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) solution for subcutaneous or intravenous use
Initial U.S. Approval: 2000

——— 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).

• Subcutaneous injection (2.2):
  o Inject subcutaneously within 5-10 minutes before a meal into the abdominal area, thigh, buttocks or upper arm.
  o Rotate injection sites within the same region from one injection to the next.
  o Should generally be used in regimens with an intermediate- or long-acting insulin.

• Continuous Subcutaneous Infusion (Insulin Pump) (2.2):
  o Change the NOVOLOG® in the reservoir at least every 4 days
  o Change the infusion set and the infusion set insertion site at least every 3 days.
  o Do not mix with other insulins or diluents in the pump

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

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

——— DOSAGE FORMS AND STRENGTHS ———

Each presentation contains 100 Units of insulin aspart per mL (U-100)
• 10 mL vials (3)
• 3 mL PenFill® cartridges for the 3 mL PenFill® cartridge device (3)
• 3 mL NOVOLOG® FlexPen® (3)
• 3 mL 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:
  o 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).
• Hyperglycemia and Ketonacidosis Due to Insulin Pump Device Malfunction: Monitor glucose and administer NOVOLOG® by subcutaneous injection if pump malfunction occurs (5.8).

——— ADVERSE REACTIONS ———

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

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

——— DRUG INTERACTIONS ———

• Drugs that may increase the risk of hypoglycemia: antidiabetic agents, ACE inhibitors, angiotensin II receptor blocker medications, disopyramide, fludrocortisone, odanacatib, tolcapone, vardenafil, warfarin, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics (7).
• Drugs that may decrease the blood glucose lowering effect: atypical antipsychotics, corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones (7).
• Drugs that may increase or decrease the blood glucose lowering effect: Alcohol, beta-blockers, clonidine, lithium salts, and pimodaine (7).
• Drugs that may blunt the signs and symptoms of hypoglycemia: beta-blockers, clonidine, guanethidine, and reserpine (7).

——— USE IN SPECIFIC POPULATIONS ———

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

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

Revised: 3/2017

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3 DOSE FORMS AND STRENGTHS
NOVOLOG® 100 units per ml (U-100) is available as a clear and colorless solution for injection in:
- 10 ml vials
- 3 ml PenFil® cartridges for the 3 ml PenFil® cartridge device with Novofine® disposable needles
- 3 ml NOVOLOG® FlexPen®
- 3 ml NOVOLOG® FlexTouch®

4 CONTRAINDICATIONS
NOVOLOG® is contraindicated in:
- During episodes of hyperglycemia (see Warnings and Precautions (5.3))
- In patients with hypersensitivity to NOVOLOG® or one of its excipients (see Warnings and Precautions (5.3))

5 WARNINGS AND PRECAUTIONS
5.1 Never Share NOVOLOG® FlexPen®, NOVOLOG® FlexTouch®, PenFill® Cartridge or PenFill® Cartridge insulin device with another person.

5.2 Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen
Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia (See Warnings and Precautions (5.3)) or hyperglycemia. These changes should be made cautiously and only under close medical supervision, and the frequency of blood glucose monitoring should be increased. For patients with type 2 diabetes, dosage adjustments of concomitant anti-diabetic products may be needed.

5.3 Hypoglycemia
Hypoglycemia is the most common adverse effect of all insulin therapies, including NOVOLOG®. Severe hypoglycemia can cause seizures, may lead to unconsciousness, and may increase risk for hypokalemia if indicated (e.g., patients using potassium-lowering blockers). Severe hypoglycemia may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and different times in the same individual. Symptoms of hypoglycemia may be less pronounced in patients with longstanding diabetes in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) (see Drug Interactions (7)), or in patients who experience recurrent hypoglycemia.

Risk Factors for Hypoglycemia
The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of NOVOLOG® may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature (see Clinical Pharmacology (12)). Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication (see Drug Interactions (7)). Patients with renal or hepatic impairment may be at higher risk of hypoglycemia (see Use in Specific Populations (8.6, 8.7)).

Risk Mitigation Strategies for Hypoglycemia
Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia, increased frequency of blood glucose monitoring is recommended. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

5.4 Hypoglycemia Due to Medication Errors
Accidental mix-ups between NOVOLOG® and other insulin products have been reported. To avoid medication errors between NOVOLOG® and other insulin products instruct patients to 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 reactions occur, discontinue NOVOLOG®, treat as anaphylaxis, and monitor until symptoms and signs resolve (see Adverse Reactions (6)). NOVOLOG® is contraindicated in patients who have had hypersensitivity reactions to insulin aspart or one of the excipients (see Contraindications (4)).

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

5.7 Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists
Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin, including NOVOLOG®, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist may be considered.

5.8 Hypoglycemia and Ketoadiabetic Due to Insulin Pump Device Malfunction
Malfunction of the insulin pump or insulin infusion set or insulin degradation can rapidly lead to hypoglycemia and ketoadiposity. Prompt identification and correction of the cause of hypoglycemia or ketosis is necessary. Interim subcutaneous insulations with NOVOLOG® may be required. Patients using continuous subcutaneous infusion pump therapy must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure.

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 of NOVOLOG® was evaluated in two treat-to-target trials of 6 months duration, conducted in subjects with type 1 diabetes or type 2 diabetes (see Clinical Studies (14)).

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® or comparator therapy

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>NOVOLOG® (n = 596)</th>
<th>Regular Human Insulin (n = 228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Injury accidental</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

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® or comparator therapy

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>NOVOLOG® (n = 91)</th>
<th>Regular Human Insulin (n = 91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Sensory disturbance</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Chest pain</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>
Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of NOVOLOG®

**Drugs**

**Increase Blood Glucose Lowering Effect**

- Alcohol, beta-blockers, clonidine, and lithium salts.

**Decrease Blood Glucose Lowering Effect**

- Beta-blockers, clonidine, guanethidine and reserpine.

**Intervention**

- Close adjustment and increased frequency of glucose monitoring may be required when NOVOLOG® is co-administered with these drugs.

**Drugs That May Blunt Signs and Symptoms of Hypoglycemia**

**Drugs**

- Beta-blockers, clonidine, and lithium salts.

**Intervention**

- Increased frequency of glucose monitoring may be required when NOVOLOG® is co-administered with these drugs.

**USE IN SPECIFIC POPULATIONS**

### 8.1 Pregnancy

**Pregnancy Category**

- Category B

**Monotriglycerides and Lipids**

- Maternal

**Intervention**

- Maternal diabetes and hyperglycemia are well controlled before conception and throughout pregnancy. Insulin levels and dose are adjusted 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 these patients. Therefore, female patients should be advised to tell their physician if they intend to become, or if they become pregnant while taking NOVOLOG®.

**Diabetes in Pregnancy**

- Pregnancy outcomes have been evaluated in several studies in which NOVOLOG® was used during pregnancy. NOVOLOG® has been shown to improve glycemic control during pregnancy. NOVOLOG® has been associated with better fetal outcome compared with regular human insulin. NOVOLOG® is generally well tolerated by maternal and fetal outcome.

**Lipid-Enhancing Effects**

- In the randomized clinical trial, mean effects on triacylglycerol (triglycerides), mean effects on total cholesterol (total cholesterol)/LDL cholesterol (low-density lipoprotein cholesterol)/HDL cholesterol (high-density lipoprotein cholesterol) were not significantly different between groups. NOVOLOG® is associated with other metabolic effects.

**Figure 1. Structural formula of insulin aspart.**

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

### 12.2 Pharmacodynamics

NOVOLOG® is a rapid-acting human insulin analog used to lower blood glucose. NOVOLOG® is homologous with regular human insulin with the exception of a single substitution of the amino acid L-proline by aspartic acid in position B28, and is produced using recombinant DNA technology utilizing Saccharomyces cerevisiae (baker’s yeast). Insulin aspart has the empirical formula C21H22N4O12S and a molecular weight of 8265.8.

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

Intensive insulin administration is also not represented in the hyperglycemia may recur after apparent clinical recovery. Hypoglycemia must be corrected appropriately.

### 11 DESCRIPTION

**NOVOLOG®** (insulin aspart injection) is a rapid-acting human insulin analog used to lower blood glucose. **NOVOLOG®** is homologous with regular human insulin with the exception of a single substitution of the amino acid L-proline by aspartic acid in position B28, and is produced using recombinant DNA technology utilizing Saccharomyces cerevisiae (baker’s yeast). Insulin aspart has the empirical formula C21H22N4O12S and a molecular weight of 8265.8.

**Intravenous administration**

A double-blind, randomized, two-way crossover study in 16 patients with type 1 diabetes demonstrated that intravenous infusion of NOVOLOG® resulted in a blood glucose profile that was similar to that after intravenous infusion with regular human insulin. NOVOLOG® or human insulin was infused until the patient’s blood glucose decreased to 36 mg/dL, or until the patient demonstrated signs of hypoglycemia (rise in heart rate and onset of sweating), defined as the time of autonomic reaction (RI) (Figure 3).
Novolog® (insulin aspart injection)

4

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=4) or mild renal function (N=7; Clcr = 50-80 ml/min), moderate (N=3; Clcr = 30-50 ml/min) or severe (but not requiring hemodialysis) (N=2; Clcr <30 ml/min) renal impairment. In this study, there was no significant effect of creatinine clearance values on AUC and Cmax of NOVOLOG®.

Hepatic Impairment: – A single subcutaneous dose of 0.06 units/kg NOVOLOG® was administered in an open-label, single-dose study of 24 subjects (N=6/group) with different degree of hepatic impairment (mild, moderate or 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 in Sprague-Dawley rats, NOVOLOG® increased the incidence of mammary gland tumors in females when compared to untreated controls. The relevance of these findings to humans is unknown.

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

In fertility studies in male and female rats, at subcutaneous doses up to 200 mg/kg/day (approximately 32 times the human subcutaneous dose), based on body weight, NOVOLOG® did not affect male fertility or female fertility, or general reproductive performance of animals was observed.

13.2 Animal Toxicology and/or Pharmacology

In standard biological assays in mice and rats, 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 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

Type 1 Diabetes—Adults (see Table 5)

Two 24-week, open-label, active-controlled studies were conducted to compare the safety and efficacy of NOVOLOG® to regular human insulin injection in adult patients with type 1 diabetes. Because the two study designs and results were similar, data are shown for only one study (see Table 5).

The mean age of the trial population was 38.9 years and mean duration of diabetes was 15.7 years. Fifty-one percent were male. Fifty-nine percent were Caucasian, 2% were Black and 4% were Other. The mean BMI was 25.6 kg/m².

NOVOLOG® was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection 30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA1c were comparable for the two treatment regimens.

Type 1 Diabetes—Pediatric (see Table 6)

An open-label, 16-week parallel design trial compared pre-prandial NOVOLOG® injection in conjunction with NPH injections to NOVOLOG® administered by continuous subcutaneous insulin injection in children with type 1 diabetes (n=26) aged 2 to 6 years with similar effects on HbA1c.

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

Type 2 Diabetes—Adults (see Table 5)

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

The mean age of the trial population was 56.6 years and mean duration of diabetes was 12.7 years. Sixty-three percent were male. Seventy-six percent were Caucasian, 9% were Black and 10% were Other. The mean BMI was approximately 29.7 kg/m².

NOVOLOG® was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection 30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA1c were comparable for the two treatment regimens.

Type 1 Diabetes—Adults (see Table 6)

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

The mean age of the trial population was 43.2 years. Thirty-nine percent were male. Ninety-eight percent were Caucasian and 2% were Black.

The two treatment regimens had comparable changes in HbA1c.

Type 1 Diabetes—Pediatric (see Table 7)

A randomized, 16-week, open-label, parallel design study of children and adolescents with type 1 diabetes (n=298) aged 4-18 years compared two subcutaneous multiple-dose treatment regimens: NOVOLOG® (n=167) or regular human insulin (n=131). NPH insulin was administered as the basal insulin. Similar effects on HbA1c were observed in both treatment groups (Table 4).

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c, Mean (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOLOG®</td>
<td>7.9 ± 1.1</td>
<td>-0.1 ± 0.8</td>
<td>0.2 (-0.1, 0.4)</td>
</tr>
<tr>
<td>Regular Human Insulin plus NPH insulin</td>
<td>8.0 ± 1.2</td>
<td>-0.1 ± 0.8</td>
<td>0.2 (-0.1, 0.4)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c, Mean (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOLOG®</td>
<td>8.0 ± 0.9</td>
<td>-0.1 ± 0.6</td>
<td>-0.2 (-0.3, 0.1)</td>
</tr>
<tr>
<td>Lispro (N=100)</td>
<td>8.2 ± 0.8</td>
<td>-0.0 ± 0.6</td>
<td>-0.2 (-0.3, 0.1)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD

14.5 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, 16-week parallel design trial compared pre-prandial NOVOLOG® injection in conjunction with NPH injections to NOVOLOG® administered by continuous subcutaneous insulin injection in 127 adults with type 2 diabetes.

Table 8. Pediatric Subcutaneous Administration of NOVOLOG® in Type 1 Diabetes (24 weeks; n=283)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c, Mean (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOLOG®</td>
<td>8.3 ± 1.2</td>
<td>0.1 ± 1.0</td>
<td>0.4 (-0.2, 0.5)</td>
</tr>
<tr>
<td>Regular Human Insulin plus NPH insulin (N=95)</td>
<td>8.3 ± 1.3</td>
<td>0.1 ± 1.1</td>
<td>0.4 (-0.2, 0.5)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD

Table 9. Subcutaneous NOVOLOG® Administration in Type 2 Diabetes (6 months; n=176)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline HbA1c (%)</th>
<th>Change from Baseline HbA1c (%)</th>
<th>Treatment Difference in HbA1c, Mean (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOLOG®</td>
<td>7.3 ± 0.7</td>
<td>-0.1 ± 0.8</td>
<td>-0.2 (-0.3, 0.1)</td>
</tr>
<tr>
<td>Regular Human Insulin plus NPH insulin (N=96)</td>
<td>7.5 ± 0.8</td>
<td>-0.1 ± 0.8</td>
<td>-0.2 (-0.3, 0.1)</td>
</tr>
</tbody>
</table>

*Values are Mean ± SD
**NovoLog** (insulin aspart injection)

The mean age of the trial population was 55.1 years. Sixty-four percent were male. Eighty percent were Caucasian, 5% were Black and 8% were Other. The mean BMI was approximately 32.2 kg/m². The two treatment groups had similar reductions in HbA1c (Table 8).

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

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

*Values are Mean ± SD

### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 16.1 How Supplied

NOVOLOG® 100 units of insulin aspart per mL (U-100) is available as a clear and colorless solution for injection in:
- 10 mL vials
- 3 mL PenFill® cartridges
- 3 mL NOVOLOG® FlexPen®
- 3 mL NOVOLOG® FlexTouch®

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

**NOVOLOG® FlexPen®, NOVOLOG® FlexTouch®, PenFill®, cartridge, and PenFill® cartridge insulin delivery devices manufactured by Novo Nordisk must never be shared between patients, even if the needle is changed.

#### 16.2 Recommended Storage

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

NOVOLOG® should not be drawn into a syringe and stored for later use. Always remove and discard the needle after each injection from the NOVOLOG® FlexPen® or NOVOLOG® FlexTouch® and store without a needle attached. This prevents contamination and/or infection, or leakage of insulin, and will ensure accurate dosing.

The storage conditions are summarized in the following table:

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

<table>
<thead>
<tr>
<th>NOVOLOG® presentation</th>
<th>Not in-use (unopened)</th>
<th>Not in-use (unopened)</th>
<th>In-use (opened)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room temperature (below 30°C/86°F)</td>
<td>Room temperature (below 30°C/86°F)</td>
<td>Refrigerated</td>
<td></td>
</tr>
<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 PenFill® cartridges</td>
<td>28 days</td>
<td>Until expiration date</td>
<td>28 days (Do not refrigerate)</td>
</tr>
<tr>
<td>3 mL NOVOLOG® FlexPen®</td>
<td>28 days</td>
<td>Until expiration date</td>
<td>28 days (Do not refrigerate)</td>
</tr>
<tr>
<td>3 mL NOVOLOG® FlexTouch®</td>
<td>28 days</td>
<td>Until expiration date</td>
<td>28 days (Do not refrigerate)</td>
</tr>
</tbody>
</table>

**Storage in External Insulin Pump:**

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

**Storage of Diluted NOVOLOG®**

NOVOLOG® diluted with insulin Diluting Medium for NOVOLOG® to a concentration equivalent to U-100 prepared as indicated under Dosage and Administration (2.2) may remain in patient use at temperatures below 30°C (86°F) for 28 days.

**Storage of NOVOLOG® in Intra-venous Infusion Fluids**

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

### 17 PATIENT COUNSELING INFORMATION

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

#### Never Share NOVOLOG® FlexPen® or NOVOLOG® FlexTouch®, PenFill® Cartridge or PenFill® Cartridge Device Between Patients

Advise patients that they must never share NOVOLOG® FlexPen®, NOVOLOG® FlexTouch®, PenFill® cartridge or PenFill® cartridge devices with another person even if the needle is changed, because doing so carries a risk for transmission of blood-borne pathogens. Advise patients using NOVOLOG® vials not to share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens. (See Warnings and Precautions (5.1)).

#### Hypoglycemia

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

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

#### Hypoglycemia with Medication Errors

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

#### Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with NOVOLOG®. Inform patients of the symptoms of hypersensitivity reactions (See Warnings and Precautions (5.3)).

#### Women of Reproductive Potential

Advise patients to inform their health care professional if they are pregnant or are contemplating pregnancy.

#### Administration

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

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

#### Patients Using Continuous Subcutaneous Insulin Pumps

- Train patients in both intensive insulin therapy with multiple injections and in the function of their pump and pump accessories.
- Instruct patients to replace insulin in the reservoir at least every 6 days; infusion sets and infusion set insertion sites should be changed at least every 3 days. By following this schedule, patients avoid insulin degradation, infusion set occlusion, and loss of the insulin preservative. NOVOLOG® is recommended for use in any reservoir and infusion sets that are compatible with insulin and the specific pump. Please see recommended reservoir and infusion set in the pump manual.
- Instruct patients to discard insulin exposed to temperatures higher than 37°C (98.6°F).
- Instruct patients to inform physician and select a new site for infusion if infusion site becomes erythematous, pruritic, or thickened.
- Instruct patients of the risk of rapid hyperglycemia and ketosis due to pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician (See Warnings and Precautions (5) and How Supplied/Storage and Handling (16.2)).
- Instruct patients of the risk of hypoglycemia from pump malfunction. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician (See Warnings and Precautions (5) and How Supplied/Storage and Handling (16.2)).

The following insulin pumps have been used in NOVOLOG® clinical or in vitro studies conducted by Novo Nordisk, the manufacturer of NOVOLOG®:

- Medtronic Paradigm® 512 and 712
- MiniMed 508

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

**Rx only**

Date of Issue: March 16, 2017

Version: 25

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The brands listed are the registered trademarks of their respective owners and are not trademarks of Novo Nordisk A/S.

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For information about NOVOLOG contact:
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Plainboro, New Jersey 08536
1-800-727-6500
www.novonordisk-us.com

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USA17INP00949  4/2017
Patient Information
NovoLog® (NÔ-vô-log)
(insulin aspart injection)

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

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

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

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

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

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

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

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USA17INP00949 4/2017
Instructions for Use

NovoLog® (Nö-vö-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 swab

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. Push down on the plunger until the black tip reaches the line for the number of units for your prescribed dose (See Figure C).

Step 4: Push the needle through the rubber stopper of the 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 is a few units past 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).

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, buttocks, upper legs or upper arms, infused in an insulin pump, or given through a needle in your arm (intravenously) by your healthcare provider.
• If you inject NovoLog®, change (rotate) your injection sites within the area you choose for each dose. Do not use the same injection site for each injection.
• If you use NovoLog® in an insulin pump, you should change your insertion site every 3 days. The insulin in the reservoir should be changed at least every 6 days even if you have not used all of the insulin.
• If you use NovoLog® in an insulin pump, see your insulin pump manual for instructions or talk to your healthcare provider.
• NPH insulin is the only type of insulin that can be mixed with NovoLog®. Do not mix NovoLog® with any other type of insulin.
• NovoLog® should only be mixed with NPH insulin if it is going to be injected right away under your skin (subcutaneously).
• NovoLog® should be drawn up into the syringe before you draw up your NPH insulin.
• Talk to your healthcare provider if you are not sure about the right way to mix NovoLog® and NPH insulin.

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

Step 11: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure K). 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).
• 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 empty 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®?
Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
• Keep NovoLog® away from heat or light.
• Store opened and unopened NovoLog® vials in the refrigerator at 36°F to 46°F (2°C to 8°C). Opened NovoLog® 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® 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®
• Always use a new syringe and needle for each injection.
• Do not share syringes or needles.
• Keep NovoLog® vials, syringes, and needles out of the reach of children.

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

Revised: March 2017
NovoLog® is a registered trademark of Novo Nordisk A/S.
Manufactured by: Novo Nordisk A/S DK-2880 Bagsvaerd, Denmark
For information about NovoLog® contact: Novo Nordisk Inc. 800 Scudders Mill Road Plainsboro, New Jersey 08536 1-800-727-6500 www.novonordisk-us.com
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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 dia-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.

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

NovoLog® FlexPen®

Rubber stopper
Cartridge scale
Pointer
Push-button
cartridge (see diagram F).

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

A. Pull off the pen cap (see diagram A). Wipe the rubber stopper with alcohol.

B. Attaching the needle
Remove the protective tab from a disposable needle. Screw the needle tightly onto your FlexPen®. It is important that the needle is put on straight (see diagram B).

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

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

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

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

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

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

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.

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 a finger. 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 NovoLog® 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® 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®?
• Store unused NovoLog® 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 28 days.
• Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
• Keep NovoLog® away from heat or light.
• Unused FlexPen® may be used until the expiration date printed on the label, if kept in the refrigerator.
• 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.

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

Revised: 04/2015
Needle
Needle
Needle

Step 1:
• 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.
• This Pen is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product.
• NovoLog® FlexTouch® Pen is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product.
• Do not share your NovoLog® FlexTouch® Penős or NovoTwist® needle
• If you do not see a drop of insulin, repeat steps 7 to 9.
• If you still do not see a drop of insulin, change the needle and repeat steps 7 to 9.
• If you still do not see a drop of insulin, change the needle and repeat steps 7 to 9.

Preparations for your injection:
• 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.
• 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.
• You may give other people a serious infection, or get a serious infection from them.
• You may give other people a serious infection, or get a serious infection from them.
• You may give other people a serious infection, or get a serious infection from them.

NovoLog® (insulin aspart injection)

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.

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.

Selecting your dose:

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

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

How should I store my NovoLog® FlexTouch® Pen?
- Store unused NovoLog® FlexTouch® Pens in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Store the Pen you are currently using out of the refrigerator below 86°F.

- Do not freeze NovoLog®. Do not use NovoLog® if it has been frozen.
- Keep NovoLog® away from heat or light.
- Unused Pens may be used until the expiration date printed on the label, if kept in the refrigerator.
- 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.
Instructions for Use
NovoLog® (Novo-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.
- This PenFill® cartridge is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product and your insulin delivery device.
- If using a new NovoLog® PenFill® cartridge, start with Step 1.
- If the NovoLog® PenFill® cartridge has already been used, start with Step 2.

Supplies you will need to give your NovoLog® injection:
- NovoLog® PenFill® cartridge
- Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device
- 1 new NovoFine®, NovoFine® Plus, or NovoTwist® needle
- Alcohol swab
- Adhesive bandage
- Cotton gauze
- A sharps container for throwing away used PenFill® cartridges and needles. See “After your injection” at the end of these instructions.

NovoFine®

How to use the NovoLog® PenFill® cartridge

- Wash your hands with soap and water.
- 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. Do not use NovoLog® if it is cloudy or colored or if the threaded end is loose (See Figure B).

Step 1:
- Insert a 3 mL cartridge with the threaded end first into your Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery device (See Figure C).
- If you drop your device, check the insulin cartridge for damage such as cracks or leaking. If your cartridge is damaged, throw it away and use a new one.

Prepare your device with a new needle

Step 2:
- Take a new needle, and tear off the paper tab. Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. Do not attach a new needle to your device until you are ready to give your injection. Do not reuse or share your needles with other people. You may give others a serious infection, or get a serious infection from them.
- Be careful not to bend or damage the needle before you use it.
- Push the needle straight onto the device. Turn the needle clockwise until it is 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.
- Push the needle straight onto the device. Turn the needle clockwise until it is tight (See Figure F).

Step 4:
- 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.

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 airshots 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, upper legs (thighs), or upper arms (See Figure I).
- 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.
- 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
  - 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. 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?

Before use:
- Store unused NovoLog® PenFill® cartridges in the refrigerator at
36°F to 46°F (2°C to 8°C).
- Do not freeze NovoLog®.
- 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.
- Keep NovoLog® away from heat or light.
- The NovoLog® PenFill® cartridge you are using should be
thrown away after 28 days, even if it still has insulin left in it.