



Approaches in Managing MEALTIME • INSULIN

Current doses of basal insulin and bolus insulin as of today.

DATE _____

 Breakfast Dose	
 Lunch Dose	
 Dinner Dose	
Basal Insulin Dose	

- 1 Record your blood sugar levels 4 times a day — before breakfast, lunch, dinner, and bedtime
- 2 Bring completed diaries to your next doctor's visit

Please consult your doctor if you have any questions about your health or medication.

Indications and Usage for NovoLog® (insulin aspart [rDNA origin] injection):

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

Important Safety Information for NovoLog®:

Do not take NovoLog® if your blood sugar is too low (hypoglycemia) or if you are allergic to anything in NovoLog®. If you take too much NovoLog® your blood sugar may fall too low.

Please see additional Important Safety Information on back cover and accompanying Prescribing Information.

Test Your Blood Sugar 4 Times a Day to Get an Average

WEEK 0					
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level	110	106	98	314	105
Before lunch sugar level	115	99	108	322	107
Before dinner sugar level	112	102	96	310	103
Bedtime sugar level	144	156	152	452	151

WEEK 1					DATE _____
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 2					DATE _____
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 3				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 4				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 5				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					



WEEK 6				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 7				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 8				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					



WEEK 9				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 10				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

WEEK 11				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					



WEEK 12				DATE _____	
	Day 1	Day 2	Day 3	Total	Average (Total/3)
Before breakfast sugar level					
Before lunch sugar level					
Before dinner sugar level					
Bedtime sugar level					

Indications and Usage for NovoLog® (insulin aspart [rDNA origin] injection):

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

Important Safety Information for NovoLog®:

Do not take NovoLog® if your blood sugar is too low (hypoglycemia) or if you are allergic to anything in NovoLog®. If you take too much NovoLog® your blood sugar may fall too low.

NovoLog® is a fast-acting insulin. You should eat a meal within 5 to 10 minutes after using NovoLog® to avoid low blood sugar. Do not inject NovoLog® if you do not plan to eat right after using NovoLog®. Check your blood sugar levels. Ask your health care provider what your blood sugars should be and when you should check your blood sugar levels. Alcohol, including beer and wine, may affect your blood sugar when you take NovoLog®.

Do not change the type of insulin you use unless told to do so by your health care provider. The amount of insulin you take as well as the best time for you to take your insulin may need to change if you take a different type of insulin.

Do not mix NovoLog® with any other insulins when used in a pump or with any insulins other than NPH when used with injections by syringe. Needles and NovoLog® FlexPen® must not be shared.

Tell your health care provider about all medicines you take and all of your medical conditions, including if you are pregnant or breastfeeding. Your NovoLog® dose may change if you take other medicines.

NovoLog® has not been studied in children with type 2 diabetes or in children with type 1 diabetes under the age of two.

The most common side effect of NovoLog® is low blood sugar (hypoglycemia). Other possible side effects include reactions at the injection site (like redness, swelling and itching), and allergic reactions. Get medical help right away if you experience signs of serious allergic reaction such as body rash, trouble with your breathing, fast heartbeat, or sweating. Ask your doctor or pharmacist for further information.

Please see additional Important Safety Information on front cover.

Please see accompanying Prescribing Information.

You are encouraged to report negative side effects of prescribing drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.



Partnership for
Prescription Assistance

If you need assistance with prescription costs, help may be available. Visit pparx.org or call 1-888-4PPA-NOW.

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 [rDNA origin] injection) solution for subcutaneous use

Initial U.S. Approval: 2000

RECENT MAJOR CHANGES

- Dosage and Administration (2.3) 7/2009
- Warnings and Precautions, Administration (5.1) 10/2009

INDICATIONS AND USAGE

- NovoLog[®] is an insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus (1.1).

DOSAGE AND ADMINISTRATION

- The dosage of NovoLog[®] must be individualized.
- *Subcutaneous injection:* NovoLog[®] should generally be given immediately (within 5-10 minutes) prior to the start of a meal (2.2).
- *Use in pumps:* 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. NovoLog[®] should not be mixed with other insulins or with a diluent when it is used in the pump (2.3).
- *Intravenous use:* NovoLog[®] should be used at concentrations from 0.05 U/mL to 1.0 U/mL insulin aspart in infusion systems using polypropylene infusion bags. NovoLog[®] has been shown to be stable in infusion fluids such as 0.9% sodium chloride (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)

CONTRAINDICATIONS

- Do not use during episodes of hypoglycemia (4).
- Do not use in patients with hypersensitivity to NovoLog[®] or one of its excipients.

WARNINGS AND PRECAUTIONS

- Hypoglycemia is the most common adverse effect of insulin therapy. Glucose monitoring is recommended for all patients with diabetes. Any change of insulin dose should be made cautiously and only under medical supervision (5.1, 5.2).
- Insulin, particularly when given intravenously or in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia (5.3).
- Like all insulins, NovoLog[®] requirements may be reduced in patients with renal impairment or hepatic impairment (5.4, 5.5).
- Severe, life-threatening, generalized allergy, including anaphylaxis, may occur with insulin products, including NovoLog[®] (5.6).

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

- The following may increase the blood-glucose-lowering effect and susceptibility to hypoglycemia: oral antidiabetic products, pramlintide, ACE inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, propoxyphene, salicylates, somatostatin analogs, sulfonamide antibiotics (7).
- The following may reduce the blood-glucose-lowering effect: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, salbutamol, terbutaline), isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), atypical antipsychotics (7).

- Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin (7).
- Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia (7).
- The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic products such as beta-blockers, clonidine, guanethidine, and reserpine (7).

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: 6/2011

FULL PRESCRIBING INFORMATION: CONTENTS*

<p>1 INDICATIONS AND USAGE</p> <p>1.1 Treatment of Diabetes Mellitus</p> <p>2 DOSAGE AND ADMINISTRATION</p> <p>2.1 Dosing</p> <p>2.2 Subcutaneous Injection</p> <p>2.3 Continuous Subcutaneous Insulin Infusion (CSII) by External Pump</p> <p>2.4 Intravenous Use</p> <p>3 DOSAGE FORMS AND STRENGTHS</p> <p>4 CONTRAINDICATIONS</p> <p>5 WARNINGS AND PRECAUTIONS</p> <p>5.1 Administration</p> <p>5.2 Hypoglycemia</p> <p>5.3 Hypokalemia</p> <p>5.4 Renal Impairment</p> <p>5.5 Hepatic Impairment</p> <p>5.6 Hypersensitivity and Allergic Reactions</p> <p>5.7 Antibody Production</p> <p>5.8 Mixing of Insulins</p> <p>5.9 Continuous Subcutaneous Insulin Infusion by External Pump</p> <p>6 ADVERSE REACTIONS</p> <p>7 DRUG INTERACTIONS</p> <p>8 USE IN SPECIFIC POPULATIONS</p> <p>8.1 Pregnancy</p>	<p>8.3 Nursing Mothers</p> <p>8.4 Pediatric Use</p> <p>8.5 Geriatric Use</p> <p>10 OVERDOSAGE</p> <p>11 DESCRIPTION</p> <p>12 CLINICAL PHARMACOLOGY</p> <p>12.1 Mechanism of Action</p> <p>12.2 Pharmacodynamics</p> <p>12.3 Pharmacokinetics</p> <p>13 NONCLINICAL TOXICOLOGY</p> <p>13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility</p> <p>13.2 Animal Toxicology and/or Pharmacology</p> <p>14 CLINICAL STUDIES</p> <p>14.1 Subcutaneous Daily Injections</p> <p>14.2 Continuous Subcutaneous Insulin Infusion (CSII) by External Pump</p> <p>14.3 Intravenous Administration of NovoLog[®]</p> <p>16 HOW SUPPLIED/STORAGE AND HANDLING</p> <p>16.1 How Supplied</p> <p>16.2 Recommended Storage</p> <p>17 PATIENT COUNSELING INFORMATION</p> <p>17.1 Physician Instructions</p> <p>17.2 Patients Using Pumps</p> <p>17.3 FDA-Approved Patient Labeling</p>
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*Sections or subsections omitted from the full prescribing information are not listed.

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®.

An open-label, randomized study compared the safety and efficacy of NovoLog® (n=157) versus regular human insulin (n=165) in 322 pregnant women with type 1 diabetes. Two-thirds of the enrolled patients were already pregnant when they entered the study. Because only one-third of the patients enrolled before conception, the study was not large enough to evaluate the risk of congenital malformations. Both groups achieved a mean HbA_{1c} of ~6% during pregnancy, and there was no significant difference in the incidence of maternal hypoglycemia.

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

8.3 Nursing Mothers

It is unknown whether insulin aspart is excreted in human milk. Use of NovoLog® is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

8.4 Pediatric Use

NovoLog® is approved for use in children for subcutaneous daily injections and for subcutaneous continuous infusion by external insulin pump. NovoLog® has not been studied in pediatric patients younger than 2 years of age. NovoLog® has not been studied in pediatric patients with type 2 diabetes. Please see Section 14 CLINICAL STUDIES for summaries of clinical studies.

8.5 Geriatric Use

Of the total number of patients (n=1,375) treated with NovoLog® in 3 controlled clinical studies, 2.6% (n=36) were 65 years of age or over. One-half of these patients had type 1 diabetes (18/1285) and the other half had type 2 diabetes (18/90). The HbA_{1c} response to NovoLog®, as compared to human insulin, did not differ by age, particularly in patients with type 2 diabetes. Additional studies in larger populations of patients 65 years of age or over are needed to permit conclusions regarding the safety of NovoLog® in elderly compared to younger patients. Pharmacokinetic/pharmacodynamic studies to assess the effect of age on the onset of NovoLog® action have not been performed.

10 OVERDOSAGE

Excess insulin administration may cause hypoglycemia and, particularly when given intravenously, hypokalemia. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise, may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

11 DESCRIPTION

NovoLog® (insulin aspart [rDNA origin] injection) is a rapid-acting human insulin analog used to lower blood glucose. NovoLog® is homologous with regular human insulin with the exception of a single substitution of the amino acid proline by aspartic acid in position B28, and is produced by recombinant DNA technology utilizing *Saccharomyces cerevisiae* (baker's yeast). Insulin aspart has the empirical formula C₂₅₆H₃₈₁N₆₅O₇₉S₆ and a molecular weight of 5825.8.

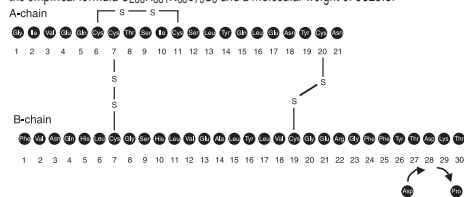


Figure 1. Structural formula of insulin aspart.

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary activity of NovoLog® is the regulation of glucose metabolism. Insulins, including NovoLog®, bind to the insulin receptors on muscle and fat cells and lower blood glucose by facilitating the cellular uptake of glucose and simultaneously inhibiting the output of glucose from the liver.

12.2 Pharmacodynamics

Studies in normal volunteers and patients with diabetes demonstrated that subcutaneous administration of NovoLog® has a more rapid onset of action than regular human insulin. In a study in patients with type 1 diabetes (n=22), the maximum glucose-lowering effect of NovoLog® occurred between 1 and 3 hours after subcutaneous injection (see Figure 2). The duration of action for NovoLog® is 3 to 5 hours. The time course of action of insulin and insulin analogs such as NovoLog® may vary considerably in different individuals or within the same individual. The parameters of NovoLog® activity (time of onset, peak time and duration) as designated in Figure 2 should be considered only as general guidelines. The rate of insulin absorption and onset of activity is affected by the site of injection, exercise, and other variables [see Warnings and Precautions (5.1)].

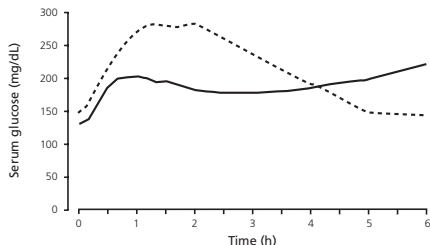


Figure 2. Serial mean serum glucose collected up to 6 hours following a single pre-meal dose of NovoLog® (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

A double-blind, randomized, two-way cross-over 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), in the setting of autonomic reaction (R) (see Figure 3).

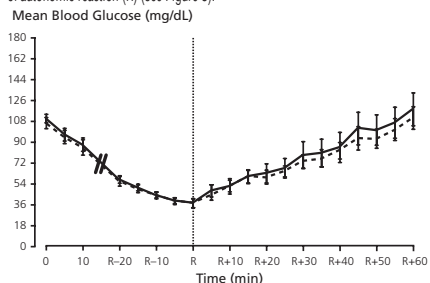


Figure 3. Mean blood glucose profiles following intravenous infusion of NovoLog® (hatched curve) and regular human insulin (solid curve) in 16 patients with type 1 diabetes. R represents the time of autonomic reaction.

12.3 Pharmacokinetics

The single substitution of the amino acid proline with aspartic acid at position B28 in NovoLog® reduces the molecule's tendency to form hexamers as observed with regular human insulin. NovoLog® is, therefore, more rapidly absorbed after subcutaneous injection compared to regular human insulin.

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

Bioavailability and Absorption - NovoLog® has a faster absorption, a faster onset of action, and a shorter duration of action than regular human insulin after subcutaneous injection (see Figure 2 and Figure 4). The relative bioavailability of NovoLog® compared to regular human insulin indicates that the two insulins are absorbed to a similar extent.

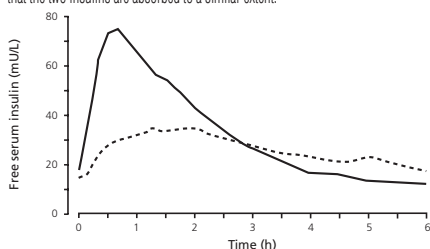


Figure 4. Serial mean serum free insulin concentration collected up to 6 hours following a single pre-meal dose of NovoLog® (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

In studies in healthy volunteers (total n=107) and patients with type 1 diabetes (total n=40), NovoLog® consistently reached peak serum concentrations approximately twice as fast as regular human insulin. The median time to maximum concentration in these trials was 40 to 50 minutes for NovoLog® versus 80 to 120 minutes for regular human insulin. In a clinical trial in patients with type 1 diabetes, NovoLog® and regular human insulin, both administered subcutaneously at a dose of 0.15 U/kg body weight, reached mean maximum concentrations of 82 and 36 mU/L, respectively. Pharmacokinetic/pharmacodynamic characteristics of insulin aspart have not been established in patients with type 2 diabetes.

The intra-individual variability in time to maximum serum insulin concentration for healthy male volunteers was significantly less for NovoLog® than for regular human insulin. The clinical significance of this observation has not been established.

In a clinical study in healthy non-obese subjects, the pharmacokinetic differences between NovoLog® and regular human insulin described above, were observed independent of the site of injection (abdomen, thigh, or upper arm).

Distribution and Elimination - NovoLog® has low binding to plasma proteins (<10%), similar to that seen with regular human insulin. After subcutaneous administration in normal male volunteers (n=24), NovoLog® was more rapidly eliminated than regular human insulin with an average apparent half-life of 81 minutes compared to 141 minutes for regular human insulin.

Specific Populations

Children and Adolescents - 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.

Gender - In healthy volunteers, no difference in insulin aspart levels was seen between men and women when body weight differences were taken into account. There was no significant difference in efficacy noted (as assessed by HbA_{1c}) between genders in a trial in patients with type 1 diabetes.

Obesity - A single subcutaneous dose of 0.1 U/kg NovoLog® was administered in a study of 23 patients with type 1 diabetes and a wide range of body mass index (BMI, 22-39 kg/m²). The pharmacokinetic parameters, AUC and C_{max}, of NovoLog® were generally unaffected by BMI in the different groups - BMI 19-23 kg/m² (N=4); BMI 23-27 kg/m² (N=7); BMI 27-32 kg/m² (N=6) and BMI >32 kg/m² (N=6). Clearance of NovoLog® was reduced by 28% in patients with BMI >32 kg/m² compared to patients with BMI <23 kg/m².

Renal Impairment - Some studies with human insulin have shown increased circulating levels of insulin in patients with renal failure. A single subcutaneous dose of 0.08 U/kg NovoLog® was administered in a study to subjects with either normal (N=6) creatinine clearance (CL_{CR}) (>80 mL/min) or mild (N=7; CL_{CR} = 50-80 mL/min), moderate (N=3; CL_{CR} = 30-50 mL/min) or severe (but not requiring hemodialysis) (N=2; CL_{CR} <30 mL/min) renal impairment. In this small study, there was no apparent effect of creatinine clearance values on AUC and C_{max} of NovoLog®. Careful glucose monitoring and dose adjustments of insulin, including NovoLog®, may be necessary in patients with renal dysfunction [see Warnings and Precautions (5.4)].

Hepatic Impairment - Some studies with human insulin have shown increased circulating levels of insulin in patients with liver failure. A single subcutaneous dose of 0.06 U/kg NovoLog® was administered in an open-label, single-dose study of 24 subjects (N=6/group) with different degree of hepatic impairment (mild, moderate and severe) having Child-Pugh Scores ranging from 0 (healthy volunteers) to 12 (severe hepatic impairment). In this small study, there was no correlation between the degree of hepatic failure and any NovoLog® pharmacokinetic parameter. Careful glucose monitoring and dose adjustments of insulin, including NovoLog®, may be necessary in patients with hepatic dysfunction [see Warnings and Precautions (5.5)].

The effect of age, ethnic origin, pregnancy and smoking on the pharmacokinetics and pharmacodynamics of NovoLog® has not been studied.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the carcinogenic potential of NovoLog®. In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with NovoLog® at 10, 50, and 200 U/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 U/kg/day, based on U/body surface area, respectively). At a dose of 200 U/kg/day, NovoLog® increased the incidence of mammary gland tumors in females when compared to untreated controls. The incidence of mammary tumors for NovoLog® was not significantly different than for regular human insulin. The relevance of these findings to humans is not known. NovoLog® was not genotoxic in the following tests: Ames test, mouse lymphoma cell forward gene mutation test, human peripheral blood lymphocyte chromosome aberration test, *in vivo* micronucleus test in mice, and in *ex vivo* UDS test in rat liver hepatocytes. In fertility studies in male and female rats, at subcutaneous doses up to 200 U/kg/day (approximately 32 times the human subcutaneous dose, based on U/body surface area), no direct adverse effects on male and female fertility, or general reproductive performance of animals was observed.

13.2 Animal Toxicology and/or Pharmacology

In standard biological assays in mice and rabbits, one unit of NovoLog® has the same glucose-lowering effect as one unit of regular human insulin. In humans, the effect of NovoLog® is more rapid in onset and of shorter duration, compared to regular human insulin, due to its faster absorption after subcutaneous injection (see Section 12 CLINICAL PHARMACOLOGY Figure 2 and Figure 4).

14 CLINICAL STUDIES

14.1 Subcutaneous Daily Injections

Two six-month, open-label, active-controlled studies were conducted to compare the safety and efficacy of NovoLog® to Novolin® R in adult patients with type 1 diabetes. Because the two study designs and results were similar, data are shown for only one study (see Table 3). NovoLog® was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA_{1c} and the incidence rates of severe hypoglycemia (as determined from the number of events requiring intervention from a third party) were comparable for the two treatment regimens in this study (Table 3) as well as in the other clinical studies that are cited in this section. Diabetic ketoacidosis was not reported in any of the adult studies in either treatment group.

Table 3. Subcutaneous NovoLog® Administration in Type 1 Diabetes (24 weeks; n=82)

	NovoLog® + NPH	Novolin® R + NPH
N	596	286
Baseline HbA _{1c} (%)*	7.9 ± 1.1	8.0 ± 1.2
Change from Baseline HbA _{1c} (%)	-0.1 ± 0.8	0.0 ± 0.8
Treatment Difference in HbA _{1c} , Mean (95% confidence interval)	-0.2 (-0.3, -0.1)	
Baseline insulin dose (U/kg/24 hours)*	0.7 ± 0.2	0.7 ± 0.2
End-of-Study insulin dose (U/kg/24 hours)*	0.7 ± 0.2	0.7 ± 0.2
Patients with severe hypoglycemia (n, %)**	104 (17%)	54 (19%)
Baseline body weight (kg)*	75.3 ± 14.5	75.9 ± 13.1
Weight change from baseline (kg)*	0.5 ± 3.3	0.9 ± 2.9

*Values are Mean ± SD

**Severe hypoglycemia refers to hypoglycemia associated with central nervous system symptoms and requiring the intervention of another person or hospitalization.

A 24-week, parallel-group study of children and adolescents with type 1 diabetes (n=283) aged 6 to 18 years compared two subcutaneous multiple-dose treatment regimens: NovoLog® (n=187) or Novolin® R (n=96). NPH insulin was administered as the basal insulin. NovoLog® achieved glycoemic control comparable to Novolin® R, as measured by change in HbA_{1c} (Table 4) and both treatment groups had a comparable incidence of hypoglycemia. Subcutaneous administration of NovoLog® and regular human insulin have also been compared in children with type 1 diabetes (n=26) aged 2 to 6 years with similar effects on HbA_{1c} and hypoglycemia.

Patient Information

NovoLog® (NÔ-vô-log)
(insulin aspart [rDNA origin] Injection)

Important:

Know your insulin. Do not change the type of insulin you use unless told to do so by your healthcare provider. The amount of insulin you take as well as the best time for you to take your insulin may need to change if you take a different type of insulin.

Make sure you know the type and strength of insulin prescribed for you. Read the Patient Information that comes with NovoLog® before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your diabetes or your treatment. Make sure you know how to manage your diabetes. Ask your healthcare provider if you have any questions about managing your diabetes.

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 use NovoLog®?**Do not take NovoLog® if:**

- Your blood sugar is too low (hypoglycemia).
- You are allergic to anything in NovoLog®. See the end of this leaflet for a complete list of ingredients in NovoLog®. Check with your healthcare provider if you are not sure.

Tell your healthcare provider:

- **about all of your medical conditions.** Medical conditions can affect your insulin needs and your dose of NovoLog®.
- **if you are pregnant or breastfeeding.** You and your healthcare provider should talk about the best way to manage your diabetes while you are pregnant or breastfeeding. NovoLog® has not been studied in nursing women.
- **about all medicines you take,** including prescriptions and non-prescription medicines, vitamins and herbal supplements. Your NovoLog® dose may change if you take other medicines.

Know the medicines you take. Keep a list of your medicines with you to show your healthcare providers when you get a new medicine.

How should I take NovoLog®?

Only use NovoLog® if it appears clear and colorless. There may be air bubbles. This is normal. If it looks cloudy, thickened, or colored, or if it contains solid particles do not use it and call Novo Nordisk at 1-800-727-6500.

NovoLog® comes in:

- 10 mL vials (small bottles) for use with syringe
- 3 mL PenFill® cartridges for use with the Novo Nordisk 3 mL PenFill® cartridge compatible insulin delivery devices and NovoFine® disposable needles. The cartridge delivery device can be used with a NovoPen® 3 PenMate®
- 3 mL NovoLog® FlexPen®

Read the instructions for use that come with your NovoLog® product.

Talk to your healthcare provider if you have any questions. Your healthcare provider should show you how to inject NovoLog® before you start taking it.

- **Take NovoLog® exactly as prescribed.** You should eat a meal within 5 to 10 minutes after using NovoLog® to avoid low blood sugar.
- **NovoLog® is a fast-acting insulin.** The effects of NovoLog® start working 10 to 20 minutes after injection or bolus pump infusion.
- **Do not inject NovoLog® if you do not plan to eat right after your injection or bolus pump infusion.**
- The greatest blood sugar lowering effect is between 1 and 3 hours after the injection or infusion. This blood sugar lowering lasts for 3 to 5 hours.
- **While using NovoLog® you may have to change your total dose of insulin, your dose of longer-acting insulin, or the number of injections of longer-acting insulin you use.** Pump users given NovoLog® may need to change the amount of total insulin given as a basal infusion.
- **Do not mix NovoLog®:**
 - with any other insulins when used in a pump
 - with any insulins other than NPH when used with injections by syringe

If your healthcare provider recommends diluting NovoLog®, follow your healthcare provider's instructions exactly so that you know:

- How to make NovoLog® more dilute (that is, a smaller number of units of NovoLog® for a given amount of liquid) and
- How to use this more dilute form of NovoLog®. **Do not use dilute insulin in a pump.**

- **Inject NovoLog® into the skin of your stomach area, upper arms, buttocks or upper legs.** NovoLog® may affect your blood sugar levels sooner if you inject it into the skin of your stomach area. **Never inject NovoLog® into a vein or into a muscle.**
- **Change (rotate) your injection site within the chosen area (for example, stomach or upper arm) with each dose. Do not inject into the exact same spot for each injection.**
- **If you take too much NovoLog®, your blood sugar may fall low (hypoglycemia).** You can treat mild low blood sugar (hypoglycemia) by drinking or eating something sugary right away (fruit juice, sugar candies, or glucose tablets). It is important to treat low blood sugar (hypoglycemia) right away because it could get worse and you could pass out (become unconscious). If you pass out you will need help from another person or emergency medical services right away, and will need treatment with a glucagon injection or treatment at a hospital. See "What are the possible side effects of NovoLog®?" for more information on low blood sugar (hypoglycemia).
- **If you forget to take your dose of NovoLog®, your blood sugar may go too high (hyperglycemia).** If high blood sugar (hyperglycemia) is not treated it can lead to serious problems, like loss of consciousness (passing out), coma or even death. Follow your healthcare provider's instructions for treating high blood sugar. Know your symptoms of high blood sugar which may include:
 - increased thirst
 - frequent urination
 - loss of appetite
 - high amounts of sugar and ketones in your urine
 - nausea, vomiting (throwing up) or stomach pain
 - fruity smell on the breath
 - drowsiness
 - a hard time breathing
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.

Your insulin dosage may need to change because of:

- illness
- stress
- change in physical activity or exercise
- change in diet
- other medicines you take

What should I avoid while using NovoLog®?

- **Alcohol.** Alcohol, including beer and wine, may affect your blood sugar when you take NovoLog®.
- **Driving and operating machinery.** You may have difficulty concentrating or reacting if you have low blood sugar (hypoglycemia). Be careful when you drive a car or operate machinery. Ask your healthcare provider if it is alright to drive if you often have:
 - low blood sugar
 - decreased or no warning signs of low blood sugar

What are the possible side effects of NovoLog®?

- **Low blood sugar (hypoglycemia).** Symptoms of low blood sugar may include:
 - sweating
 - blurred vision
 - trouble concentrating or confusion
 - dizziness or lightheadedness
 - hunger
 - shakiness
 - slurred speech
 - fast heart beat
 - tingling of lips and tongue
 - anxiety, irritability or mood changes
 - headache

Severe low blood sugar can cause unconsciousness (passing out), seizures, and death. Know your symptoms of low blood sugar. Follow your healthcare provider's instructions for treating low blood sugar. Talk to your healthcare provider if low blood sugar is a problem for you.

- **Serious allergic reaction (whole body reaction).** Get medical help right away, if you develop a rash over your whole body, have trouble breathing, a fast heartbeat, or sweating.
- **Reactions at the injection site (local allergic reaction).** You may get redness, swelling, and itching at the injection site. If you keep having skin reactions or they are serious talk to your healthcare provider. You may need to stop using NovoLog® and use a different insulin. Do not inject insulin into skin that is red, swollen, or itchy.
- **Skin thickens or pits at the injection site (lipodystrophy).** Change (rotate) where you inject your insulin to help to prevent these skin changes from happening. Do not inject insulin into this type of skin.

- **Swelling of your hands and feet**
- **Vision changes**
- **Low potassium in your blood (hypokalemia)**
- **Weight gain**

These are not all of the possible side effects from NovoLog®.

Ask your healthcare provider or pharmacist for more information. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store NovoLog®?**All Unopened NovoLog®:**

- **Keep all unopened NovoLog® in the refrigerator between 36° to 46°F (2° to 8°C).**
- Do not freeze. Do not use NovoLog® if it has been frozen.
- Keep unopened NovoLog® in the carton to protect from light.

NovoLog® in use:

- **Vials**
 - Keep in the refrigerator or at room temperature below 86°F (30°C) for up to 28 days.
 - Keep vials away from direct heat or light.
 - Throw away an opened vial after 28 days of use, even if there is insulin left in the vial.
 - Do not draw up NovoLog® into a syringe and store for later use.
 - Unopened vials can be used until the expiration date on the NovoLog® label, if the medicine has been stored in a refrigerator.
- **PenFill® Cartridges or NovoLog® FlexPen®**
 - Keep at room temperature below 86°F (30°C) for up to 28 days.
 - Do not store a PenFill® cartridge or NovoLog® FlexPen® that you are using in the refrigerator.
 - Keep PenFill® cartridges and NovoLog® FlexPen® away from direct heat or light.
 - Throw away a used PenFill® cartridge or NovoLog® FlexPen® after 28 days, even if there is insulin left in the cartridge or syringe.
- **NovoLog® in the pump reservoir and the complete external pump infusion set**
 - The infusion set and the infusion site should be changed at **least 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. Change the infusion set and the infusion site more often than every 3 days if you have high blood sugar (hyperglycemia), the pump alarm sounds, or the insulin flow is blocked (occlusion).

General advice about NovoLog®

Medicines are sometimes prescribed for conditions that are not mentioned in the patient leaflet. 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 you have. It may harm them.

This leaflet summarizes the most important information about NovoLog®. If you would like more information about NovoLog® or diabetes, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about NovoLog® that is written for healthcare professionals. Call 1-800-727-6500 or visit www.novonordisk-us.com for more information.

Helpful information for people with diabetes is published by the American Diabetes Association, 1701 N Beauregard Street, Alexandria, VA 22311 and on www.diabetes.org.

NovoLog® ingredients include:

- insulin aspart
- glycerin
- metacresol
- disodium hydrogen phosphate dihydrate
- water for injection
- zinc
- phenol
- sodium chloride

All NovoLog® vials, PenFill® cartridges and NovoLog® FlexPen® are latex free.

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Novo Nordisk®, NovoLog®, PenFill®, FlexPen®, NovoPen®, NovoFine®, and PenMate® are registered trademarks of Novo Nordisk A/S.

NovoLog® is covered by US Patent Nos. 5,618,913, 5,866,538, and other patents pending.

FlexPen® is covered by US Patent Nos. 6,582,404, 6,004,297, 6,235,004, and other patents pending.

PenFill® is covered by US Patent No. 5,693,027.

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novonordisk®

Patient Instructions for Use

NovoLog® FlexPen®

Introduction

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

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® needles.

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

Getting ready

Make sure you have the following items:

- NovoLog® FlexPen®
- New NovoFine® needle
- Alcohol swab

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® should look clear.

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

B. Attaching the needle

Remove the protective tab from a disposable needle. Screw the needle tightly onto your FlexPen®. It is important that the needle is put on straight (see diagram B). Never place a disposable needle on your NovoLog® FlexPen® until you are ready to take your injection.

- C. Pull off the big outer needle cap (see diagram C).
- D. Pull off the inner needle cap and dispose of it (see diagram D).
△ Always use a new needle for each injection to help ensure sterility and prevent blocked needles.
△ 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 select 2 units (see diagram E).
- F. Hold your NovoLog® FlexPen® with the needle pointing up. Tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge (see diagram F).
- G. Keep the needle pointing upwards, press the push-button all the way in (see diagram G). The dose selector returns to 0.
A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.
If you do not see a drop of insulin after 6 times, do not use the NovoLog® FlexPen® and contact Novo Nordisk at 1-800-727-6500.
A small air bubble may remain at the needle tip, but it will not be injected.

Selecting your dose

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

- H. Turn the dose selector to the number of units you need to inject. The pointer should line up with your dose.
The dose can be corrected either up or down by turning the dose selector in either direction until the correct dose lines up with the pointer (see diagram H). When turning the dose selector, be careful not to press the push-button as insulin will come out.
You cannot select a dose larger than the number of units left in the cartridge.
You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear.

△ 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.

- 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 NovoLog® at the needle tip. This is normal and has no effect on the dose you just received. If blood appears after you take the needle out of your skin, press the injection site lightly with 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. This helps to prevent infection, leakage of insulin, and will help to make sure you inject the right dose of insulin.

△ Put the needle and any empty NovoLog® FlexPen® or any used NovoLog® FlexPen® still containing insulin in a sharps container or some type of hard plastic or metal container with a screw top such as a detergent bottle or empty coffee can. These containers should be sealed and thrown away the right way. Check with your healthcare provider about the right way to throw away used needles and syringes. Do not throw away used needles and syringes in household trash or recycling bins.

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).

Function Check

- L. If your NovoLog® FlexPen® is not working the right way, follow the steps below:
 - Screw on a new NovoFine® needle.
 - Remove the big outer needle cap and the inner needle cap.
 - Do an airshot as described in "Giving the airshot before each injection".
 - Put the big outer needle cap onto the needle. Do not put on the inner needle cap.
 - Turn the dose selector so the dose indicator window shows 20 units.
 - Hold the NovoLog® FlexPen® so the needle is pointing down.
 - Press the push-button all the way in.

The insulin should fill the lower part of the big outer needle cap (see diagram L). If the NovoLog® FlexPen® has released too much or too little insulin, do the function check again. If the same problem happens again, do not use your NovoLog® FlexPen® and contact Novo Nordisk at 1-800-727-6500.

Maintenance

Your FlexPen® is designed to work accurately and safely. It must be handled 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.
- △ Needles and NovoLog® FlexPen® must not be shared. 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.

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