

NovoLog[®] Mix 70/30

70% insulin aspart protamine suspension and 30% insulin aspart injection
(rDNA origin)

DESCRIPTION

NovoLog Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin]) is a human insulin analogue suspension containing 70% insulin aspart protamine crystals and 30% soluble insulin aspart. NovoLog Mix 70/30 is a blood glucose-lowering agent with a rapid onset and an intermediate duration of action. Insulin aspart is homologous with regular human insulin with the exception of a single substitution of the amino acid proline by aspartic acid in position B28, and is produced by recombinant DNA technology utilizing *Saccharomyces cerevisiae* (baker's yeast) as the production organism. Insulin aspart (NovoLog[®]) has the empirical formula C₂₅₆H₃₈₁N₆₅O₇₉S₆ and a molecular weight of 5825.8 Da.

Structural formula:

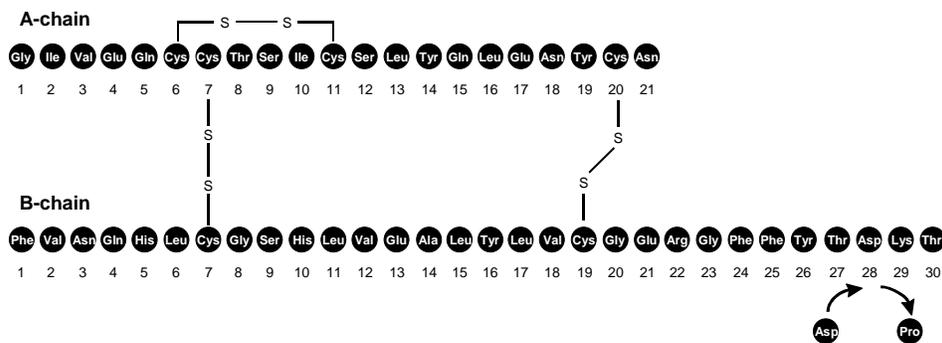


Figure 1. Structural formula of insulin aspart

NovoLog Mix 70/30 is a uniform, white, sterile suspension that contains insulin aspart (B28 asp regular human insulin analogue) 100 Units/mL, mannitol 36.4 mg/mL, phenol 1.50 mg/mL, metacresol 1.72 mg/mL, zinc 19.6 µg/mL, disodium hydrogen phosphate dihydrate 1.25 mg/mL, sodium chloride 0.58 mg/mL, and protamine sulfate 0.33 mg/mL. NovoLog Mix 70/30 has a pH of 7.20 - 7.44. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

CLINICAL PHARMACOLOGY

Mechanism of action

The primary activity of NovoLog Mix 70/30 is the regulation of glucose metabolism. Insulins, including NovoLog Mix 70/30, exert their specific action through binding to insulin receptors. Insulin

34 binding activates mechanisms to lower blood glucose by facilitating cellular uptake of glucose into
35 skeletal muscle and fat, simultaneously inhibiting the output of glucose from the liver.

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37 In standard biological assays in mice and rabbits, one unit of NovoLog[®] has the same glucose-lowering
38 effect as one unit of regular human insulin. However, the effect of NovoLog Mix 70/30 is more rapid in
39 onset compared to Novolin[®] (human insulin) 70/30 due to its faster absorption after subcutaneous
40 injection.

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42 **Pharmacokinetics**

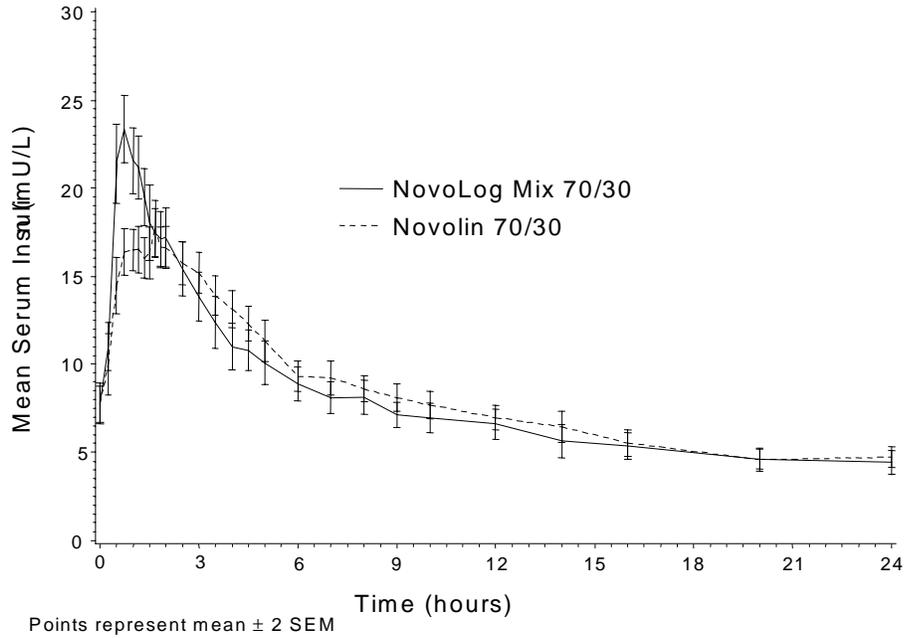
43 **Bioavailability and absorption**

44 The single substitution of the amino acid proline with aspartic acid at position B28 in insulin aspart
45 (NovoLog[®]) reduces the molecule's tendency to form hexamers as observed with regular human
46 insulin. The rapid absorption characteristics of NovoLog[®] are maintained by NovoLog Mix 70/30. The
47 insulin aspart in the soluble component of NovoLog Mix 70/30 is absorbed more rapidly from the
48 subcutaneous layer than regular human insulin. The remaining 70% is in crystalline form as insulin
49 aspart protamine which has a prolonged absorption profile after subcutaneous injection.

50
51 The relative bioavailability of NovoLog Mix 70/30 compared to NovoLog[®] and Novolin 70/30
52 indicates that they are absorbed to similar degrees. In euglycemic clamp studies in healthy
53 volunteers (n=23) after dosing with 0.2 U/kg of NovoLog Mix 70/30, a mean maximum serum
54 concentration (C_{max}) of 23.4 ± 5.3 mU/L was reached after 60 minutes. The mean half-life
55 (t_{1/2}) of NovoLog Mix 70/30 was about 8 to 9 hours. Serum insulin levels returned to baseline
56 15 to 18 hours after a subcutaneous dose. Similar data were seen in a separate euglycemic clamp
57 study in healthy volunteers (n=24) after dosing with 0.3 U/kg of NovoLog Mix 70/30. A C_{max}
58 of 61.3 ± 20.1 mU/L was reached after 85 minutes. Serum insulin levels returned to baseline 12
59 hours after a subcutaneous dose.

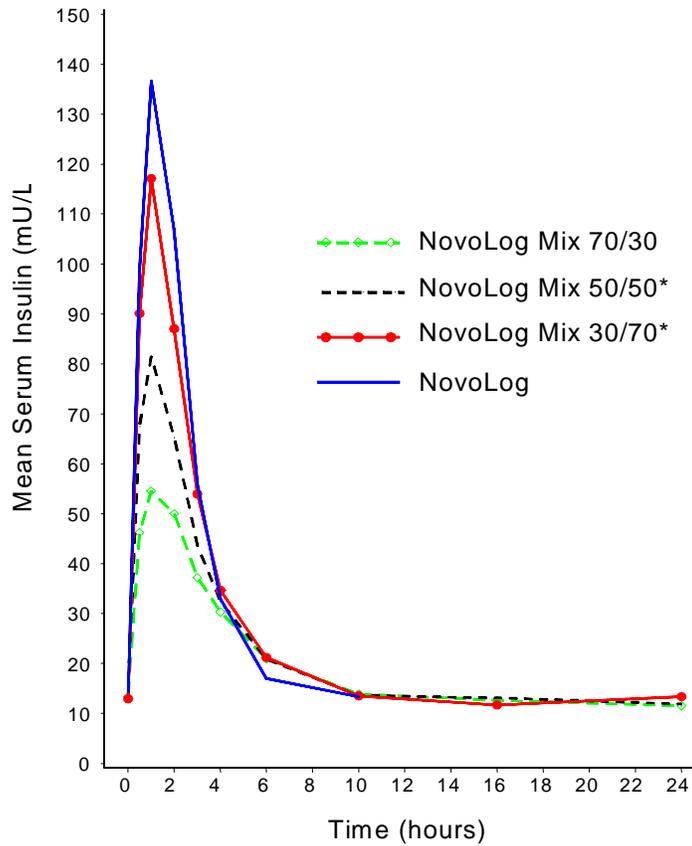
60
61 The C_{max} and the area under the insulin concentration-time curve (AUC) after administration of
62 NovoLog Mix 70/30 differed by approximately 20% from those after administration of NovoLog
63 Mix 50/50 (investigational drug, not marketed.) and Novolin 70/30 (see Fig. 2 and 3 for
64 pharmacokinetic profiles).

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Figure 2. Pharmacokinetic Profiles of NovoLog Mix 70/30 and Novolin® 70/30



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72 **Figure 3 Pharmacokinetic profiles for NovoLog Mix 70/30 and other proportional mixes (***
73 **investigational drugs, not marketed).**

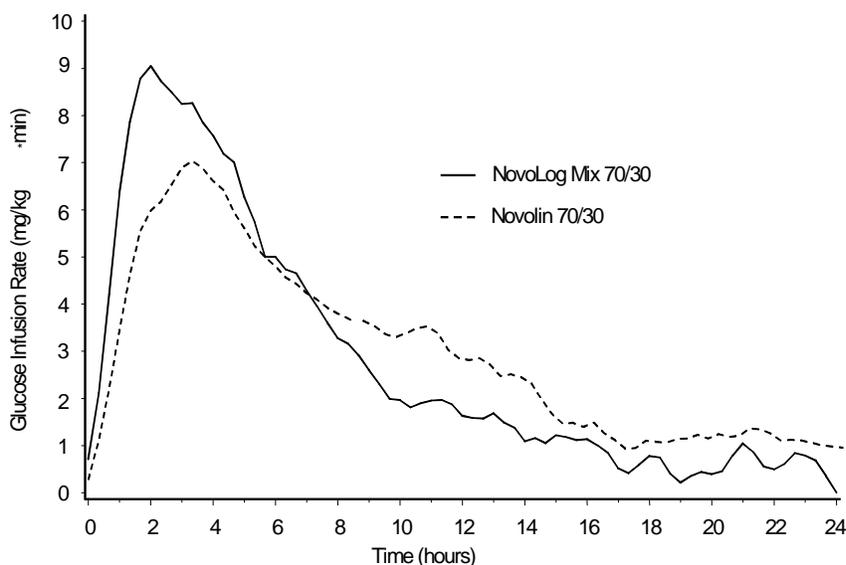
74
75 Pharmacokinetic measurements were generated in clamp studies employing insulin doses of 0.3
76 U/kg. Insulin kinetics exhibit significant inter- and intra-patient variability. The rate of insulin
77 absorption and consequently the onset of activity is known to be affected by the site of injection,
78 exercise, and other variables (see PRECAUTIONS, General). Differences in pharmacokinetics
79 between NovoLog Mix 70/30 and products to which it has been compared are not associated
80 with differences in overall glycemic control.

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

88
89 **Pharmacodynamics**

90 The two euglycemic clamp studies described above assessed glucose utilization after dosing of healthy
91 volunteers. NovoLog Mix 70/30 has a more rapid onset of action than regular human insulin in studies
92 of normal volunteers and patients with diabetes. The peak pharmacodynamic effect of NovoLog Mix
93 70/30 occurs between 1 and 4 hours after injection. The duration of action may be as long as 24 hours
94 (see Figures 4 and 5).

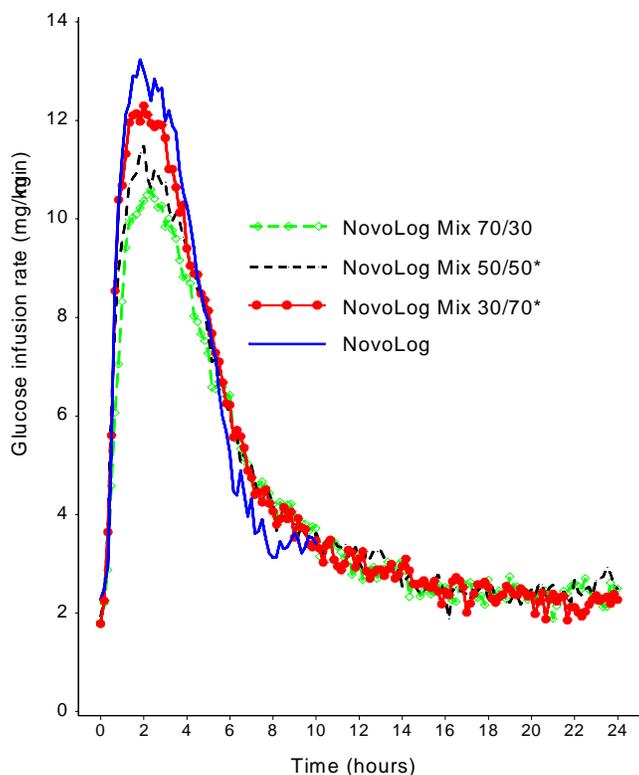
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99 **Fig 4: Pharmacodynamic Activity Profile of NovoLog Mix 70/30 and Novolin 70/30 in healthy**
100 **subjects.**

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Figure 5. Pharmacodynamic Activity Profiles for NovoLog Mix 70/30 and other proportional mixes (* investigational drugs, not marketed)

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Special populations

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Children and adolescents-The pharmacokinetic and pharmacodynamic properties of NovoLog Mix 70/30 have not been assessed in children and adolescents less than 18 years of age.

Geriatrics-The effect of age on the pharmacokinetics and pharmacodynamics of NovoLog Mix 70/30 has not been studied.

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123 *Gender*- The effect of gender on the pharmacokinetics and pharmacodynamics of NovoLog Mix 70/30
124 has not been studied.

125
126 *Obesity*-The effect of obesity and/or subcutaneous fat thickness on the pharmacokinetics and
127 pharmacodynamics of NovoLog Mix 70/30 has not been studied but data on the rapid acting component
128 (NovoLog®) show no significant effect.

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130 *Ethnic origin*-The effect of ethnic origin on the pharmacokinetics and pharmacodynamics of NovoLog
131 Mix 70/30 has not been studied.

132
133 *Renal impairment*-The effect of renal function on the pharmacokinetics and pharmacodynamics of
134 NovoLog Mix 70/30 has not been studied but data on the rapid acting component (NovoLog®) show no
135 significant effect. Some studies with human insulin have shown increased circulating levels of insulin in
136 patients with renal failure. Careful glucose monitoring and dose adjustments of insulin, including
137 NovoLog Mix 70/30, may be necessary in patients with renal dysfunction (see PRECAUTIONS, Renal
138 Impairment).

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140 *Hepatic impairment*- The effect of hepatic impairment on the pharmacokinetics and pharmacodynamics
141 of NovoLog Mix 70/30 has not been studied but data on the rapid-acting component (NovoLog®) show
142 no significant effect. Some studies with human insulin have shown increased circulating levels of
143 insulin in patients with liver failure. Careful glucose monitoring and dose adjustments of insulin,
144 including NovoLog Mix 70/30, may be necessary in patients with hepatic dysfunction (see
145 PRECAUTIONS, Hepatic Impairment).

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147 *Pregnancy*-The effect of pregnancy on the pharmacokinetics and pharmacodynamics of NovoLog Mix
148 70/30 has not been studied (see PRECAUTIONS, Pregnancy).

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150 *Smoking*-The effect of smoking on the pharmacokinetics and pharmacodynamics of NovoLog Mix 70/30
151 has not been studied.

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154 **CLINICAL STUDIES**

155 In a three-month, open-label trial, patients with Type 1 (n=146) or Type 2 (n=178) diabetes were treated
156 BID (before breakfast and before supper) with NovoLog Mix 70/30 or Novolin® 70/30. The small
157 changes in HbA1c were comparable across the treatment groups (see Table 1).

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Table 1: Glycemic Parameters at the End of Treatment [Mean (SD)]

	NovoLog Mix 70/30	Novolin 70/30
Type 1, N=92		
Fasting Blood Glucose (mg/dL)	173 (62.3)	141 (58.7)
1.5 Hour Post Breakfast	185 (80.1)	198 (80.1)
1.5 Hour Post Dinner	158 (76.5)	169 (65.9)
HbA1c (%)	8.4 (1.1)	8.3 (1.0)
Type 2, N=169		
Fasting Blood Glucose (mg/dL)	151 (39.2)	151 (67.6)
1.5 Hour Post Breakfast	180 (64.1)	198 (80.1)
1.5 Hour Post Dinner	166 (49.8)	189 (49.8)
HbA1c (%)	7.9 (1.0)	8.1 (1.1)

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

Specific anti-insulin antibodies as well as cross-reacting anti-insulin antibodies were monitored in the 3-month open-label comparator trial as well as in a long-term extension trial (see PRECAUTIONS, Allergy).

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INDICATIONS AND USAGE

NovoLog Mix 70/30 is indicated for the treatment of patients with diabetes mellitus for the control of hyperglycemia.

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CONTRAINDICATIONS

NovoLog Mix 70/30 is contraindicated during episodes of hypoglycemia and in patients hypersensitive to NovoLog Mix 70/30 or one of its excipients.

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WARNINGS

Because NovoLog Mix 70/30 has peak pharmacodynamic activity one hour after injection, it should be administered with meals.

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NovoLog Mix 70/30 should not be administered intravenously.

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NovoLog Mix 70/30 is not to be used in insulin infusion pumps.

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

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Hypoglycemia is the most common adverse effect of insulin therapy, including NovoLog Mix 70/30. As with all insulins, the timing of hypoglycemia may differ among various insulin formulations.

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198 Glucose monitoring is recommended for all patients with diabetes.
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200 Any change of insulin dose should be made cautiously and only under medical supervision. Changes in
201 insulin strength, manufacturer, type (e.g., regular, NPH, analog), species (animal, human), or method of
202 manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage.
203

204 **PRECAUTIONS**

206 **General**

207 Hypoglycemia and hypokalemia are among the potential clinical adverse effects associated with the use
208 of all insulins. Because of differences in the action of NovoLog Mix 70/30 and other insulins, care
209 should be taken in patients in whom such potential side effects might be clinically relevant (e.g., patients
210 who are fasting, have autonomic neuropathy, or are using potassium-lowering drugs or patients taking
211 drugs sensitive to serum potassium level)
212

213 Fixed ratio insulins are typically dosed on a twice daily basis, i.e., before breakfast and supper, |
214 with each dose intended to cover two meals or a meal and snack (see DOSAGE AND
215 ADMINISTRATION). Because there is diurnal variation in insulin resistance and endogenous
216 insulin secretion, variability in the time and content of meals, and variability in the time and
217 extent of exercise, fixed ratio insulin mixtures may not provide optimal glycemic control for all
218 patients. The dose of insulin required to provide adequate glycemic control for one of the meals
219 may result in hyper- or hypoglycemia for the other meal. The pharmacodynamic profile may
220 also be inadequate for patients (e.g. pregnant women) who require more frequent meals.

221
222 Adjustments in insulin dose or insulin type may be needed during illness, emotional stress, and
223 other physiologic stress in addition to changes in meals and exercise.
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225 The pharmacokinetic and pharmacodynamic profiles of all insulins may be altered by the site
226 used for injection and the degree of vascularization of the site. Smoking, temperature, and
227 exercise contribute to variations in blood flow and insulin absorption. These and other factors
228 contribute to inter- and intra-patient variability.
229

230 Lipodystrophy and hypersensitivity are among other potential clinical adverse effects associated with the
231 use of all insulins.
232

233 **Hypoglycemia**-As with all insulin preparations, hypoglycemic reactions may be associated with the
234 administration of NovoLog Mix 70/30. Rapid changes in serum glucose concentrations may induce
235 symptoms of hypoglycemia in persons with diabetes, regardless of the glucose value. Early warning
236 symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long
237 duration of diabetes, diabetic nerve disease, use of medications such as beta-blockers, or intensified
238 diabetes control.
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240 **Renal Impairment**- Clinical or pharmacology studies with NovoLog Mix 70/30 in diabetic patients
241 with various degrees of renal impairment have not been conducted. As with other insulins, the
242 requirements for NovoLog Mix 70/30 may be reduced in patients with renal impairment.

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244 **Hepatic Impairment**-Clinical or pharmacology studies with NovoLog Mix 70/30 in diabetic patients
245 with various degrees of hepatic impairment have not been conducted.—As with other insulins, the
246 requirements for NovoLog Mix 70/30 may be reduced in patients with hepatic impairment.

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248 **Allergy-**

249 Local Reactions- Erythema, swelling, and pruritus at the injection site have been observed with
250 NovoLog Mix 70/30 as with other insulin therapy. Reactions may be related to the insulin molecule,
251 other components in the insulin preparation including protamine and cresol, components in skin
252 cleansing agents, or injection techniques.

253

254 Systemic Reactions- Less common, but potentially more serious, is generalized allergy to insulin,
255 which may cause rash (including pruritus) over the whole body, shortness of breath, wheezing, reduction
256 in blood pressure, rapid pulse, or sweating. Severe cases of generalized allergy, including anaphylactic
257 reaction, may be life threatening. Localized reactions and generalized myalgias have been reported with
258 the use of cresol as an injectable excipient.

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261 **Antibody production**-Specific anti-insulin antibodies as well as cross-reacting anti-insulin antibodies
262 were monitored in the 3-month, open-label comparator trial as well as in a long-term extension trial.
263 Changes in cross-reactive antibodies were more common after NovoLog Mix 70/30 than with Novolin®
264 70/30 but these changes did not correlate with change in HbA1c or increase in insulin dose. The clinical
265 significance of these antibodies has not been established. Antibodies did not increase further after long-
266 term exposure (>6 months) to NovoLog Mix 70/30.

267

268 **Information for patients-**

269 Patients should be informed about potential risks and advantages of NovoLog Mix 70/30 therapy
270 including the possible side effects. Patients should also be offered continued education and advice on
271 insulin therapies, injection technique, life-style management, regular glucose monitoring, periodic
272 glycosylated hemoglobin testing, recognition and management of hypo- and hyperglycemia, adherence
273 to meal planning, complications of insulin therapy, timing of dose, instruction for use of injection
274 devices, and proper storage of insulin.

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276 Female patients should be advised to discuss with their physician if they intend to, or if they become,
277 pregnant because information is not available on the use of NovoLog Mix 70/30 during pregnancy or
278 lactation (see PRECAUTIONS, Pregnancy).

279

280 **Laboratory Tests**- The therapeutic response to NovoLog Mix 70/30 should be assessed by measurement
281 of serum or blood glucose and glycosylated hemoglobin.

282

283 **Drug Interactions** A number of substances affect glucose metabolism and may require insulin dose
284 adjustment and particularly close monitoring. The following are examples of substances that may
285 increase the blood-glucose-lowering effect and susceptibility to hypoglycemia: oral antidiabetic
286 products, ACE inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors,
287 propoxyphene, salicylates, somatostatin analog (e.g. octreotide), sulfonamide antibiotics.

288

289 The following are examples of substances that may reduce the blood-glucose-lowering effect:
290 corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, salbutamol,
291 terbutaline), isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens,
292 progestogens (e.g., in oral contraceptives).

293
294 Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-
295 lowering effect of insulin.

296
297 Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

298
299 In addition, under the influence of sympatholytic medical products such as beta-blockers, clonidine,
300 guanethidine, and reserpine, the signs of hypoglycemia may be reduced or absent (see CLINICAL
301 PHARMACOLOGY).

304 **Mixing of insulins**

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

307 **Carcinogenicity, Mutagenicity, Impairment of Fertility**

308 Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the carcinogenic
309 potential of NovoLog Mix 70/30. In 52-week studies, Sprague-Dawley rats were dosed subcutaneously
310 with NovoLog®, the rapid-acting component of NovoLog Mix 70/30, at 10, 50, and 200 U/kg/day
311 (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 U/kg/day, based on U/body
312 surface area, respectively). At a dose of 200 U/kg/day, NovoLog® increased the incidence of mammary
313 gland tumors in females when compared to untreated controls. The incidence of mammary tumors for
314 NovoLog® was not significantly different than for regular human insulin. The relevance of these
315 findings to humans is not known. NovoLog® was not genotoxic in the following tests: Ames test,
316 mouse lymphoma cell forward gene mutation test, human peripheral blood lymphocyte chromosome
317 aberration test, in vivo micronucleus test in mice, and in ex vivo UDS test in rat liver hepatocytes. In
318 fertility studies in male and female rats, NovoLog® at subcutaneous doses up to 200 U/kg/day
319 (approximately 32 times the human subcutaneous dose, based on U/body surface area) had no direct
320 adverse effects on male and female fertility, or on general reproductive performance of animals.

322 **Pregnancy: Teratogenic Effects: Pregnancy Category C:**

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

334 These doses are approximately 8 times the human subcutaneous dose of 1.0 U/kg/day for rats and equal
335 to the human subcutaneous dose of 1.0 U/kg/day for rabbits based on U/body surface area.

336
337 It is not known whether NovoLog Mix 70/30 can cause fetal harm when administered to a pregnant
338 woman or can affect reproductive capacity. There are no adequate and well-controlled studies of the use
339 of NovoLog Mix 70/30 or NovoLog® in pregnant women. NovoLog Mix 70/30 should be used during
340 pregnancy only if the potential benefit justifies the potential risk to the fetus.

341
342 *Nursing mothers*-It is unknown whether NovoLog Mix 70/30 is excreted in human milk as is human
343 insulin. There are no adequate and well-controlled studies of the use of NovoLog Mix 70/30 or
344 NovoLog® in lactating women.

345
346 *Pediatric Use*-Safety and effectiveness of NovoLog Mix 70/30 in children have not been established.

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348 *Geriatric Use*- Clinical studies of NovoLog Mix 70/30 did not include sufficient numbers of patients
349 aged 65 and over to determine whether they respond differently than younger patients. In general, dose
350 selection for an elderly patient should be cautious, usually starting at the low end of the dosing range
351 reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant
352 disease or other drug therapy in this population.

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355 **ADVERSE REACTIONS**

356 Clinical trials comparing NovoLog Mix 70/30 with Novolin® 70/30 did not demonstrate a difference in
357 frequency of adverse events between the two treatments.

358 Adverse events commonly associated with human insulin therapy include the following:

359

360 **Body as whole:** *allergic reactions* (see PRECAUTIONS, Allergy).

361 **Skin and Appendages:** *Local injection site reactions or rash or pruritus, as with other insulin*
362 *therapies, occurred in 7% of all patients on NovoLog Mix 70/30 and 5% on Novolin® 70/30. Rash led*
363 *to withdrawal of therapy in <1% of patients on either drug* (see PRECAUTIONS, Allergy).

364 **Hypoglycemia:** see WARNINGS and PRECAUTIONS.

365 **Other:** Small elevations in alkaline phosphatase were observed in patients treated in NovoLog®
366 controlled clinical trials. There have been no clinical consequences of these laboratory findings.

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369 **OVERDOSAGE**

370 Hypoglycemia may occur as a result of an excess of insulin relative to food intake, energy expenditure,
371 or both. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug
372 dosage, meal patterns, or exercise, may be needed. More severe episodes with coma, seizure, or
373 neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated
374 intravenous glucose. Sustained carbohydrate intake and observation may be necessary because
375 hypoglycemia may recur after apparent clinical recovery.

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378 **DOSAGE AND ADMINISTRATION**

379 General:

380 Fixed ratio insulins are typically dosed on a twice daily basis, i.e. before breakfast and supper,
381 with each dose intended to cover two meals or a meal and snack. NovoLog Mix 70/30 is
382 intended only for subcutaneous injection (into the abdominal wall, thigh, or upper arm).
383 NovoLog Mix 70/30 should not be administered intravenously. The absorption rate of NovoLog
384 Mix 70/30 from the subcutaneous tissue allows dosing within 15 minutes of meal initiation.

385 Dose regimens of NovoLog Mix 70/30 will vary among patients and should be determined by
386 the health care professional familiar with the patient's metabolic needs, eating habits, and other
387 lifestyle variables. As with all insulins, the duration of action may vary according to the dose,
388 injection site, blood flow, temperature, and level of physical activity and conditioning.

389

390 Table 2 Summary of pharmacodynamic properties of insulin products (pooled cross-study
391 comparison) and recommended interval between dosing and meal initiation

392

<i>Insulin Products</i>	<i>Dose (U/kg) Used in Study</i>	<i>Recommended interval between dosing and meal initiation (minutes)*</i>	<i>Time of Peak Activity (hours after dosing) (mean ± SD)</i>	<i>Percent of Total Activity Occurring in the First 4 hours (mean, range)</i>
NovoLog®	0.3	10-20	2.2 ± 0.98	65% ± 11%
Novolin® R	0.2	30	3.3	60% ± 16%
Novolin® 50/50	0.5	30	4.0 ± 0.6	54% ± 12%
NovoLog Mix 70/30	0.3	10-20	2.4 ± 0.80	45% ± 22%
Novolin® 70/30	0.3	30	4.2 ± 0.39	25% ± 5%
Novolin® N	0.3	n/a	8.0 ± 5.3	21% ± 11%

393 *Applicable only to Novolin® R and NovoLog® alone or as components of insulin mixes.

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396 **Administration using PenFill® Cartridges for 3 mL PenFill® cartridge compatible delivery**
397 **devices, NovoLog® Mix 70/30 FlexPen Prefilled syringes, or vials:**

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399 **PenFill® Cartridges for 3 mL PenFill® cartridge compatible delivery devices*:** NovoLog Mix
400 70/30 PenFill® suspension should be visually inspected and resuspended immediately before
401 use. The resuspended ~~liquid~~ **NovoLog Mix 70/30** must appear uniformly white and cloudy.
402 Before ~~insertion~~ **inserting the cartridge** into the insulin delivery system, roll the cartridge
403 between your palms 10 times. Thereafter, turn the cartridge upside down so that the glass ball
404 moves from one end of the cartridge to the other. Do this at least 10 times. The rolling and
405 turning procedure must be repeated until the ~~liquid~~ **suspension** appears uniformly white and
406 cloudy. Inject immediately. Before each subsequent injection, turn the 3 mL PenFill® cartridge
407 compatible delivery devices* upside down so that the glass ball moves from one end of the
408 cartridge to the other. Repeat this 10 times until the ~~liquid~~ **suspension** appears uniformly white
409 and cloudy. Inject immediately. **After use, needles on the insulin pen delivery devices should**
410 **not be recapped. Used syringes, needles, or lancets should be placed in sharps containers**
411 **(such as red biohazard containers), hard plastic containers (such as detergent bottles), or**
412 **metal containers (such as an empty coffee can). Such containers should be sealed and**
413 **disposed of properly.**

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416 * NovoLog® Mix 70/30 PenFill® cartridges are for use with the following 3 mL PenFill® cartridge
417 compatible delivery devices: NovoPen® 3, Innovo®, and InDuo™.
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420 ***Disposable NovoLog Mix 70/30 FlexPen™ Prefilled Syringes:***

421 NovoLog Mix 70/30 suspension should be visually inspected and resuspended immediately
422 before use. The resuspended ~~liquid~~ NovoLog Mix 70/30 must appear uniformly white and
423 cloudy. Before use, roll the disposable NovoLog Mix 70/30 FlexPen prefilled syringe between
424 your palms 10 times. Thereafter, turn the disposable NovoLog Mix 70/30 FlexPen prefilled
425 syringe upside down so that the glass ball moves from one end of the reservoir to the other. Do
426 this at least 10 times. The rolling and turning procedure must be repeated until the ~~liquid~~
427 suspension appears uniformly white and cloudy. Inject immediately. Before each subsequent
428 injection, turn the disposable NovoLog Mix 70/30 FlexPen Prefilled® syringe upside down so
429 that the glass ball moves from one end of the reservoir to the other at least 10 times and until the
430 ~~liquid~~ suspension appears uniformly white and cloudy. Inject immediately. **After use, needles**
431 **on the disposable NovoLog Mix 70/30 FlexPen prefilled syringes should not be recapped.**
432 **Used syringes, needles, or lancets should be placed in sharps containers (such as red**
433 **biohazard containers), hard plastic containers (such as detergent bottles), or metal**
434 **containers (such as an empty coffee can). Such containers should be sealed and disposed of**
435 **properly.**
436

437 ***Vial:*** NovoLog Mix 70/30 vial must be resuspended immediately before use. Roll the vial gently 10
438 times in your hand to mix it. The resuspended NovoLog Mix 70/30 must appear uniformly white and
439 cloudy.
440

441
442 **HOW SUPPLIED**

443 NovoLog Mix 70/30 is available in the following package sizes: each presentation contains 100 Units of
444 insulin aspart per mL (U-100).
445

446 10 mL vials	NDC xxxx-xxxx-xx
447 3 mL PenFill® cartridges*	NDC xxxx-xxxx-xx
448 3 mL NovoLog® Mix 70/30 FlexPen® Prefilled Syringe	NDC xxxx-xxxx-xx

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451 * NovoLog Mix 70/30 PenFill® cartridges are for use with the following 3 mL PenFill® cartridge
452 compatible delivery devices: NovoPen® 3, Innovo®, and InDuo™.
453

454 **RECOMMENDED STORAGE**

455 NovoLog Mix 70/30 should be stored between 2°C and 8°C (36° F to 46°F). *Do not freeze. Do*
456 **not use NovoLog Mix 70/30 if it has been frozen.**
457

458 ***Vials:***
459

460 The vials should be stored in a refrigerator, not in a freezer. If refrigeration is not possible, the
461 bottle in use can be kept unrefrigerated at room temperature below 30°C (86°F) for up to 28
462 days, as long as it is kept as cool as possible and away from direct heat and light.

463
464 Unpunctured vials can be used until the expiration date printed on the label if they are stored in a
465 refrigerator. Keep unused vials in the carton so they will stay clean and protected from light.

466
467 ***PenFill® cartridges or NovoLog Mix 70/30 FlexPen™ Prefilled syringes:***

468
469 Once a cartridge or a NovoLog Mix 70/30 FlexPen® prefilled syringe is punctured, it may be
470 used for up to 14 days if it is kept at room temperature below 30°C (86°F). Cartridges or
471 NovoLog Mix 70/30 FlexPen® prefilled syringes in use must NOT be stored in the refrigerator.
472 Keep all PenFill® cartridges and disposable NovoLog® Mix 70/30 FlexPen® Prefilled syringes
473 away from direct heat and sunlight. Unpunctured PenFill® cartridges and NovoLog Mix 70/30
474 FlexPen® Prefilled syringes can be used until the expiration date printed on the label if they are
475 stored in a refrigerator. Keep unused PenFill® cartridges and NovoLog® Mix 70/30 FlexPen®
476 Prefilled syringes in the carton so they will stay clean and protected from light.

477
478 Rx Only.

479
480 Date of issue: [date]

481
482 Manufactured by:
483 Novo Nordisk A/S
484 2880 Bagsvaerd, Denmark

485
486
487 Manufactured for:
488 Novo Nordisk Pharmaceuticals, Inc.
489 Princeton, NJ 08540

490
491 www.novonordisk-us.com

492 8-xxxx-xx-xxx-x

493

1 **Patient Information for 10 mL vials and 3 mL PenFill cartridges (100 Units/mL, U-**
2 **100)**

3 **NovoLog® Mix 70/30**

4 70% insulin aspart protamine suspension and 30% insulin aspart injection
5 ~~30% insulin aspart injection~~ (rDNA origin)

6
7
8 **What is the most important information I should know about NovoLog Mix 70/30?**

9
10 **WARNINGS**

11 THIS NOVO NORDISK® HUMAN INSULIN ANALOG MIXTURE IS DIFFERENT
12 FROM OTHER INSULIN MIXTURES BECAUSE IT HAS A RAPID ONSET OF
13 ACTION. THE RAPID ONSET OF ACTION MEANS THAT YOU SHOULD TAKE
14 YOUR DOSE OF NOVOLOG MIX 70/30 (70% INSULIN ASPART PROTAMINE
15 SUSPENSION AND 30% INSULIN ASPART INJECTION, [rDNA ORIGIN]) WITHIN
16 15 MINUTES OF A MEAL.

17 ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY
18 UNDER MEDICAL SUPERVISION. CHANGES IN STRENGTH,
19 MANUFACTURER, TYPE (E.G., REGULAR, NPH, ANALOG), SPECIES (BEEF,
20 PORK, BEEF-PORK, HUMAN), OR METHOD OF MANUFACTURE (rDNA
21 VERSUS ANIMAL-SOURCE INSULIN) MAY RESULT IN THE NEED FOR A
22 CHANGE IN THE TIMING OR DOSAGE OF NOVOLOG MIX 70/30.
23 PATIENTS TAKING NOVOLOG MIX 70/30 MAY REQUIRE A CHANGE IN
24 DOSAGE FROM THAT USED WITH OTHER INSULINS. IF AN ADJUSTMENT IS
25 NEEDED, IT MAY OCCUR WITH THE FIRST DOSE OR DURING THE FIRST
26 SEVERAL WEEKS OR MONTHS.

27
28
29
30 **What is NovoLog Mix 70/30?**

31
32 NovoLog Mix 70/30 (NO-voe-log-MIX-SEV-en-tee-THIR-tee) is a mixed insulin analog
33 similar to human insulin mixes used to treat diabetes. The active ingredient in NovoLog
34 Mix 70/30 is insulin aspart, which is made through biotechnology. Another ingredient,
35 protamine, is used to slow the absorption of the insulin analog by your body.

36
37 NovoLog Mix 70/30 comes in:

- 38 • 10 mL vials (small bottles) for use with a syringe
39 • 3 mL PenFill® cartridges for use with 3 mL PenFill® cartridge compatible delivery
40 devices*
41 • 3 mL NovoLog Mix 70/30 FlexPen Prefilled syringe
42 *3 mL PenFill® cartridge compatible delivery devices: NovoPen® 3, Innovo®, and
43 InDuo™.
44

45 **Who should NOT take NovoLog Mix 70/30?**

46

47 **Do NOT take NovoLog Mix 70/30 if:**

- 48 • Your blood sugar is too low (hypoglycemia).
49 • You are allergic to NovoLog Mix 70/30 or any of its ingredients. Check with your
50 doctor or pharmacist if you want information about ingredients.
51 • You are not planning to eat within 15 minutes of your injection.

52

53 **Tell your doctor if:**

- 54 • **You have liver or kidney problems.** Your dose may need to be changed.
55 • **You are pregnant or planning to become pregnant.** It is not known whether
56 NovoLog Mix 70/30 can cause any harm to the baby if it is taken during pregnancy.
57 • **You are breast-feeding or planning to breast-feed.** It is not known whether
58 NovoLog Mix 70/30 is passed through in human milk as is human insulin. Many
59 drugs, including human insulin, are present in human milk, and may affect the baby.
60 • **You take any other medicines,** including prescription and non-prescription
61 medicines and herbal supplements. Your NovoLog Mix 70/30 need may change if
62 you take other medicines. Be sure to mention if you take the following:
63 • oral hypoglycemic medicines (medicines you take by mouth to treat non insulin-
64 dependent [Type 2] diabetes)
65 • monoamine oxidase (MAO) inhibitors (used to treat depression)
66 • beta-blocking agents (used to treat certain heart conditions or high blood pressure)
67 • angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart
68 conditions or high blood pressure)
69 • salicylates, including aspirin (used to relieve pain or lower fever)
70 • anabolic steroids and glucocorticoids
71 • oral contraceptives (used for birth control)
72 • diuretics such as thiazides (used to treat high blood pressure or swelling [edema])
73 • thyroid hormones (used to treat thyroid gland problems)
74 • danazol (used to treat endometriosis)
75 • octreotide (used to treat gigantism or other rare endocrine tumors)
76 • sulfa antibiotics (used to treat infections)

77

78

79 **How should I take NovoLog Mix 70/30?**

80

- 81 • Follow your doctor's instructions about monitoring your blood sugar.
82 • Before injecting, make sure that you have the correct type and strength of insulin.
83 Carefully follow the instructions on how to use your insulin syringe or pen
84 • Inject your NovoLog Mix 70/30 fifteen-minutes or less before a meal.
85 • Inject NovoLog Mix 70/30 under your skin (subcutaneously). Never inject it into a
86 vein.

- 87 • The effect of an injected insulin dose may occur faster if the insulin is injected into
88 your abdomen (stomach area). However, you may also inject under the skin of your
89 thigh, or upper arm.
- 90 • Change (rotate) injection sites within the same body area.
- 91 • Measure your blood sugar level as directed by your doctor.
- 92 • Carefully follow the instructions given by your doctor about the type of insulin you
93 are using, its dose, and time of its injection. Any change in insulin should be made
94 cautiously and only with your doctor's guidance. Your insulin needs may change due
95 to a number of factors, such as illness, stress, medicines, or changes in diet or exercise
96 routines. Follow your doctor's instructions to make these changes in your dose
97 regimen.
- 98 • Clean your hands and the injection site with soap and water or with alcohol before
99 you start the injection process.

100

101 **See the end of this patient information for instructions about preparing and giving**
102 **the injection.**

103

104 **What should I do during illness?**

105

106 Even if you have a short term (acute) illness, especially with vomiting or fever, continue
107 taking your insulin. If possible, stay on your regular diet. If you have trouble eating,
108 drink fruit juices, regular soft drinks, or clear soups. If you can, eat small amounts of
109 bland foods. Test your urine for glucose and ketones and, if possible, test your blood
110 glucose. Note the results and contact your health care provider for possible insulin dose
111 adjustment. If you have severe and continued vomiting, get emergency medical care.

112

113 **What should I avoid while taking NovoLog Mix 70/30?**

114

115 Alcohol, including beer and wine, may increase and lengthen the risk of hypoglycemia
116 (too low blood sugar) when you take NovoLog Mix 70/30.

117

118 Be careful when you drive a car or operate machinery. Your ability to concentrate or
119 react may be reduced if you have hypoglycemia. Ask your doctor if you should drive if
120 you have:

- 121 • frequent hypoglycemia
- 122 • reduced or absent warning signs of hypoglycemia

123

124 **What are the possible side effects of NovoLog Mix 70/30?**

125

126 **Common side effects include blood sugar that is too low (hypoglycemia).**

127 Hypoglycemia (too little glucose in the blood) is one of the most frequent problems
128 experienced by insulin users. It can be brought about by:

- 129 1. Missing or delaying meals.
- 130 2. Taking too much insulin
- 131 3. Exercising or working more than usual
- 132 4. An infection or illness (especially with diarrhea or vomiting)
- 133 5. A change in the body's need for insulin
- 134 6. Diseases of the adrenal, pituitary, or thyroid gland, or kidney or liver disease
135 that is getting worse
- 136 7. Interactions with other drugs that lower blood glucose, such as oral (taken by
137 mouth) antidiabetic medicines, salicylates (for example, aspirin), sulfa
138 antibiotics, and certain antidepressants
- 139 8. Drinking of alcohol

140

141 What are symptoms of **mild to moderate** hypoglycemia:

- 142 • Sweating
- 143 • Dizziness
- 144 • Palpitation (fast heart beat)
- 145 • Tremor (shakiness)
- 146 • Hunger
- 147 • Restlessness
- 148 • Tingling in the hands, feet, lips, or tongue
- 149 • Lightheadedness
- 150 • Trouble concentrating
- 151 • Headache
- 152 • Drowsiness
- 153 • Sleep problems
- 154 • Anxiety
- 155 • Blurred vision
- 156 • Slurred speech
- 157 • Depressed mood
- 158 • Irritability
- 159 • Abnormal behavior
- 160 • Unsteady movement
- 161 • Personality change

162

163 What are symptoms of **severe** hypoglycemia:

- 164 • Disorientation
- 165 • Unconsciousness
- 166 • Seizures (convulsions)

167 • Death

168
169 If you develop serious hypoglycemic reactions, get medical help right away.

170
171 Without recognition of early warning symptoms, you may not be able to take steps to
172 avoid more serious hypoglycemia. Be alert for all of the various types of symptoms that
173 may indicate hypoglycemia. Patients who experience hypoglycemia without early
174 warning symptoms should monitor their blood glucose frequently, especially prior to
175 activities such as driving. If the blood glucose is below your normal fasting glucose, you
176 should consider eating or drinking sugar-containing foods to treat your hypoglycemia.
177 Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain
178 sugar. Patients should always carry a quick source of sugar, such as candy mints or
179 glucose tablets. More severe hypoglycemia may require the assistance of another person.
180 Patients who are unable to take sugar orally or who are unconscious require an injection
181 of glucagon or should be treated with intravenous administration of glucose at a medical
182 facility. You should learn to recognize your own symptoms of hypoglycemia. If you are
183 uncertain about these symptoms, you should monitor your blood glucose frequently to
184 help you learn to recognize the symptoms that your experience with hypoglycemia.

185
186 If you have frequent episodes of hypoglycemia or experience difficulty in recognizing the
187 symptoms, you should consult your doctor to discuss possible changes in therapy, meal
188 plans, and/or exercise programs to help you avoid hypoglycemia.

189
190 **Common side effects include blood sugar that is too high (hyperglycemia) and**
191 **diabetic ketoacidosis.**

192 Hyperglycemia (too much glucose in the blood) may develop if your body has too little
193 insulin. Hyperglycemia can be brought about by any of the following:

- 194 1. Not taking your insulin or taking less than the doctor has prescribed
195 2. Eating much more than your meal plan suggests
196 3. Developing a fever, infection, or being under stress

197
198
199 In patients with type 1 or insulin-dependent diabetes, long-lasting hyperglycemia can
200 cause diabetic ketoacidosis (DKA). The first symptoms of DKA usually come on
201 slowly, over a period of hours or days, and include feeling drowsy, flushed face,
202 thirst, loss of appetite, and fruity odor on the breath. With DKA, urine tests show
203 large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more
204 severe symptoms. If uncorrected, long-lasting hyperglycemia or DKA can lead to
205 nausea, vomiting, stomach pains, dehydration, loss of consciousness, or even death.
206 Therefore, it is important that you obtain medical help right away.

207
208
209 **Other possible side effects include the following:**

- 211 • **Serious allergic reaction.**
212 Get medical help right away if you develop a rash over your whole body, have
213 trouble breathing, a fast heartbeat, or sweating. These are signs of a dangerous
214 allergic reaction (systemic allergic reaction). These reactions are not common.
215
216 • **Reaction at the injection site** (local allergic reaction). You may get redness,
217 swelling and itching at the injection site. If you have serious or continuing
218 reactions, you may need to stop using NovoLog Mix 70/30 and use another
219 insulin. Do not inject insulin into skin sites with these reactions. No type of
220 insulin should be injected into skin sites with these reactions.
221
222 • **Skin thickens or pits at the injection site**, especially if the injection site is not
223 rotated (changed).
224
225 • **Vision changes** that may require evaluation by an ophthalmologist (medical
226 doctor specializing in eye disease) or changes in your eyeglasses or contact lens
227 prescription.
228 • **Fluid retention or swelling of your hands and feet.**
229
230 • **Low potassium in your blood** (hypokalemia)

231
232 There are other possible side effects from NovoLog Mix 70/30. Ask your doctor or
233 pharmacist for further information. Tell your doctor or pharmacist if you have any other
234 unwanted effects that you believe are caused by this insulin.
235

236 **How should I store NovoLog Mix 70/30?**

- 237 • **Unused insulin:**
238 Store insulin in a refrigerator (2°C to 8°C [36°F to 46°F]), but not in a freezer.
239 Do not use NovoLog Mix 70/30 if it has been frozen. Keep unused PenFill®
240 cartridges and vials in the carton so they will stay clean and protected from light.
241 • **After starting to use the insulin:**
242 Do not refrigerate the disposable PenFill® cartridge in use (the rubber stopper has
243 been punctured). However, keep it as cool as possible (below 30°C [86°F]). The
244 vials should be stored in a refrigerator, not in a freezer. If refrigeration is not
245 possible, the bottle that you are currently using can be kept unrefrigerated at room
246 temperature (below 30°C [86°F]) up to 28 days, as long as it is kept as cool as
247 possible. Keep all PenFill® cartridges and vials away from direct heat and
248 sunlight.
249 • **Throw away unrefrigerated disposable NovoLog Mix 70/30 PenFill®**
250 **cartridges after 14 days, even if they still contain insulin. Throw away**
251 **unrefrigerated vials after 28 days, even if they still contain insulin.**
252

253 **General information about NovoLog Mix 70/30**

254 Use NovoLog Mix 70/30 only to treat your diabetes. **Do not** share it with anyone else.
255 Ask your doctor or pharmacist about any concerns you have. They can answer your
256 questions and give you written information about NovoLog Mix 70/30 written for health
257 care professionals.

258

259 **How should I prepare and deliver the injection using different delivery devices?**

260 **Using the 10 ml vial:**

- 261 1. At your first use, remove the tamper-resistant cap of the vial. If the cap has already
262 been removed, do not use this vial and return it to your pharmacy.
- 263 2. Wipe the rubber stopper with an alcohol swab.
- 264 3. Roll the vial gently 10 times in your hands to mix it. Do not shake it vigorously.
265 Vigorous shaking right before the dose is drawn into the syringe may cause bubbles or
266 froth, which could cause dosage errors. The insulin should be used only if it uniformly
267 appears white and cloudy.
- 268 4. Pull back the plunger until the black tip reaches the marking for the number of units
269 you will inject.
- 270 5. Push the needle through the rubber stopper into the vial.
- 271 6. Push the plunger all the way in. This inserts air into the vial.
- 272 7. Turn the vial and syringe upside down together and slowly pull the plunger back to a
273 few units beyond the correct dose.
- 274 8. If there are air bubbles in the syringe, tap the syringe gently with your finger to raise
275 the air bubbles to the needle. Then slowly push the plunger to the correct unit
276 marking.
- 277 9. Lift the vial off the syringe.
- 278 10. Inject right away. If there is a delay after you rolled the vial, you will have to roll it
279 again to remix the insulin. (See injection instructions “How should I inject NovoLog
280 Mix 70/30 with a syringe)
- 281 11. After the injection, remove the needle **without recapping** and dispose of it in a
282 puncture-resistant container. Used syringes, needles, or lancets should be placed in
283 sharps containers (such as red biohazard containers), hard plastic containers (such as
284 detergent bottles), or metal containers (such as an empty coffee can). Such containers
285 should be sealed and disposed of properly.

286

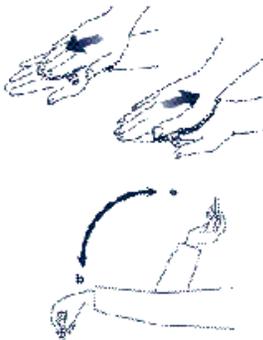
287 **Using the NovoLog Mix 70/30 3mL PenFill® cartridge in 3 mL PenFill® cartridge**
288 **compatible delivery devices* (*see 3 mL PenFill® cartridge compatible delivery**
289 **devices section):**

290

- 291 1. Read the instruction manuals for the 3 mL PenFill cartridge compatible delivery
292 devices* before the device is used.
- 293 2. For PenFill cartridge:
294 Before inserting the PenFill cartridge into the 3 mL PenFill cartridge compatible
295 delivery devices* for the first time, roll the cartridge between your palms 10 times.
296

297 Then turn the PenFill cartridge up and down between positions **a** and **b** (see
298 Diagram 1) so the glass ball moves from one end of the cartridge to the other. Do
299 this at least 10 times. The procedure must be repeated until the insulin appears
300 uniformly white and cloudy. Insert the PenFill® cartridge into the 3 mL PenFill®
301 cartridge compatible delivery devices* and inject right away.
302

303 Diagram #1



304
305

- 306 3. Place the needle onto the 3 mL PenFill® cartridge compatible delivery devices*
307 immediately before use.
- 308 4. Airshots/priming should be done prior to each injection. Directions for performing
309 an airshot or priming are provided in your insulin delivery device instruction
310 manual.
- 311 5. Inject the insulin right away. If there is a delay after you mix the insulin and the
312 injection, you will have to mix the insulin again before injecting the insulin. (See
313 below “How should I inject NovoLog Mix 70/30 insulin with a syringe or 3 mL
314 PenFill® cartridge compatible delivery devices*?”)
- 315 6. After the injection, remove the needle **without recapping** and dispose of it in a
316 puncture-resistant container. Used syringes, needles, or lancets should be placed
317 in sharps containers (such as red biohazard containers), hard plastic containers
318 (such as detergent bottles), or metal containers (such as an empty coffee can).
319 Such containers should be sealed and disposed of properly.
320

321

322 **After the first use of PenFill® cartridge:**

- 323 1 If the PenFill® cartridge is already in the 3 mL PenFill® cartridge compatible
324 delivery devices*, it should be turned upside down between positions **a** and **b** (see
325 diagram 1), so that the glass ball moves from one end of the PenFill® cartridge to
326 the other. Do this until the insulin appears uniformly white and cloudy.
- 327 2. Airshots/priming should be done prior to each injection. Directions for
328 performing an airshot or priming are provided in your insulin delivery device
329 instruction manual.
- 330 3 Inject right away. If there is a delay between mixing of the insulin and the
331 injection, the insulin will need to be mixed again. (See below “How should I

- 332 inject NovoLog Mix 70/30 insulin with a syringe or 3 mL PenFill® cartridge
333 compatible delivery devices*?)
334 3. After the injection, remove the needle **without recapping** and dispose of it in a
335 puncture-resistant container. Used syringes, needles, or lancets should be placed in
336 sharps containers (such as red biohazard containers), hard plastic containers (such as
337 detergent bottles), or metal containers (such as an empty coffee can). Such containers
338 should be sealed and disposed of properly.

339
340

341 **How should I inject NovoLog Mix 70/30 insulin with a syringe or 3 mL PenFill®**
342 **cartridge compatible delivery devices*?**

- 343 1. Pinch your skin between two fingers, push the needle into the skinfold, and push the
344 plunger to inject the insulin under your skin. The needle should be perpendicular to
345 the skin. This means the needle will be straight in.
346 2. Keep the needle under your skin for at least 6 seconds to make sure you have injected
347 all the insulin.
348 3. If blood appears after you pull the needle from your skin, press the injection site
349 lightly with a finger. Do not rub the area.

350
351

352 ***3 mL PenFill® cartridge compatible delivery devices**

353 NovoPen® 3, Innovo®, InDuo™

354
355

356 Helpful information for people with diabetes is published by the American Diabetes
357 Association, 1660 Duke Street, Alexandria, VA 22314.

358

359 For information about NovoLog® Mix 70/30 contact:

360 Novo Nordisk Pharmaceuticals, Inc.

361 100 College Road West

362 Princeton, New Jersey 08540

363 1-800-727-6500

364 www.novonordisk-us.com

365

366 Manufactured by

367 Novo Nordisk A/S

368 DK-2880 Bagsvaerd, Denmark

369

370 Novo Nordisk®, NovoLog®, FlexPen®, Innovo®, Novolin®, NovoPen®, PenFill®, and
371 NovoFine® are trademarks owned by Novo Nordisk A/S.

372 InDuo™ is a trademark of LifeScan, Inc., a Johnson & Johnson company.

373 License under U.S. Patent No. 5,618,913 and Des. 347,894

374

375 Date of Issue: [date]

376

377 Printed in USA

378

379 8-xxxx-xx-xxx-x

380

1
2 **Patient Information for NovoLog® Mix 70/30 FlexPen® Prefilled syringe (100**
3 **Units/mL, U-100)**
4

5 **NovoLog® Mix 70/30**

6 70% insulin aspart protamine suspension and 30% insulin aspart injection
7 ~~30% insulin aspart injection~~ (rDNA origin)
8
9

10 **What is the most important information I should know about NovoLog Mix**
11 **70/30?**
12

13 **WARNINGS**

14 THIS NOVO NORDISK® HUMAN INSULIN ANALOG MIXTURE IS DIFFERENT
15 FROM OTHER INSULIN MIXTURES BECAUSE IT HAS A RAPID ONSET OF
16 ACTION. THE RAPID ONSET OF ACTION MEANS THAT YOU SHOULD TAKE
17 YOUR DOSE OF NOVOLOG MIX 70/30 (70% INSULIN ASPART PROTAMINE
18 SUSPENSION AND 30% INSULIN ASPART INJECTION, [rDNA ORIGIN])
19 WITHIN 15 MINUTES OF A MEAL.

20 ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY
21 UNDER MEDICAL SUPERVISION. CHANGES IN STRENGTH,
22 MANUFACTURER, TYPE (E.G., REGULAR, NPH, ANALOG), SPECIES (BEEF,
23 PORK, BEEF-PORK, HUMAN), OR METHOD OF MANUFACTURE (rDNA
24 VERSUS ANIMAL-SOURCE INSULIN) MAY RESULT IN THE NEED FOR A
25 CHANGE IN THE TIMING OR DOSAGE OF NOVOLOG MIX 70/30.

26 PATIENTS TAKING NOVOLOG MIX 70/30 MAY REQUIRE A CHANGE IN
27 DOSAGE FROM THAT USED WITH OTHER INSULINS. IF AN ADJUSTMENT
28 IS NEEDED, IT MAY OCCUR WITH THE FIRST DOSE OR DURING THE FIRST
29 SEVERAL WEEKS OR MONTHS.
30

31
32 **What is NovoLog Mix 70/30?**
33

34 NovoLog Mix 70/30 (NO-voe-log-MIX-SEV-en-tee-THIR-tee) is a mixed insulin
35 analog similar to human insulin mixes used to treat diabetes. The active ingredient in
36 NovoLog Mix 70/30 is insulin aspart, which is made through biotechnology. Another
37 ingredient, protamine, is used to slow the absorption of the insulin analog by your body.
38

39 NovoLog Mix 70/30 comes in:

- 40 • 10 mL vials (small bottles) for use with a syringe
41 • 3 mL PenFill® cartridges for use with 3 mL PenFill® cartridge compatible delivery
42 devices*
43 • 3 mL NovoLog Mix 70/30 FlexPen® Prefilled syringe

44 *3 mL PenFill® cartridge compatible delivery devices: NovoPen® 3, Innovo®, and
45 InDuo™.

46

47 **Who should NOT take NovoLog Mix 70/30?**

48

49 **Do NOT take NovoLog Mix 70/30 if:**

- 50 • Your blood sugar is too low (hypoglycemia).
- 51 • You are allergic to NovoLog Mix 70/30 or any of its ingredients. Check with your
52 doctor or pharmacist if you want information about the ingredients.
- 53 • You are not planning to eat within 15 minutes of your injection.

54

55 **Tell your doctor if:**

- 56 • **You have liver or kidney problems.** Your dose may need to be changed.
- 57 • **You are pregnant or planning to become pregnant.** It is not known whether
58 NovoLog Mix 70/30 can cause any harm to the baby if it is taken during pregnancy.
- 59 • **You are breast-feeding or planning to breast-feed.** It is not known whether
60 NovoLog Mix 70/30 is passed through in human milk, as is human insulin. Many
61 drugs, including human insulin, are present in human milk, and may affect the baby.
- 62 • **You take any other medicines**, including prescription and non-prescription
63 medicines and herbal supplements. Your NovoLog Mix 70/30 need may change if
64 you take other medicines. Be sure to mention if you take the following:
 - 65 • oral hypoglycemic medicines (medicines you take by mouth to treat non insulin-
66 dependent [Type 2] diabetes)
 - 67 • monoamine oxidase (MAO) inhibitors (used to treat depression)
 - 68 • beta-blocking agents (used to treat certain heart conditions or high blood
69 pressure)
 - 70 • angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart
71 conditions or high blood pressure)
 - 72 • salicylates, including aspirin (used to relieve pain or lower fever)
 - 73 • anabolic steroids and glucocorticoids
 - 74 • oral contraceptives (used for birth control)
 - 75 • diuretics such as thiazides (used to treat high blood pressure or swelling [edema])
 - 76 • thyroid hormones (used to treat thyroid gland problems)
 - 77 • danazol (used to treat endometriosis)
 - 78 • octreotide (used to treat gigantism or other rare endocrine tumors)
 - 79 • sulfa antibiotics (used to treat infections)

80

81 **How should I take NovoLog Mix 70/30?**

82

- 83 • Follow your doctor's instructions about monitoring your blood sugar.
- 84 • Before injecting, make sure that you have the correct type and strength of insulin.
85 Carefully follow the instructions on how to use your insulin syringe or pen.
- 86 • Inject your NovoLog Mix 70/30 fifteen-minutes or less before a meal.

- 87 • Inject NovoLog Mix 70/30 under your skin (subcutaneously). Never inject it into a
88 vein.
- 89 • The effect of an injected insulin dose may occur faster if the insulin is injected into
90 your abdomen (stomach area). However, you may also inject under the skin of your
91 thigh, or upper arm.
- 92 • Change (rotate) injection sites within the same body area.
- 93 • Measure your blood sugar level as directed by your doctor.
- 94 • Carefully follow the instructions given by your doctor about the type of insulin you
95 are using, its dose, and time of its injection. Any change in insulin should be made
96 cautiously and only with your doctor's guidance. Your insulin needs may change
97 due to a number of factors, such as illness, stress, medicines, or changes in diet or
98 exercise routines. Follow your doctor's instructions to make these changes in your
99 dose regimen.
- 100 • Clean your hands and the injection site with soap and water or with alcohol before
101 you start the injection process.
- 102

103 **See the end of this patient information for instructions about preparing and giving**
104 **the injection.**

105

106 **What should I do during illness?**

107 Even if you have a short-term (acute) illness, especially with vomiting or fever, continue taking
108 your insulin. If possible, stay on your regular diet. If you have trouble eating, drink fruit juices,
109 regular soft drinks, or clear soups. If you can, eat small amounts of bland foods. Test your urine
110 for glucose and ketones and, if possible, test your blood glucose. Note the results and contact
111 your health care provider for possible insulin dose adjustment. If you have severe and continued
112 vomiting, get emergency medical care.

113

114 **What should I avoid while taking NovoLog Mix 70/30?**

115

116 Alcohol, including beer and wine, may increase and lengthen the risk of hypoglycemia
117 (too low blood sugar) when you take NovoLog Mix 70/30.

118

119 Be careful when you drive a car or operate machinery. Your ability to concentrate or
120 react may be reduced if you have hypoglycemia. Ask your doctor if you should drive if
121 you have:

- 122 • frequent hypoglycemia
123 • reduced or absent warning signs of hypoglycemia
- 124

125
126 **What are the possible side effects of NovoLog Mix 70/30?**

127

128 **Common side effects include blood sugar that is too low (hypoglycemia).**

129 Hypoglycemia (too little glucose in the blood) is one of the most frequent problems
130 experienced by insulin users. It can be brought about by:

- 131 1. Missing or delaying meals
- 132 2. Taking too much insulin
- 133 3. Exercising or working more than usual
- 134 4. An infection or illness (especially with diarrhea or vomiting)
- 135 5. A change in the body's need for insulin
- 136 6. Diseases of the adrenal, pituitary, or thyroid gland, or kidney or liver disease
137 that is getting worse
- 138 7. Interactions with other drugs that lower blood glucose, such as oral (taken
139 by mouth) antidiabetic medicines, salicylates (for example, aspirin), sulfa
140 antibiotics, and certain antidepressants
- 141 8. Drinking of alcohol

142

143 What are symptoms of **mild to moderate** hypoglycemia:

- 144 • Sweating
- 145 • Dizziness
- 146 • Palpitation (fast heart beat)
- 147 • Tremor (shakiness)
- 148 • Hunger
- 149 • Restlessness
- 150 • Tingling in the hands, feet, lips, or tongue
- 151 • Lightheadedness
- 152 • Trouble concentrating
- 153 • Headache
- 154 • Drowsiness
- 155 • Sleep problems
- 156 • Anxiety
- 157 • Blurred vision
- 158 • Slurred speech
- 159 • Depressed mood
- 160 • Irritability
- 161 • Abnormal behavior
- 162 • Unsteady movement
- 163 • Personality change

164

165 What are symptoms of **severe** hypoglycemia:

- 166 • Disorientation
- 167 • Unconsciousness
- 168 • Seizures (convulsions)

- 169 • Death
170

171

172

If you develop serious hypoglycemic reactions, get medical help right away.

173

174 Without recognition of early warning symptoms, you may not be able to take steps to avoid
175 more serious hypoglycemia. Be alert for all of the various types of symptoms that may
176 indicate hypoglycemia. Patients who experience hypoglycemia without early warning
177 symptoms should monitor their blood glucose frequently, especially prior to activities such as
178 driving. If the blood glucose is below your normal fasting glucose, you should consider
179 eating or drinking sugar-containing foods to treat your hypoglycemia. Mild to moderate
180 hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should
181 always carry a quick source of sugar, such as candy mints or glucose tablets. More severe
182 hypoglycemia may require the assistance of another person. Patients who are unable to take
183 sugar orally or who are unconscious require an injection of glucagon or should be treated
184 with intravenous administration of glucose at a medical facility. You should learn to
185 recognize your own symptoms of hypoglycemia. If you are uncertain about these symptoms,
186 you should monitor your blood glucose frequently to help you learn to recognize the
187 symptoms that you experience with hypoglycemia.

188

189 If you have frequent episodes of hypoglycemia or experience difficulty in recognizing
190 the symptoms, you should consult your doctor to discuss possible changes in therapy,
191 meal plans, and/or exercise programs to help you avoid hypoglycemia.

192

193 **Common side effects include blood sugar that is too high (hyperglycemia) and**
194 **diabetic ketoacidosis.**

195 Hyperglycemia (too much glucose in the blood) may develop if your body has too little
196 insulin. Hyperglycemia can be brought about by any of the following:

- 197 1. Not taking your insulin or taking less than the doctor has prescribed
198 2. Eating much more than your meal plan suggests
199 3. Developing a fever, infection, or being under stress

200

201 In patients with type 1 or insulin-dependent diabetes, long-lasting hyperglycemia can
202 cause diabetic ketoacidosis (DKA). The first symptoms of DKA usually come on
203 slowly, over a period of hours or days, and include feeling drowsy, flushed face, thirst,
204 loss of appetite, and fruity odor on the breath. With DKA, urine tests show large
205 amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe
206 symptoms. If uncorrected, long-lasting hyperglycemia or DKA can lead to nausea,
207 vomiting, stomach pains, dehydration, loss of consciousness, or even death. Therefore,
208 it is important that you obtain medical help right away.

209

210 **Other possible side effects include the following:**

211

212 • **Serious allergic reaction.**

213 Get medical help right away if you develop a rash over your whole body, have
214 trouble breathing, a fast heartbeat, or sweating. These are signs of a dangerous
215 allergic reaction (systemic allergic reaction). These reactions are not common.

216

217 • **Reaction at the injection site** (local allergic reaction). You may get redness,
218 swelling and itching at the injection site. If you have serious or continuing
219 reactions, you may need to stop using NovoLog Mix 70/30 and use another
220 insulin. Do not inject insulin into skin sites with these reactions. No type of
221 insulin should be injected into skin sites with these reactions.

222

223 • **Skin thickens or pits at the injection site**, especially if the injection site is not
224 rotated (changed).

225

226 • **Vision changes** that may require evaluation by an ophthalmologist (medical
227 doctor specializing in eye disease) or changes in your eyeglasses or contact lens
228 prescription.

229

230 • **Fluid retention or swelling of your hands and feet.**

231

232 • **Low potassium in your blood** (hypokalemia)

233

234 There are other possible side effects from NovoLog Mix 70/30. Ask your doctor or
235 pharmacist for further information. Tell your doctor or pharmacist if you have any
236 other unwanted effects that you believe are caused by this insulin.

237

238 **How should I store NovoLog Mix 70/30?**

239 • **Unused insulin:**

240 Store insulin in a refrigerator (2°C to 8°C [36°F to 46°F]), but not in a freezer.
241 Do not use NovoLog Mix 70/30 if it has been frozen. Keep unused disposable
242 NovoLog Mix 70/30 FlexPen® Prefilled syringes in the carton so they will stay
243 clean and protected from light.

244 • **After starting to use the insulin:**

245 Do not refrigerate disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe
246 in use (the rubber stopper has been punctured). However, keep them as cool as
247 possible (below 30°C [86°F]). Keep all disposable NovoLog Mix 70/30
248 FlexPen® Prefilled syringes away from direct heat and sunlight.

249 • **Throw away unrefrigerated disposable NovoLog Mix 70/30 FlexPen® Prefilled**
250 **syringes after 14 days, even if they still contain insulin.**

251

252 **General information about NovoLog Mix 70/30**

253 Use NovoLog Mix 70/30 only to treat your diabetes. **Do not** share it with anyone else.

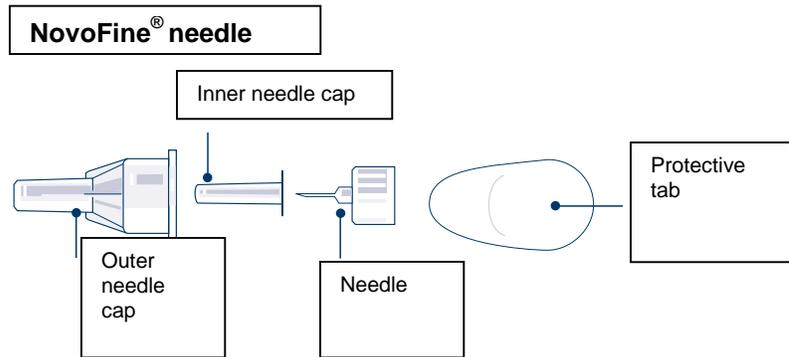
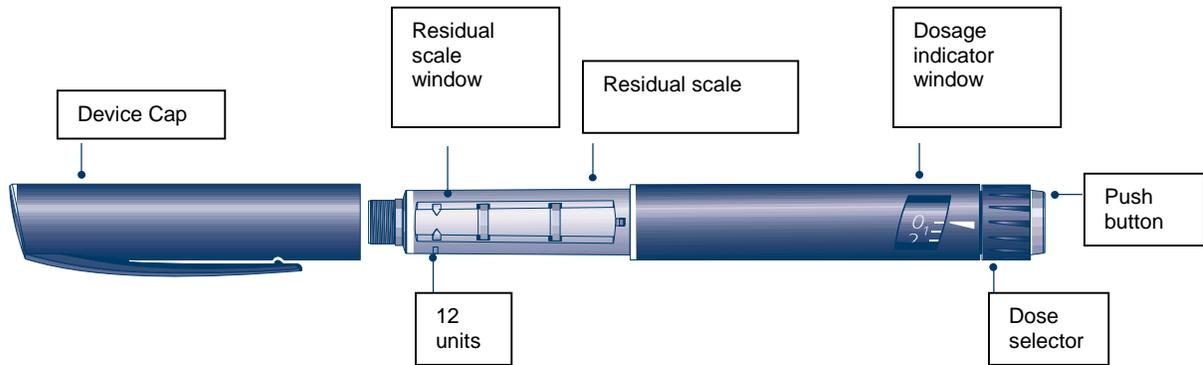
254 Ask your doctor or pharmacist about any concerns you have. They can answer your
255 questions and give you written information about NovoLog Mix 70/30 written for
256 health care professionals.

257

258 **Using the disposable NovoLog Mix 70/30 3mL FlexPen® Prefilled syringe**

259
260 NovoLog Mix 70/30 FlexPen Prefilled syringe is a disposable dial-a-dose insulin
261 delivery system able to deliver 1 to a maximum of 60 units. The dose can be adjusted
262 in increments of 1 unit. NovoLog Mix 70/30 FlexPen Prefilled syringe is designed for
263 use with NovoFine® single use needles. NovoLog Mix 70/30 FlexPen® Prefilled
264 syringe is not recommended for the blind or severely visually impaired without the
265 assistance of a sighted individual trained in the proper use of the product.

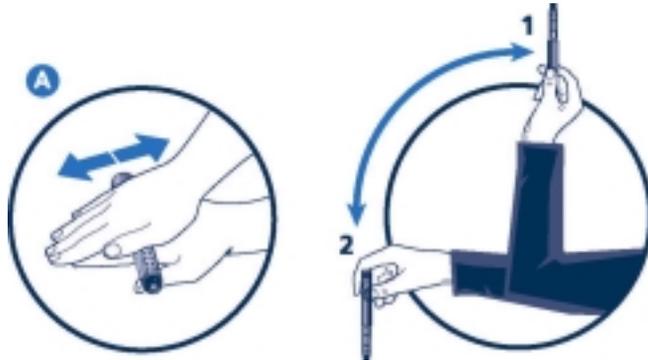
266
267 **Please read these instructions completely before using this device.**



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1. PREPARING THE FLEXPEN PREFILLED SYRINGE:

- a. Pull off the device cap.
- b. Wipe the rubber stopper with an alcohol swab.



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- c. Before using the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe for the first time, roll the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe between your palms 10 times (see diagram A). Thereafter, turn the pen up and down between position **1** and **2** so that the glass ball moves from one end of the insulin reservoir to the other (see diagram A). Do this at least 10 times. This procedure must be repeated until the insulin appears uniformly white and cloudy.

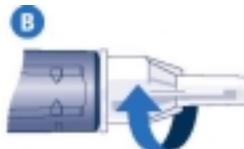
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To ensure even mixing of the remaining insulin, there must be at least 12 units of insulin left in the reservoir. If there are less than 12 units left, do not use the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe.

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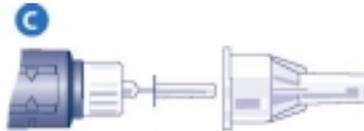
The numbers on the insulin reservoir can be used to estimate the amount of insulin left in the syringe. Do not use these numbers to measure the insulin dose. You cannot set a dose greater than the number of units remaining in the reservoir.

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- d. Place the needle onto the disposable prefilled syringe immediately before use. Remove the protective tab from the disposable needle and screw the needle tightly onto the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe (see diagram B)



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- e. Pull off the outer and inner needle caps (see diagram C). Do not discard the outer needle cap.

If there is a delay between mixing of the insulin and the injection, the insulin will need to be mixed again. The NovoLog Mix 70/30 FlexPen® Prefilled syringe should be turned upside down between positions **1** and **2** (see diagram A), so that the glass ball moves from one end of the insulin reservoir to the other. Do this until the insulin appears uniformly white and cloudy.

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f. **Giving the airshot before each injection:**

Small amounts of air may collect in the needle and insulin reservoir during normal use. **To avoid injecting air and to ensure proper dosing**, hold the syringe with the needle pointing up and tap the syringe gently with your finger so any air bubbles collect in the top of the reservoir. Remove both the plastic outer cap and the needle cap.



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g. Dial 2 units (see diagram D).



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h. Holding the syringe with the needle pointing up, tap the reservoir gently with your finger a few times (see diagram E). Still with the needle pointing up, press the push button as far as it will go and see if a drop of insulin appears at the needle tip. If not, repeat the procedure until insulin appears. Before the first use of each disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe, you may need to perform up to 6 airshots to get a droplet of insulin at the needle tip. If you need to make more than 6 airshots, do not use the syringe, and contact Novo Nordisk® at 1-800-727-6500. A small air bubble may remain but it will not be injected because the operating mechanism prevents the reservoir from being completely emptied.

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2. SETTING THE DOSE



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Check that the dose selector is set at **0** (see diagram F). Dial the number of units you need to inject. The dose can be corrected either up or down by turning the dose selector in either direction. When dialing back, be careful not to push the push button as insulin will come out. You cannot set a dose larger than the number of units left in the reservoir.

3. GIVING THE INJECTION

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Use the injection technique recommended by your doctor or health care professionals.



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- a. Pinch the skin between two fingers; push the needle into the skinfold (see diagram G).



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386 b. Deliver the dose by pressing the push button all the way in (see diagram H). Be
387 careful only to push the push button when injecting.

388 c. After the injection, the needle should remain under the skin for at least 6 seconds.
389 Keep the push button fully depressed until the needle is withdrawn from the skin.
390 This will ensure that the full dose has been delivered. If blood appears after you pull
391 the needle from your skin, press the injection site lightly with a finger. Do not rub the
392 area.

393 d. After the injection, remove the needle **without recapping** and dispose of it in a
394 puncture-resistant container. Used syringes, needles, or lancets should be
395 placed in sharps containers (such as red biohazard containers), hard plastic
396 containers (such as detergent bottles), or metal containers (such as an empty
397 coffee can). Such containers should be sealed and disposed of properly.

398

399 **It is important that you use a new needle for each injection. Health care**
400 **professionals, relatives, and other caregivers, should follow general precautionary**
401 **measures for removal and disposal of needles to eliminate the risk of unintended**
402 **needle stick.**

403

404

405 **4. LATER (SUBSEQUENT) INJECTIONS**

406

407 **It is important that you use a new needle for each injection.** Follow the directions
408 in steps 1 – 3.

409

410 Before each injection: turn the disposable NovoLog Mix 70/30 FlexPen® Prefilled
411 syringe up and down between position **1** and **2** (diagram A) so that the glass ball moves
412 from one end of the insulin reservoir to the other. Do this at least 10 times. This
413 procedure must be repeated until the insulin appears uniformly white and cloudy.
414 Inject immediately. If there is a delay between mixing of the insulin and the injection,
415 the insulin will need to be mixed again as described above.

416

417 To ensure even mixing of the remaining insulin, there must be at least 12 units of
418 insulin left in the reservoir. If there are less than 12 units left, do not use the disposable
419 NovoLog Mix 70/30 FlexPen® Prefilled syringe.

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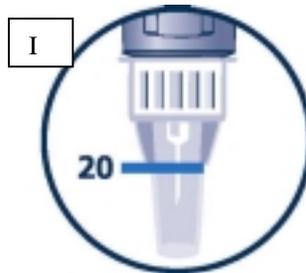
421 The numbers on the insulin reservoir can be used to estimate the amount of insulin left
422 in the syringe. Do not use these numbers to measure the insulin dose.

423 You cannot set a dose greater than the number of units remaining in the reservoir.

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5. FUNCTION CHECK



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If your disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe is not working properly, follow this procedure:

- Screw on a new NovoFine needle
- Give an airshot as described in sections f and g
- Put the outer needle cap onto the needle
- Dispense 20 units into the outer needle cap, holding the FlexPen® with the needle pointing down.

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The insulin should fill the lower part of the cap (as shown in diagram I). If the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe has released too much, or too little insulin, repeat the test. If it happens again, do not use your disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe and contact Novo Nordisk® at 1-800-727-6500.

Dispose of the used NovoLog Mix 70/30 FlexPen® Prefilled syringe carefully without the needle attached.

448

6. IMPORTANT NOTES

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- If you need to perform more than 6 airshots before the first use of the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe to get a droplet of insulin at the needle tip, do not use the FlexPen®.
- Remember to perform an air shot before each injection. See diagrams D and E.
- Take care not to drop the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe.
- Remember to keep the disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe with you. Don't leave it in a car or other location where it can get too hot or too cold.
- NovoLog Mix 70/30 FlexPen® Prefilled syringe is designed for use with NovoFine® disposable needles.
- Never place a disposable needle on this disposable prefilled syringe until you are ready to use it. Remove the needle right after use without recapping.

460

- 461 • **Dispose of used needles properly, so other people will not be harmed.**
- 462 • Throw away the used NovoLog™ Mix® 70/30 FlexPen® Prefilled syringe, without
463 the needle attached.
- 464 • Always carry a spare disposable NovoLog Mix 70/30 FlexPen® Prefilled syringe
465 with you in case it is damaged or lost.
- 466 • To avoid possible transmission of disease, do not let anyone else use your disposable
467 NovoLog Mix 70/30 FlexPen® Prefilled syringe, even if you attach a new needle.
468
- 469 • **Novo Nordisk is not responsible for harm due to using this insulin delivery
470 system with products other than PenFill® 3 mL insulin cartridges and
471 NovoFine® single use needles.**
472
- 473 • Keep this disposable FlexPen® prefilled syringe out of the reach of children.
474

475

476

477 Call 1-800-727-6500 for additional information.

478

479

480 Helpful information for people with diabetes is published by the American Diabetes
481 Association, 1660 Duke Street, Alexandria, VA 22314.

482

483

484 For information about NovoLog Mix 70/30 contact:

485

Novo Nordisk Pharmaceuticals
Inc.,
100 College Road West,
Princeton, New Jersey 08540
www.novonordisk-us.com

486

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490

491 Manufactured by:

492 Novo Nordisk A/S

493 DK-2880 Bagsvaerd, Denmark

494

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496

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501

502 Date of Issue:

503

504 8-XXXX-XX-XXX-X

NDA 21-172
NovoLog Mix 70/30 70%
insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 1

*Novo Nordisk
Pharmaceuticals, Inc.*

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation

Trade Carton Label:

Front:

NDC xxx-xxx-xx List xxxxxx
NovoLog Mix 70/30 70% insulin aspart protamine suspension and 30% insulin aspart injection (rDNA origin)
10 mL 100 units/mL Rx only U-100
Novo Nordisk®

Side:

Store at 2°-8° C (36°-46° F). Avoid freezing. Protect from light. Warning: Any change of insulin should be made cautiously and only under medical supervision (see package insert). For parenteral use.
Each mL contains 100 Units of insulin aspart; mannitol 36.4 mg, phenol 1.50 mg, metacresol 1.72 mg, zinc 19.6 µg, disodium hydrogen phosphate dihydrate 1.25 mg, sodium chloride 0.58 mg, and protamine sulfate 0.33 mg.
NovoLog® is a trademark owned by Novo Nordisk® A/S

Back

BAR CODE XXXXX
For information contact:: Novo Nordisk Pharmaceuticals, Inc. Princeton, NJ 08540 www.novonordisk-us.com 1-800-727-6500
Manufactured by Novo Nordisk A/S 2880 Bagsvaerd, Denmark

NDA 21-172
NovoLog Mix 70/30 70%
insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 2

*Novo Nordisk
Pharmaceuticals, Inc.*

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation (cont'd)

Trade Carton Label

Top

U-100

NovoLog® Mix 70/30
70% insulin aspart protamine
suspension and 30% insulin aspart
injection (rDNA origin)

100 Units/mL
Rx only
U-100

Bottom

Exp. Date/Control

NDA 21-172
NovoLog Mix 70/30 70%
insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 3

*Novo Nordisk
Pharmaceuticals, Inc.*

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation

Sample Carton Label:

Front:

NDC XXXX-XXXX-XX List XXXXXX
NovoLog Mix 70/30 70% insulin aspart protamine suspension and 30% insulin aspart injection, (rDNA origin)
10 mL 100 units/mL
Rx only U-100
Sample. Not for resale Novo Nordisk®

Side:

Store at 2°-8° C (36°-46° F) Avoid freezing. Protect from light. Warning: Any change of insulin should be made cautiously and only under medical supervision (see package insert). For parenteral use.
Each mL contains 100 Units of insulin aspart; mannitol 36.4 mg, phenol 1.50 mg, metacresol 1.72 mg, zinc 19.6 µg, disodium hydrogen phosphate dihydrate 1.25 mg, sodium chloride 0.58 mg, and protamine sulfate 0.33 mg.
NovoLog® is a trademark owned by Novo Nordisk® A/S

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BAR CODE XXXXX
For information contact:: Novo Nordisk Pharmaceuticals, Inc. Princeton, NJ 08540 www.novonordisk-us.com 1-800-727-6500
Manufactured by Novo Nordisk A/S 2880 Bagsvaerd, Denmark

NDA 21-172
NovoLog Mix 70/30 70%
insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 4

*Novo Nordisk
Pharmaceuticals, Inc.*

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation (cont'd)

Sample Carton Label

Side:

Sample. Not for resale

Top

U-100

NovoLog® Mix 70/30
70% insulin aspart protamine
suspension and 30% insulin aspart
injection (rDNA origin)

100 Units/mL
Rx only
U-100
Sample. Not for resale

Bottom

Exp. Date/Control

NDA 21-172
NovoLog Mix 70/30 70%insulin
aspart protamine suspension and
30% insulin aspart injection
(rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 1

*Novo Nordisk
Pharmaceuticals, Inc.*

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation

Trade Vial Label

Front:

NovoLog® Mix 70/30
70% insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL 100 units/mL (U-100)

- Important: see insert
- Store at 2°-8° C (36°-46° F)
- Avoid freezing

Rx only

Side:

NDC XXXX-XXXX-XX
List XXXXXX

Novo Nordisk Pharmaceuticals, Inc.
Princeton, NJ 08540
1-800-727-6500

Manufactured by
Novo Nordisk A/S
2880 Bagsvaerd, Denmark

Exp. Date/Control:

NovoLog Mix 70/30 Draft Labeling: 10 ml Vial Presentation (cont'd)

Sample Vial Label

Front:

NovoLog® Mix 70/30
70% insulin aspart protamine
suspension and 30% insulin
aspart injection (rDNA origin)

10 mL 100 units/mL (U-100)

- Important: see insert
- Store at 2°-8° C (36°-46° F)
- Avoid freezing

Rx only
Sample. Not for resale

NDA 21-172
NovoLog Mix 70/30 70%insulin
aspart protamine suspension and
30% insulin aspart injection
(rDNA origin)

10 mL vial labeling

Date: November 8, 2002

Final Version
Page 2

*Novo Nordisk
Pharmaceuticals, Inc.*

Side:

NDC XXXX-XXXX-XX
List XXXXXX

Novo Nordisk Pharmaceuticals, Inc.
Princeton, NJ 08540
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Novo Nordisk A/S
2880 Bagsvaerd, Denmark

Exp. Date/Control: