

A1.0 NL 5731 AMP
A1.0 NL 6822 AMP
A1.0 NL 5761 AMP

INFORMATION FOR THE PATIENT
10 mL Vial (1000 Units per vial)

HUMALOG[®]
INSULIN LISPRO INJECTION, USP
(rDNA ORIGIN)
100 UNITS PER ML (U-100)

WARNINGS

THIS LILLY HUMAN INSULIN ANALOG IS DIFFERENT FROM OTHER INSULINS BECAUSE IT HAS A RAPID ONSET AND SHORTER DURATION OF ACTION. THE RAPID ONSET OF ACTION MEANS THAT YOU SHOULD TAKE YOUR DOSE OF HUMALOG[®] [INSULIN LISPRO INJECTION, USP (rDNA ORIGIN)] WITHIN 15 MINUTES BEFORE OR IMMEDIATELY AFTER EATING. THE SHORT DURATION OF ACTION OF HUMALOG MEANS THAT IF YOU HAVE TYPE 1 DIABETES, YOU ALSO NEED TO USE A LONGER-ACTING INSULIN TO GIVE THE BEST GLUCOSE CONTROL (EXCEPT WHEN USING AN EXTERNAL INSULIN PUMP). IF YOU HAVE TYPE 2 DIABETES, HUMALOG MAY BE USED WITHOUT A LONGER-ACTING INSULIN WHEN USED IN COMBINATION THERAPY WITH SULFONYLUREA AGENTS.

ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY UNDER MEDICAL SUPERVISION. CHANGES IN STRENGTH, MANUFACTURER, TYPE (E.G., REGULAR, NPH, ANALOG), SPECIES, OR METHOD OF MANUFACTURE MAY RESULT IN THE NEED FOR A CHANGE IN THE TIMING OR DOSAGE OF HUMALOG OR THE LONGER-ACTING INSULIN, OR BOTH.

PATIENTS TAKING HUMALOG MAY REQUIRE A CHANGE IN DOSAGE FROM THAT USED WITH OTHER INSULINS. IF AN ADJUSTMENT IS NEEDED, IT MAY OCCUR WITH THE FIRST DOSE OR DURING THE FIRST SEVERAL WEEKS OR MONTHS.

EXTERNAL INSULIN PUMP: WHEN USED IN AN EXTERNAL INSULIN PUMP, HUMALOG SHOULD NOT BE DILUTED OR MIXED WITH ANY OTHER INSULIN. CAREFULLY READ AND FOLLOW THE EXTERNAL INSULIN PUMP MANUFACTURER'S INSTRUCTIONS AND THIS INSERT BEFORE USING HUMALOG (*see* INSTRUCTIONS FOR INSULIN VIAL USE section).

DIABETES

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin products to keep your blood glucose at a near-normal level. You have been instructed to test your blood and/or your urine regularly for glucose. Studies have shown that some chronic complications of diabetes such as eye disease, kidney disease, and nerve disease can be significantly reduced if the blood sugar

44 is maintained as close to normal as possible. The American Diabetes Association recommends
45 that if your pre-meal glucose levels are consistently above 130 mg/dL or your hemoglobin A_{1c}
46 (HbA_{1c}) is more than 7%, you should talk to your doctor. A change in your diabetes therapy may
47 be needed. If your blood tests consistently show below-normal glucose levels, you should also let
48 your doctor know. Proper control of your diabetes requires close and constant cooperation with
49 your doctor. Despite diabetes, you can lead an active and healthy life if you eat a balanced diet,
50 exercise regularly, and take your insulin injections as prescribed by your doctor.

51 Always keep an extra supply of insulin as well as a spare syringe and needle on hand. Always
52 wear diabetic identification so that appropriate treatment can be given if complications occur
53 away from home.

54

HUMALOG

Description

56 Humalog [insulin lispro injection, USP (rDNA origin)] is made by a special
57 non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically
58 altered to produce this human insulin analog. Humalog consists of zinc-insulin lispro crystals
59 dissolved in a clear fluid. The time course of Humalog action, like that of other insulins, may
60 vary in different individuals or at different times in the same individual, based on dose, site of
61 injection, blood supply, temperature, and physical activity. Humalog is a sterile solution and is
62 for subcutaneous injection. It should not be used intramuscularly. The concentration of Humalog
63 is 100 units/mL (U-100).

64 Humalog starts lowering blood glucose more quickly and has a shorter duration of action
65 compared with Regular human insulin. This means that your dose of Humalog should be given
66 within 15 minutes before or immediately after a meal (Regular human insulin works best when
67 given 30 to 60 minutes before a meal). The short duration of action of Humalog means that if
68 you have type 1 diabetes, you also need to use a longer-acting insulin to give the best glucose
69 control (except when using an external insulin pump). If you have type 2 diabetes, Humalog may
70 be used without a longer-acting insulin when used in combination therapy with sulfonylurea
71 agents.

Identification

73 Insulin lispro injection, USP (rDNA origin) from Eli Lilly and Company, has the trademark
74 Humalog. Your doctor has prescribed the type of insulin that he/she believes is best for you.

75 **DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND**
76 **DIRECTION.**

77 Always check the carton and bottle label of the Humalog you receive from your pharmacy to
78 make sure it is the same as prescribed by your doctor.

79 Always check the appearance of your bottle of Humalog before withdrawing each dose.
80 Humalog is a clear and colorless liquid with a water-like appearance and consistency.

81 Do not use Humalog:

- 82 • if it appears cloudy, thickened, or slightly colored, or
- 83 • if solid particles are visible.

84 If you see anything unusual in the appearance of Humalog solution in your bottle or notice
85 your insulin requirements changing, talk to your doctor.

Storage

87 Humalog may be diluted with the appropriate sterile diluent only under the direction of your
88 doctor. **However, do not dilute Humalog when used in an external insulin pump.**

89 After withdrawal of the initial dose, diluted Humalog should be discarded 28 days after first
90 use when refrigerated and 14 days after first use when stored at room temperature.

91 **Not in-use (unopened):** Humalog bottles not in-use should be stored in a refrigerator, but not
92 in the freezer.

93 **In-use (opened):** The Humalog bottle you are currently using can be kept unrefrigerated, for
94 **up to 28 days**, as long as it is kept at room temperature [below 86°F (30°C)] away from direct
95 heat and light. The Humalog bottle you are currently using must be discarded **28 days** after the
96 first use, even if it still contains Humalog.

97 Humalog in the external insulin pump reservoir and the complete infusion set should be
98 replaced and a new infusion site selected every 48 hours or less. Humalog in an external
99 insulin pump should not be exposed to temperatures above 98.6°F (37°C), such as in a sauna or
100 hot tub, hot showers, direct sunlight, or radiant heater.

101 **Do not use Humalog after the expiration date stamped on the label or if it has been**
102 **frozen.**

103 INSTRUCTIONS FOR INSULIN VIAL USE

104 *Use with Syringes*

105 **NEVER SHARE NEEDLES AND SYRINGES.**

106 **Correct Syringe Type**

107 Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc).
108 With Humalog, it is important to use a syringe that is marked for U-100 insulin preparations.
109 Failure to use the proper syringe can lead to a mistake in dosage, causing serious problems for
110 you, such as a blood glucose level that is too low or too high.

111 **Syringe Use**

112 To help avoid contamination and possible infection, follow these instructions exactly.

113 Disposable syringes and needles should be used only once and then discarded by placing the
114 used needle in a puncture-resistant disposable container. Properly dispose of the puncture-
115 resistant container as directed by your Health Care Professional.

116 **Preparing the Dose**

- 117 1. Wash your hands.
- 118 2. Inspect the insulin. Humalog solution should look clear and colorless. Do not use
119 Humalog if it appears cloudy, thickened, or slightly colored, or if you see particles in the
120 solution. Do not use Humalog if you notice anything unusual in its appearance.
- 121 3. If using a new Humalog bottle, flip off the plastic protective cap, but **do not** remove the
122 stopper. Wipe the top of the bottle with an alcohol swab.
- 123 4. If you are mixing insulins, refer to the “Mixing Humalog with Longer-Acting Human
124 Insulins” section below.
- 125 5. Draw an amount of air into the syringe that is equal to the Humalog dose. Put the needle
126 through rubber top of the Humalog bottle and inject the air into the bottle.
- 127 6. Turn the Humalog bottle and syringe upside down. Hold the bottle and syringe firmly in
128 one hand.
- 129 7. Making sure the tip of the needle is in the Humalog solution, withdraw the correct dose of
130 Humalog into the syringe.
- 131 8. Before removing the needle from the Humalog bottle, check the syringe for air bubbles. If
132 bubbles are present, hold the syringe straight up and tap its side until the bubbles float to
133 the top. Push the bubbles out with the plunger and then withdraw the correct dose.
- 134 9. Remove the needle from the bottle and lay the syringe down so that the needle does not
135 touch anything.

- 136 10. If you do not need to mix your Humalog with a longer-acting insulin, go to the “Injection
137 Instructions” section below and follow the directions.

138 **Mixing Humalog with Longer-Acting Human Insulins**

139 **Humalog should not be mixed with any other insulin when used in an external
140 insulin pump.**

- 141 1. Humalog should be mixed with longer-acting human insulins only on the advice of your
142 doctor.
- 143 2. Draw an amount of air into the syringe that is equal to the amount of longer-acting insulin
144 you are taking. Insert the needle into the longer-acting insulin bottle and inject the air.
145 Withdraw the needle.
- 146 3. Draw an amount of air into the syringe that is equal to the amount of Humalog you are
147 taking. Insert the needle into the Humalog bottle and inject the air, but **do not** withdraw
148 the needle.
- 149 4. Turn the Humalog bottle and syringe upside down.
- 150 5. Making sure the tip of the needle is in the Humalog solution, withdraw the correct dose of
151 Humalog into the syringe.
- 152 6. Before removing the needle from the Humalog bottle, check the syringe for air bubbles. If
153 bubbles are present, hold the syringe straight up and tap its side until the bubbles float to
154 the top. Push the bubbles out with the plunger and then withdraw the correct dose.
- 155 7. Remove the syringe with the needle from the Humalog bottle and insert it into the
156 longer-acting insulin bottle. Turn the longer-acting insulin bottle and syringe upside
157 down. Hold the bottle and syringe firmly in one hand and shake gently. Making sure the
158 tip of the needle is in the longer-acting insulin, withdraw the correct dose of longer-acting
159 insulin.
- 160 8. Remove the needle from the bottle and lay the syringe down so that the needle does not
161 touch anything.
- 162 9. Follow the directions under “Injection Instructions” section below.

163 When you are mixing two types of insulin, always draw Humalog into the syringe first.

164 Always mix the insulin preparations in this same sequence in order to maintain purity of the
165 Humalog bottle. You should inject your insulins immediately after mixing.

166 Syringes from different manufacturers may vary in the amount of space between the bottom
167 line and the needle. Because of this, do not change:

- 168 • the sequence of mixing, or
- 169 • the model and brand of syringe or needle that your doctor has prescribed.

170 **Injection Instructions**

- 171 1. To avoid tissue damage, choose a site for each injection that is at least 1/2 inch from the
172 previous injection site. The usual sites of injection are abdomen, thighs, and arms.
- 173 2. Cleanse the skin with alcohol where the injection is to be made.
- 174 3. With one hand, stabilize the skin by spreading it or pinching up a large area.
- 175 4. Insert the needle as instructed by your doctor.
- 176 5. Push the plunger in as far as it will go.
- 177 6. Pull the needle out and apply gentle pressure over the injection site for several seconds.
178 **Do not rub the area.**
- 179 7. Place the used needle in a puncture-resistant disposable container and properly dispose of
180 the puncture-resistant container as directed by your Health Care Professional.

181 Use in an External Insulin Pump

182 Your doctor should train you on intensive insulin therapy. You should also be trained on the
183 use of your external insulin pump and pump accessories.

184 Humalog may be used with the MiniMed®¹ Models 506, 507, and 508 insulin pumps using
185 MiniMed®¹ Polyfin®¹ infusion sets. Humalog may also be used in the Disetronic®²

186 H-TRONplus® V100 insulin pump (with plastic 3.15 mL insulin reservoir), using the
187 Disetronic®² Rapid®² infusion set.

188 Follow the external insulin pump manufacturer's instructions for use of Humalog in an
189 external insulin pump. Humalog should not be diluted or mixed with any other insulin when used
190 in an external insulin pump.

191 You should replace the infusion set (reservoir syringe, tubing, and catheter) and Humalog in
192 the external insulin pump reservoir every 48 hours or less. You should also choose a new
193 infusion site every 48 hours or less. Contact your doctor if your infusion sites are red, itching, or
194 thickened, and then choose a new infusion site.

195 **DOSAGE**

196 Your doctor has told you which insulin to use, how much, and when and how often to inject it.
197 Because each patient's diabetes is different, this schedule has been individualized for you. Your
198 usual dose of Humalog may be affected by changes in your diet, activity, or work schedule.
199 Carefully follow your doctor's instructions to allow for these changes. Other things that may
200 affect your Humalog dose are:

201 **Illness**

202 Illness, especially with nausea and vomiting, may cause your insulin requirements to change.
203 Even if you are not eating, you will still require insulin. You and your doctor should establish a
204 sick day plan for you to use in case of illness. When you are sick, test your blood glucose
205 frequently. If instructed by your doctor, test your ketones and report the results to your doctor.

206 **Pregnancy**

207 Good control of diabetes is especially important for you and your unborn baby. Pregnancy may
208 make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or
209 are nursing a baby, talk to your doctor. Humalog has not been tested in pregnant or nursing
210 women.

211 **Geriatric Use**

212 Elderly patients using Humalog had HbA_{1c} values and hypoglycemia rates similar to those
213 observed in younger patients. The onset of action of Humalog may be different in elderly
214 patients.

215 **Medication**

216 Insulin requirements may be increased if you are taking other drugs with blood-glucose-raising
217 activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy. Insulin
218 requirements may be reduced in the presence of drugs with blood-glucose-lowering activity,
219 such as oral antidiabetic agents, salicylates (for example, aspirin), sulfa antibiotics, alcohol,
220 certain antidepressants and some kidney and blood pressure medicines. Your Health Care
221 Professional may be aware of other medications that may affect your diabetes control. Therefore,
222 always discuss any medications you are taking with your doctor.

223 **Exercise**

224 Exercise may lower your body's need for insulin during and for some time after the physical
225 activity. Exercise may also speed up the effect of an insulin dose, especially if the exercise
226 involves the area of injection site (for example, the leg should not be used for injection just prior
227 to running). Discuss with your doctor how you should adjust your insulin regimen to
228 accommodate exercise.

229 **Travel**

230 When traveling across more than 2 time zones, you should talk to your doctor concerning
231 adjustments in your insulin schedule.

COMMON PROBLEMS OF DIABETES

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Hypoglycemia (Low Blood Sugar)

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

1. **Missing or delaying meals.**
2. Taking too much insulin.
3. Exercising or working more than usual.
4. An infection or illness associated with diarrhea or vomiting.
5. A change in the body's need for insulin.
6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease.
7. Interactions with other drugs that lower blood glucose, such as oral antidiabetic agents, salicylates (for example, aspirin), sulfa antibiotics, certain antidepressants and some kidney and blood pressure medicines.
8. Consumption of alcoholic beverages.

Symptoms of mild to moderate hypoglycemia may occur suddenly and can include:

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| • sweating | • drowsiness |
| • dizziness | • sleep disturbances |
| • palpitation | • anxiety |
| • tremor | • blurred vision |
| • hunger | • slurred speech |
| • restlessness | • depressed mood |
| • tingling in the hands, feet, lips, or tongue | • irritability |
| • lightheadedness | • abnormal behavior |
| • inability to concentrate | • unsteady movement |
| • headache | • personality changes |

Signs of severe hypoglycemia can include:

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| • disorientation | • seizures |
| • unconsciousness | • death |

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Therefore, it is important that assistance be obtained immediately.

Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetic nerve disease, use of medications such as beta-blockers, changing insulin preparations, or intensified control (3 or more injections per day) of diabetes. A few patients who have experienced hypoglycemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycemia were less pronounced or different from those experienced with their previous insulin.

Without recognition of early warning symptoms, you may not be able to take steps to avoid more serious hypoglycemia. Be alert for all of the various types of symptoms that may indicate hypoglycemia. Patients who experience hypoglycemia without early warning symptoms should monitor their blood glucose frequently, especially prior to activities such as driving. If the blood glucose is below your normal fasting glucose, you should consider eating or drinking sugar-containing foods to treat your hypoglycemia.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as hard candy or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious require an injection of glucagon or should be treated with intravenous administration of glucose at a medical facility.

267 You should learn to recognize your own symptoms of hypoglycemia. If you are uncertain
 268 about these symptoms, you should monitor your blood glucose frequently to help you learn to
 269 recognize the symptoms that you experience with hypoglycemia.

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

273 **Hyperglycemia (High Blood Sugar) and Diabetic Ketoacidosis (DKA)**

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

- 276 1. Omitting your insulin or taking less than your doctor has prescribed.
- 277 2. Eating significantly more than your meal plan suggests.
- 278 3. Developing a fever, infection, or other significant stressful situation.

279 In patients with type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in
 280 DKA (a life-threatening emergency). The first symptoms of DKA usually come on gradually,
 281 over a period of hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite,
 282 and fruity odor on the breath. With DKA, blood and urine tests show large amounts of glucose
 283 and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected,
 284 prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, dehydration, loss
 285 of consciousness, or death. Therefore, it is important that you obtain medical assistance
 286 immediately.

287 **Lipodystrophy**

288 Rarely, administration of insulin subcutaneously can result in lipoatrophy (seen as an apparent
 289 depression of the skin) or lipohypertrophy (seen as a raised area of the skin). If you notice either
 290 of these conditions, talk to your doctor. A change in your injection technique may help alleviate
 291 the problem.

292 **Allergy**

293 *Local Allergy* — Patients occasionally experience redness, swelling, and itching at the site of
 294 injection. This condition, called local allergy, usually clears up in a few days to a few weeks. In
 295 some instances, this condition may be related to factors other than insulin, such as irritants in the
 296 skin cleansing agent or poor injection technique. If you have local reactions, talk to your doctor.

297 *Systemic Allergy* — Less common, but potentially more serious, is generalized allergy to
 298 insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in
 299 blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life
 300 threatening. If you think you are having a generalized allergic reaction, call your doctor
 301 immediately.

302 **ADDITIONAL INFORMATION**

303 Information about diabetes may be obtained from your diabetes educator.

304 Additional information about diabetes and Humalog can be obtained by calling The Lilly
 305 Answers Center at 1-800-LillyRx (1-800-545-5979) or by visiting www.LillyDiabetes.com.

306
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308 ² Disetronic®, H-TRONplus®, and Rapid® are registered trademarks of Roche Diagnostics GMBH.

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