

A1.0 NL 5771 AMP
A1.0 NL 4851 AMP**INFORMATION FOR THE PATIENT**
10 mL Vial (1000 Units per vial)**HUMALOG[®] Mix75/25[™]**
75% INSULIN LISPRO PROTAMINE SUSPENSION AND
25% INSULIN LISPRO INJECTION
(rDNA ORIGIN)
100 UNITS PER ML (U-100)**WARNINGS**

THIS LILLY HUMAN INSULIN ANALOG MIXTURE IS DIFFERENT FROM OTHER INSULIN MIXTURES IN THAT ITS ONSET OF ACTION IS VERY QUICK. THE QUICK ONSET OF ACTION MEANS THAT YOU SHOULD TAKE YOUR DOSE OF HUMALOG[®] Mix75/25[™] [75% INSULIN LISPRO PROTAMINE SUSPENSION AND 25% INSULIN LISPRO INJECTION, (rDNA ORIGIN)] WITHIN 15 MINUTES BEFORE YOU EAT.

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 Mix75/25.

PATIENTS TAKING HUMALOG Mix75/25 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.

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 is maintained as close to normal as possible. The American Diabetes Association recommends that if your pre-meal glucose levels are consistently above 130 mg/dL, bedtime glucose levels are consistently above 160 mg/dL or your hemoglobin A_{1c} (HbA_{1c}) is more than 7%, you should talk to your doctor. A change in your diabetes therapy may be needed. If your blood tests consistently show below-normal glucose levels, you should also let your doctor know. Proper control of your diabetes requires close and constant cooperation with your doctor. Despite diabetes, you can lead an active and healthy life if you eat a balanced diet, exercise regularly, and take your insulin injections as prescribed by your doctor.

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

45 HUMALOG Mix75/25

46 Description

47 Humalog [insulin lispro injection, USP (rDNA origin)] is made by a special
48 non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically
49 altered to produce this human insulin analog. Humalog Mix75/25 is a mixture of 75% insulin
50 lispro protamine suspension and 25% insulin lispro injection, (rDNA origin). It is a longer-acting
51 insulin combined with the more rapid onset of action of Humalog. The duration of activity is
52 similar to that of Humulin[®] 70/30 and may last up to 24 hours following injection. The time
53 course of Humalog Mix75/25 action, like that of other insulins, may vary in different individuals
54 or at different times in the same individual, based on dose, site of injection, blood supply,
55 temperature, and physical activity. Humalog Mix75/25 is a sterile suspension and is for
56 subcutaneous injection only. It should not be used intravenously. The concentration of
57 Humalog Mix75/25 is 100 units/mL (U-100).

58 Humalog Mix75/25 starts lowering blood glucose more quickly than Regular human insulin,
59 allowing for convenient dosing immediately before a meal (within 15 minutes). In contrast,
60 mixtures containing Regular human insulin should be given 30 to 60 minutes before a meal.

61 Identification

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

64 **DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND**
65 **DIRECTION. YOU SHOULD NOT MIX HUMALOG Mix75/25 WITH ANOTHER**
66 **INSULIN.**

67 Always check the carton and bottle label of the Humalog Mix75/25 you receive from your
68 pharmacy to make sure it is the same as prescribed by your doctor.

69 Always check the appearance of your bottle of Humalog Mix75/25 before withdrawing each
70 dose. Before each injection the Humalog Mix75/25 bottle must be carefully shaken or rotated
71 several times to completely mix the insulin. Humalog Mix75/25 suspension should look
72 uniformly cloudy or milky after mixing. If not, repeat the above step until contents are mixed.

73 Do not use Humalog Mix75/25:

- 74 • if the insulin substance (the white material) remains at the bottom of the bottle after
75 mixing or
- 76 • if there are clumps in the insulin after mixing, or
- 77 • if solid white particles stick to the bottom or wall of the bottle, giving a frosted
78 appearance.

79 If you see anything unusual in the appearance of Humalog Mix75/25 suspension in your bottle
80 or notice your insulin requirements changing, talk to your doctor.

81 Storage

82 **Not in-use (unopened):** Humalog Mix75/25 bottles not in-use should be stored in a
83 refrigerator, but not in the freezer.

84 **In-use (opened):** The Humalog Mix75/25 bottle you are currently using can be kept
85 unrefrigerated, for **up to 28 days**, as long as it is kept at room temperature [below 86°F (30°C)]
86 away from direct heat and light. The Humalog Mix75/25 bottle you are currently using must be
87 discarded **28 days** after the first use, even if it still contains Humalog Mix75/25.

88 **Do not use Humalog Mix75/25 after the expiration date stamped on the label or if it has**
 89 **been frozen.**

90 INSTRUCTIONS FOR INSULIN VIAL USE

91 *Use with Syringes*

92 **NEVER SHARE NEEDLES AND SYRINGES.**

93 **Correct Syringe Type**

94 Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc).
 95 With Humalog Mix75/25, it is important to use a syringe that is marked for U-100 insulin
 96 preparations. Failure to use the proper syringe can lead to a mistake in dosage, causing serious
 97 problems for you, such as a blood glucose level that is too low or too high.

98 **Syringe Use**

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

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

103 **Preparing the Dose**

- 104 1. Wash your hands.
- 105 2. Carefully shake or rotate the bottle of insulin several times to completely mix the insulin.
- 106 3. Inspect the insulin. Humalog Mix75/25 suspension should look uniformly cloudy or
 107 milky. Do not use Humalog Mix75/25 if you notice anything unusual in its appearance.
- 108 4. If using a new Humalog Mix75/25 bottle, flip off the plastic protective cap, but **do not**
 109 remove the stopper. Wipe the top of the bottle with an alcohol swab.
- 110 5. Draw an amount of air into the syringe that is equal to the Humalog Mix75/25 dose. Put
 111 the needle through rubber top of the Humalog Mix75/25 bottle and inject the air into the
 112 bottle.
- 113 6. Turn the Humalog Mix75/25 bottle and syringe upside down. Hold the bottle and syringe
 114 firmly in one hand and shake gently.
- 115 7. Making sure the tip of the needle is in the Humalog Mix75/25 suspension, withdraw the
 116 correct dose of Humalog Mix75/25 into the syringe.
- 117 8. Before removing the needle from the Humalog Mix75/25 bottle, check the syringe for air
 118 bubbles. If bubbles are present, hold the syringe straight up and tap its side until the
 119 bubbles float to the top. Push the bubbles out with the plunger and then withdraw the
 120 correct dose.
- 121 9. Remove the needle from the bottle and lay the syringe down so that the needle does not
 122 touch anything.

123 **Injection Instructions**

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

134 **DOSAGE**

135 Your doctor has told you which insulin to use, how much, and when and how often to inject it.
 136 Because each patient's diabetes is different, this schedule has been individualized for you. Your

137 usual dose of Humalog Mix75/25 may be affected by changes in your diet, activity, or work
138 schedule. Carefully follow your doctor's instructions to allow for these changes. Other things
139 that may affect your Humalog Mix75/25 dose are:

140 **Illness**

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

145 **Pregnancy**

146 Good control of diabetes is especially important for you and your unborn baby. Pregnancy may
147 make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or
148 are nursing a baby, talk to your doctor. Humalog Mix75/25 has not been tested in pregnant or
149 nursing women.

150 **Medication**

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

158 **Exercise**

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

164 **Travel**

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

167 **COMMON PROBLEMS OF DIABETES**

168 **Hypoglycemia (Low Blood Sugar)**

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

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

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

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

Signs of severe hypoglycemia can include:

- disorientation
- unconsciousness
- seizures
- death

183 Therefore, it is important that assistance be obtained immediately.

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

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

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

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

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

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

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

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

214 In patients with type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in
215 DKA (a life-threatening emergency). The first symptoms of DKA usually come on gradually,
216 over a period of hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite,
217 and fruity odor on the breath. With DKA, blood and urine tests show large amounts of glucose

218 and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected,
219 prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, dehydration, loss
220 of consciousness, or death. Therefore, it is important that you obtain medical assistance
221 immediately.

222 **Lipodystrophy**

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

227 **Allergy**

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

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

237 **ADDITIONAL INFORMATION**

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

239 Additional information about diabetes and Humalog Mix75/25 can be obtained by calling The
240 Lilly Answers Center at 1-800-LillyRx (1-800-545-5979) or by visiting www.LillyDiabetes.com.

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244 **Lilly France, F-67640 Fegersheim, France**

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