

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

HUMALOG[®] Mix50/50[™]
50% INSULIN LISPRO PROTAMINE SUSPENSION AND
50% 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[®] Mix50/50[™] [50% INSULIN LISPRO PROTAMINE SUSPENSION AND 50% 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 Mix50/50.

PATIENTS TAKING HUMALOG Mix50/50 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.

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

HUMALOG Mix50/50

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Description

Humalog [insulin lispro injection, USP (rDNA origin)] is made by a special non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically altered to produce this human insulin analog. Humalog Mix50/50 is a mixture of 50% insulin lispro protamine suspension and 50% insulin lispro injection, (rDNA origin). It is a longer-acting insulin combined with the more rapid onset of action of Humalog. The duration of activity is similar to that of Humulin[®] 50/50 and may last up to 16 hours following injection. The time course of Humalog Mix50/50 action, like that of other insulins, may vary in different individuals or at different times in the same individual, based on dose, site of injection, blood supply, temperature, and physical activity. Humalog Mix50/50 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously. The concentration of Humalog Mix50/50 is 100 units/mL (U-100).

Humalog Mix50/50 starts lowering blood glucose more quickly than Regular human insulin, allowing for convenient dosing immediately before a meal (within 15 minutes). In contrast, mixtures containing Regular human insulin should be given 30 to 60 minutes before a meal.

Identification

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

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION. YOU SHOULD NOT MIX HUMALOG Mix50/50 WITH ANOTHER INSULIN.

Always check the carton and bottle label of the Humalog Mix50/50 you receive from your pharmacy to make sure it is the same as prescribed by your doctor.

Always check the appearance of your bottle of Humalog Mix50/50 before withdrawing each dose. Before each injection the Humalog Mix50/50 bottle must be carefully shaken or rotated several times to completely mix the insulin. Humalog Mix50/50 suspension should look uniformly cloudy or milky after mixing. If not, repeat the above step until contents are mixed.

Do not use Humalog Mix50/50:

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

If you see anything unusual in the appearance of Humalog Mix50/50 suspension in your bottle or notice your insulin requirements changing, talk to your doctor.

Storage

Not in-use (unopened): Humalog Mix50/50 bottles not in-use should be stored in a refrigerator, but not in the freezer.

In-use (opened): The Humalog Mix50/50 bottle you are currently using can be kept unrefrigerated, for **up to 28 days**, as long as it is kept at room temperature [below 86°F (30°C)] away from direct heat and light. The Humalog Mix50/50 bottle you are currently using must be discarded **28 days** after the first use, even if it still contains Humalog Mix50/50.

Do not use Humalog Mix50/50 after the expiration date stamped on the label or if it has been frozen.

INSTRUCTIONS FOR INSULIN VIAL USE

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90 *Use with Syringes*91 **NEVER SHARE NEEDLES AND SYRINGES.**92 **Correct Syringe Type**93 Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc).94 With Humalog Mix50/50, it is important to use a syringe that is marked for U-100 insulin
95 preparations. Failure to use the proper syringe can lead to a mistake in dosage, causing serious
96 problems for you, such as a blood glucose level that is too low or too high.97 **Syringe Use**

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

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

- 103 1. Wash your hands.
- 104 2. Carefully shake or rotate the bottle of insulin several times to completely mix the insulin.
- 105 3. Inspect the insulin. Humalog Mix50/50 suspension should look uniformly cloudy or
106 milky. Do not use Humalog Mix50/50 if you notice anything unusual in its appearance.
- 107 4. If using a new Humalog Mix50/50 bottle, flip off the plastic protective cap, but **do not**
108 remove the stopper. Wipe the top of the bottle with an alcohol swab.
- 109 5. Draw an amount of air into the syringe that is equal to the Humalog Mix50/50 dose. Put
110 the needle through rubber top of the Humalog Mix50/50 bottle and inject the air into the
111 bottle.
- 112 6. Turn the Humalog Mix50/50 bottle and syringe upside down. Hold the bottle and syringe
113 firmly in one hand and shake gently.
- 114 7. Making sure the tip of the needle is in the Humalog Mix50/50 suspension, withdraw the
115 correct dose of Humalog Mix50/50 into the syringe.
- 116 8. Before removing the needle from the Humalog Mix50/50 bottle, check the syringe for air
117 bubbles. If bubbles are present, hold the syringe straight up and tap its side until the
118 bubbles float to the top. Push the bubbles out with the plunger and then withdraw the
119 correct dose.
- 120 9. Remove the needle from the bottle and lay the syringe down so that the needle does not
121 touch anything.

122 **Injection Instructions**

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

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DOSAGE

134 Your doctor has told you which insulin to use, how much, and when and how often to inject it.

135 Because each patient's diabetes is different, this schedule has been individualized for you. Your

136 usual dose of Humalog Mix50/50 may be affected by changes in your diet, activity, or work

137 schedule. Carefully follow your doctor's instructions to allow for these changes. Other things
138 that may affect your Humalog Mix50/50 dose are:

139 **Illness**

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

144 **Pregnancy**

145 Good control of diabetes is especially important for you and your unborn baby. Pregnancy may
146 make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or
147 are nursing a baby, talk to your doctor. Humalog Mix50/50 has not been tested in pregnant or
148 nursing women.

149 **Medication**

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

157 **Exercise**

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

163 **Travel**

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

166 **COMMON PROBLEMS OF DIABETES**

167 **Hypoglycemia (Low Blood Sugar)**

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

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

181 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

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

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

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

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

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

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

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

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

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

213 In patients with type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in
214 DKA (a life-threatening emergency). The first symptoms of DKA usually come on gradually,
215 over a period of hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite,

216 and fruity odor on the breath. With DKA, blood and urine tests show large amounts of glucose
217 and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected,
218 prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, dehydration, loss
219 of consciousness, or death. Therefore, it is important that you obtain medical assistance
220 immediately.

221 **Lipodystrophy**

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

226 **Allergy**

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

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

236 **ADDITIONAL INFORMATION**

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

238 Additional information about diabetes and Humalog Mix50/50 can be obtained by calling The
239 Lilly Answers Center at 1-800-LillyRx (1-800-545-5979) or by visiting www.LillyDiabetes.com.

240 Patient Information issued/revised Month dd, yyyy

241 **Vials manufactured by**
242 **Eli Lilly and Company, Indianapolis, IN 46285, USA**

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A1.0 NL 5801 AMP

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