

INFORMATION FOR THE PATIENT

HUMULIN[®] R
REGULAR
INSULIN HUMAN INJECTION, USP
(rDNA ORIGIN)
100 Units per mL (U-100)

WARNINGS

THIS LILLY HUMAN INSULIN PRODUCT DIFFERS FROM ANIMAL-SOURCE INSULINS BECAUSE IT IS STRUCTURALLY IDENTICAL TO THE INSULIN PRODUCED BY YOUR BODY'S PANCREAS AND BECAUSE OF ITS UNIQUE MANUFACTURING PROCESS.

ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY UNDER MEDICAL SUPERVISION. CHANGES IN STRENGTH, MANUFACTURER, TYPE (E.G., REGULAR, NPH, LENTE[®]), SPECIES (BEEF, PORK, BEEF-PORK, HUMAN), OR METHOD OF MANUFACTURE (rDNA VERSUS ANIMAL-SOURCE INSULIN) MAY RESULT IN THE NEED FOR A CHANGE IN DOSAGE.

SOME PATIENTS TAKING HUMULIN[®] (HUMAN INSULIN, rDNA ORIGIN) MAY REQUIRE A CHANGE IN DOSAGE FROM THAT USED WITH ANIMAL-SOURCE 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 140 mg/dL or your hemoglobin A_{1c} (HbA_{1c}) is more than 8%, consult 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.

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.

REGULAR HUMAN INSULIN**Description**

Humulin is synthesized in a special non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically altered by the addition of the gene for human insulin production. Humulin R consists of zinc-insulin crystals dissolved in a clear fluid. Humulin R has

48 had nothing added to change the speed or length of its action. It takes effect rapidly and has a
 49 relatively short duration of activity (4 to 12 hours) as compared with other insulins. The time
 50 course of action of any insulin may vary considerably in different individuals or at different
 51 times in the same individual. As with all insulin preparations, the duration of action of
 52 Humulin R is dependent on dose, site of injection, blood supply, temperature, and physical
 53 activity. Humulin R is a sterile solution and is for subcutaneous injection. It should not be used
 54 intramuscularly. The concentration of Humulin R is 100 units/mL (U-100).

55 **Identification**

56 Human insulin by Eli Lilly and Company has the trademark Humulin and is available in
 57 6 formulations — Regular (**R**), NPH (**N**), Lente (**L**), Ultralente[®] (**U**), 50% Human Insulin
 58 Isophane Suspension [NPH]/50% Human Insulin Injection [regular] (**50/50**), and 70% Human
 59 Insulin Isophane Suspension [NPH]/30% Human Insulin Injection [regular] (**70/30**). Your doctor
 60 has prescribed the type of insulin that he/she believes is best for you. **DO NOT USE ANY**
 61 **OTHER INSULIN EXCEPT ON HIS/HER ADVICE AND DIRECTION.**

62 Always check the carton and the bottle label for the name and letter designation of the insulin
 63 you receive from your pharmacy to make sure it is the same as that your doctor has prescribed.

64 Always examine the appearance of your bottle of insulin before withdrawing each dose.
 65 Humulin R is a clear and colorless liquid with a water-like appearance and consistency. Do not
 66 use if it appears cloudy, thickened, or slightly colored or if solid particles are visible. Always
 67 check the appearance of your bottle of insulin before using, and if you note anything unusual in
 68 the appearance of your insulin or notice your insulin requirements changing markedly, consult
 69 your doctor.

70 **Storage**

71 Humulin R should be stored in a refrigerator (2° to 8° C [36° to 46° F]), but not in the freezer. If
 72 refrigeration is not possible, the bottle of Humulin R that you are currently using can be kept
 73 unrefrigerated as long as it is kept as cool as possible (below 30°C [86° F]), and away from heat
 74 and light. Do not use Humulin R if it has been frozen. Do not use a bottle of Humulin R after the
 75 expiration date stamped on the label.

76 **INJECTION PROCEDURES**

77 **Correct Syringe**

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

82 **Syringe Use**

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

84 Disposable syringes and needles should be used only once and then discarded. **NEEDLES**
 85 **AND SYRINGES MUST NOT BE SHARED.**

86 Reusable syringes and needles must be sterilized before each injection. **Follow the package**
 87 **directions supplied with your syringe.** Described below are 2 methods of sterilizing.

88 **Boiling**

- 89 1. Put syringe, plunger, and needle in strainer, place in saucepan, and cover with water. Boil
 90 for 5 minutes.
- 91 2. Remove articles from water. When they have cooled, insert plunger into barrel, and fasten
 92 needle to syringe with a slight twist.
- 93 3. Push plunger in and out several times until water is completely removed.

94 **Isopropyl Alcohol**

95 If the syringe, plunger, and needle cannot be boiled, as when you are traveling, they may be
 96 sterilized by immersion for at least 5 minutes in Isopropyl Alcohol, 91%. Do not use bathing,
 97 rubbing, or medicated alcohol for this sterilization. If the syringe is sterilized with alcohol, it
 98 must be absolutely dry before use.

99 Preparing the Dose

- 100 1. Wash your hands.
- 101 2. Inspect the insulin. Humulin R should look clear and colorless. Do not use Humulin R if it
- 102 appears cloudy, thickened, or slightly colored or if solid particles are visible.
- 103 3. If using a new bottle, flip off the plastic protective cap, but **do not** remove the stopper.
- 104 When using a new bottle, wipe the top of the bottle with an alcohol swab.
- 105 4. If you are mixing insulins, refer to the instructions for mixing that follow.
- 106 5. Draw air into the syringe equal to your insulin dose. Put the needle through rubber top of
- 107 the insulin bottle and inject the air into the bottle.
- 108 6. Turn the bottle and syringe upside down. Hold the bottle and syringe firmly in one hand.
- 109 7. Making sure the tip of the needle is in the insulin, withdraw the correct dose of insulin
- 110 into the syringe.
- 111 8. Before removing the needle from the bottle, check your syringe for air bubbles which
- 112 reduce the amount of insulin in it. If bubbles are present, hold the syringe straight up and
- 113 tap its side until the bubbles float to the top. Push them out with the plunger and withdraw
- 114 the correct dose.
- 115 9. Remove the needle from the bottle and lay the syringe down so that the needle does not
- 116 touch anything.

117 Mixing Humulin R with Longer-acting Human Insulins

- 118 1. Regular human insulin should be mixed with longer-acting human insulins only on the
- 119 advice of your doctor.
- 120 2. Draw air into your syringe equal to the amount of longer-acting insulin you are taking.
- 121 Insert the needle into the longer-acting insulin bottle and inject the air. Withdraw the
- 122 needle.
- 123 3. Now inject air into your regular human insulin bottle in the same manner, but **do not**
- 124 withdraw the needle.
- 125 4. Turn the bottle and syringe upside down.
- 126 5. Making sure the tip of the needle is in the insulin, withdraw the correct dose of regular
- 127 insulin into the syringe.
- 128 6. Before removing the needle from the bottle, check your syringe for air bubbles which
- 129 reduce the amount of insulin in it. If bubbles are present, hold the syringe straight up and
- 130 tap its side until the bubbles float to the top. Push them out with the plunger and withdraw
- 131 the correct dose.
- 132 7. Remove the needle from the bottle of regular insulin and insert it into the bottle of the
- 133 longer-acting insulin. Turn the bottle and syringe upside down. Hold the bottle and
- 134 syringe firmly in one hand and shake gently. Making sure the tip of the needle is in the
- 135 insulin, withdraw your dose of longer-acting insulin.
- 136 8. Remove the needle and lay the syringe down so that the needle does not touch anything.

137 Follow your doctor's instructions on whether to mix your insulins ahead of time or just before

138 giving your injection. It is important to be consistent in your method.

139 Syringes from different manufacturers may vary in the amount of space between the bottom

140 line and the needle. Because of this, do not change:

- 141 • the sequence of mixing, or
- 142 • the model and brand of syringe or needle that the doctor has prescribed.

143 Injection

144 Cleanse the skin with alcohol where the injection is to be made. Stabilize the skin by spreading

145 it or pinching up a large area. Insert the needle as instructed by your doctor. Push the plunger in

146 as far as it will go. Pull the needle out and apply gentle pressure over the injection site for

147 several seconds. **Do not rub the area.** To avoid tissue damage, give the next injection at a site at

148 least 1/2" from the previous site. Place the used needle in a puncture-resistant disposable

149 container and properly dispose of it as directed by your Health Care Professional.

150 **DOSAGE**

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

154 Your usual insulin dose may be affected by changes in your food, activity, or work schedule.
155 Carefully follow your doctor's instructions to allow for these changes. Other things that may
156 affect your insulin dose are:

157 **Illness**

158 Illness, especially with nausea and vomiting, may cause your insulin requirements to change.
159 Even if you are not eating, you will still require insulin. You and your doctor should establish a
160 sick day plan for you to use in case of illness. When you are sick, test your blood/urine
161 frequently and call your doctor as instructed.

162 **Pregnancy**

163 Good control of diabetes is especially important for you and your unborn baby. Pregnancy may
164 make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or
165 are nursing a baby, consult your doctor.

166 **Medication**

167 Insulin requirements may be increased if you are taking other drugs with hyperglycemic
168 activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy. Insulin
169 requirements may be reduced in the presence of drugs with hypoglycemic activity, such as oral
170 hypoglycemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants.
171 Always discuss any medications you are taking with your doctor.

172 **Exercise**

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

177 **Travel**

178 Persons traveling across more than 2 time zones should consult their doctor concerning
179 adjustments in their insulin schedule.

180 **COMMON PROBLEMS OF DIABETES**

181 **Hypoglycemia (Insulin Reaction)**

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

- 184 1. Taking too much insulin
- 185 2. Missing or delaying meals
- 186 3. Exercising or working more than usual
- 187 4. An infection or illness (especially with diarrhea or vomiting)
- 188 5. A change in the body's need for insulin
- 189 6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver
190 disease
- 191 7. Interactions with other drugs that lower blood glucose, such as oral hypoglycemics,
192 salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants
- 193 8. Consumption of alcoholic beverages

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

- | | |
|-------------------|----------------------|
| 195 • sweating | • drowsiness |
| 196 • dizziness | • sleep disturbances |
| 197 • palpitation | • anxiety |
| 198 • tremor | • blurred vision |
| 199 • hunger | • slurred speech |

- 200 • restlessness
- 201 • tingling in the hands, feet, lips, or tongue
- 202 • lightheadedness
- 203 • inability to concentrate
- 204 • headache
- depressed mood
- irritability
- abnormal behavior
- unsteady movement
- personality changes

205 Signs of severe hypoglycemia can include:

- 206 • disorientation
- 207 • unconsciousness
- seizures
- death

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

209 Early warning symptoms of hypoglycemia may be different or less pronounced under certain
210 conditions, such as long duration of diabetes, diabetic nerve disease, medications such as
211 beta-blockers, change in insulin preparations, or intensified control (3 or more insulin injections
212 per day) of diabetes.

213 **A few patients who have experienced hypoglycemic reactions after transfer from**
214 **animal-source insulin to human insulin have reported that the early warning symptoms of**
215 **hypoglycemia were less pronounced or different from those experienced with their**
216 **previous insulin.**

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

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

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

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

234 **Hyperglycemia and Diabetic Acidosis**

235 Hyperglycemia (too much glucose in the blood) may develop if your body has too little insulin.
236 Hyperglycemia can be brought about by:

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

240 In patients with insulin-dependent diabetes, prolonged hyperglycemia can result in diabetic
241 acidosis. The first symptoms of diabetic acidosis usually come on gradually, over a period of
242 hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite, and fruity odor
243 on the breath. With acidosis, urine tests show large amounts of glucose and acetone. Heavy
244 breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia
245 or diabetic acidosis can lead to nausea, vomiting, dehydration, loss of consciousness or death.
246 Therefore, it is important that you obtain medical assistance immediately.

247 **Lipodystrophy**

248 Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the
249 skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these

250 conditions, consult your doctor. A change in your injection technique may help alleviate the
251 problem.

252 **Allergy to Insulin**

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

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

263 **ADDITIONAL INFORMATION**

264 Additional information about diabetes may be obtained from your diabetes educator.

265 **DIABETES FORECAST** is a national magazine designed especially for patients with
266 diabetes and their families and is available by subscription from the American Diabetes
267 Association, National Service Center, 1660 Duke Street, Alexandria, Virginia 22314,
268 1-800-DIABETES (1-800-342-2383).

269 Another publication, **DIABETES COUNTDOWN**, is available from the Juvenile Diabetes
270 Foundation International (JDF), 120 Wall Street, 19th Floor, New York, New York 10005,
271 1-800-JDF-CURE (1-800-533-2873).

272 Additional information about Humulin can be obtained by calling 1-888-88-LILLY
273 (1-888-885-4559).

274

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IMPORTANT—SEE WARNINGS
ON ACCOMPANYING CIRCULAR

**CARTON HAS
BEEN OPENED**

NL 3820 AMS
SMA 3820 AMS

Exp. Date/Control No.

Humulin R
REGULAR insulin human
injection, USP
(rDNA origin)

Warning:
Any change of Insulin
should be made cautiously
and only under medical
supervision. See enclosed
circular.

As with any drug, if you
are pregnant or nursing a
baby, seek professional
advice when using this
product.

Contains Metacresol 0.25%
added during manufacture
as a preservative.

Neutral

For information call
1-888-885-4559

Manufactured by Abbott Laboratories
North Chicago, IL 60064, USA
for Eli Lilly and Company
Indianapolis, IN 46285, USA

 NDC 0002-8215-01
10 mL HI-210

Humulin[®]

R

REGULAR
insulin human
injection, USP
(rDNA origin)



U-100

100 units per mL

 **U-100**

NDC 0002-8215-01
10 mL HI-210
100 units per mL



Humulin R

REGULAR
insulin human
injection, USP
(rDNA origin)

Keep in a cold place.
Avoid freezing.



0002-8215-01

U-100

NL 3820 AMS

C-671



AZ20



Exp. Date/Control No.
● NL 4050 AMX ●

Lilly

NDC 0002-8215-01

10 mL HI-210

100 units per mL

Humulin[®] R

REGULAR
insulin human
injection, USP
(rDNA origin)



U-100

Important: See enclosed insert.
Keep in a cold place. Avoid freezing.

Neutral

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Humulin R

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