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

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, ANALOG), SPECIES, OR METHOD OF MANUFACTURE 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 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 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.

REGULAR HUMAN INSULIN

Description

Humulin is synthesized in a special non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically altered to produce human insulin. Humulin R [Regular insulin human injection, USP (rDNA origin)] consists of zinc-insulin crystals dissolved in a clear fluid. Humulin R has had nothing added to change the speed or length of its action. It takes effect

47 rapidly and has a relatively short duration of activity (4 to 12 hours) as compared with other
48 insulins. The time course of action of any insulin may vary considerably in different individuals
49 or at different times in the same individual. As with all insulin preparations, the duration of
50 action of Humulin R is dependent on dose, site of injection, blood supply, temperature, and
51 physical activity. Humulin R is a sterile solution and is for subcutaneous injection. It should not
52 be used intramuscularly. The concentration of Humulin R is 100 units/mL (U-100).

53 **Identification**

54 Human insulin from Eli Lilly and Company has the trademark Humulin. Your doctor has
55 prescribed the type of insulin that he/she believes is best for you.

56 **DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND** 57 **DIRECTION.**

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

60 Always check the appearance of your bottle of Humulin R before withdrawing each dose.
61 Humulin R is a clear and colorless liquid with a water-like appearance and consistency. Do not
62 use Humulin R:

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

65 If you see anything unusual in the appearance of Humulin R solution in your bottle or notice
66 your insulin requirements changing, talk to your doctor.

67 **Storage**

68 **Not in-use (unopened):** Humulin R bottles not in-use should be stored in a refrigerator, but
69 not in the freezer.

70 **In-use (opened):** The Humulin R bottle you are currently using can be kept unrefrigerated as
71 long as it is kept as cool as possible [below 86°F (30°C)] away from heat and light.

72 **Do not use Humulin R after the expiration date stamped on the label or if it has been**
73 **frozen.**

74 **INSTRUCTIONS FOR INSULIN VIAL USE**

75 **NEVER SHARE NEEDLES AND SYRINGES.**

76 **Correct Syringe Type**

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

81 **Syringe Use**

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

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

86 **Preparing the Dose**

- 87 1. Wash your hands.
- 88 2. Inspect the insulin. Humulin R solution should look clear and colorless. Do not use
89 Humulin R if it appears cloudy, thickened, or slightly colored, or if you see particles in the
90 solution. Do not use Humulin R if you notice anything unusual in its appearance.
- 91 3. If using a new Humulin R bottle, flip off the plastic protective cap, but **do not** remove the
92 stopper. Wipe the top of the bottle with an alcohol swab.
- 93 4. If you are mixing insulins, refer to the "Mixing Humulin R with Longer-Acting Human
94 Insulins" section below.
- 95 5. Draw an amount of air into the syringe that is equal to the Humulin R dose. Put the needle
96 through rubber top of the Humulin R bottle and inject the air into the bottle.

- 97 6. Turn the Humulin R bottle and syringe upside down. Hold the bottle and syringe firmly in
98 one hand.
- 99 7. Making sure the tip of the needle is in the Humulin R solution, withdraw the correct dose
100 of Humulin R into the syringe.
- 101 8. Before removing the needle from the Humulin R bottle, check the syringe for air bubbles.
102 If bubbles are present, hold the syringe straight up and tap its side until the bubbles float
103 to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
- 104 9. Remove the needle from the bottle and lay the syringe down so that the needle does not
105 touch anything.
- 106 10. If you do not need to mix your Humulin R with a longer-acting insulin, go to the
107 “Injection Instructions” section below and follow the directions.

Mixing Humulin R with Longer-Acting Human Insulins

- 109 1. Humulin R should be mixed with longer-acting human insulins only on the advice of your
110 doctor.
- 111 2. Draw an amount of air into the syringe that is equal to the amount of longer-acting insulin
112 you are taking. Insert the needle into the longer-acting insulin bottle and inject the air.
113 Withdraw the needle.
- 114 3. Draw an amount of air into the syringe that is equal to the amount of Humulin R you are
115 taking. Insert the needle into the Humulin R bottle and inject the air, but **do not** withdraw
116 the needle.
- 117 4. Turn the Humulin R bottle and syringe upside down.
- 118 5. Making sure the tip of the needle is in the Humulin R solution, withdraw the correct dose
119 of Humulin R into the syringe.
- 120 6. Before removing the needle from the Humulin R bottle, check the syringe for air bubbles.
121 If bubbles are present, hold the syringe straight up and tap its side until the bubbles float
122 to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
- 123 7. Remove the syringe with the needle from the Humulin R bottle and insert it into the
124 longer-acting insulin bottle. Turn the longer-acting insulin bottle and syringe upside
125 down. Hold the bottle and syringe firmly in one hand and shake gently. Making sure the
126 tip of the needle is in the longer-acting insulin, withdraw the correct dose of longer-acting
127 insulin.
- 128 8. Remove the needle from the bottle and lay the syringe down so that the needle does not
129 touch anything.
- 130 9. Follow the directions under “Injection Instructions” section below.

131 Follow your doctor’s instructions on whether to mix your insulins ahead of time or just before
132 giving your injection. It is important to be consistent in your method.

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

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

Injection Instructions

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

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DOSAGE

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

Your usual dose of Humulin R may be affected by changes in your diet, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your Humulin R dose are:

Illness

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

Pregnancy

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

Medication

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

Exercise

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

Travel

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

COMMON PROBLEMS OF DIABETES

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 certain drugs, 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:

- sweating
- drowsiness
- dizziness
- sleep disturbances

- 198 • palpitation
- 199 • tremor
- 200 • hunger
- 201 • restlessness
- 202 • tingling in the hands, feet, lips, or tongue
- 203 • lightheadedness
- 204 • inability to concentrate
- 205 • headache
- 206 Signs of severe hypoglycemia can include:
- 207 • disorientation
- 208 • unconsciousness
- anxiety
- blurred vision
- slurred speech
- depressed mood
- irritability
- abnormal behavior
- unsteady movement
- personality changes
- seizures
- death

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

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

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

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

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

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

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

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

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

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

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

249 **Lipodystrophy**

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

254 **Allergy**

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

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

264 **ADDITIONAL INFORMATION**

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

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

268 Patient Information revised Month dd, yyyy

269 **Vials manufactured by**
270 **Eli Lilly and Company, Indianapolis, IN 46285, USA**
271
272 **for Wal-Mart Stores, Inc.**

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