

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 1

NL 4480 AMP

**INFORMATION FOR THE PATIENT**

**HUMULIN<sup>®</sup> L  
LENTE<sup>®</sup>  
HUMAN INSULIN (rDNA ORIGIN)  
ZINC SUSPENSION  
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<sup>®</sup>), 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<sup>®</sup> (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 premeal glucose levels are consistently above 140 mg/dL or your hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) 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.

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 2

## LENTE 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 L is an amorphous and crystalline suspension of human insulin with zinc providing an intermediate-acting insulin with a slower onset and a longer duration of activity (up to 24 hours) than regular insulin. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of Humulin L is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin L is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously or intramuscularly. The concentration of Humulin L is 100 units/mL (U-100).

### Identification

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

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

Always examine the appearance of your bottle of insulin before withdrawing each dose. A bottle of Humulin L must be carefully shaken or rotated before each injection so that the contents are uniformly mixed. Humulin L should look uniformly cloudy or milky after mixing. Do not use it if the insulin substance (the white material) remains at the bottom of the bottle after mixing. Do not use a bottle of Humulin L if there are clumps in the insulin after mixing. Always check the appearance of your bottle of insulin before using, and if you note anything unusual in the appearance of your insulin or notice your insulin requirements changing markedly, consult your doctor.

### Storage

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

## INJECTION PROCEDURES

### Correct Syringe

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

### Syringe Use

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

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

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

### Boiling

1. Put syringe, plunger, and needle in strainer, place in saucepan, and cover with water. Boil for 5 minutes.

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 3

2. Remove articles from water. When they have cooled, insert plunger into barrel, and fasten needle to syringe with a slight twist.
3. Push plunger in and out several times until water is completely removed.

### **Isopropyl Alcohol**

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

### **Preparing the Dose**

1. Wash your hands.
2. Carefully shake or rotate the insulin bottle several times to completely mix the insulin.
3. Inspect the insulin. Humulin L should look uniformly cloudy or milky. Do not use it if you notice anything unusual in the appearance.
4. If using a new bottle, flip off the plastic protective cap, but **do not** remove the stopper. When using a new bottle, wipe the top of the bottle with an alcohol swab.
5. If you are mixing insulins, refer to the instructions for mixing that follow.
6. Draw air into the syringe equal to your insulin dose. Put the needle through rubber top of the insulin bottle and inject the air into the bottle.
7. Turn the bottle and syringe upside down. Hold the bottle and syringe firmly in **one** hand and shake gently.
8. Making sure the tip of the needle is in the insulin, withdraw the correct dose of insulin into the syringe.
9. Before removing the needle from the bottle, check your syringe for air bubbles which reduce the amount of insulin in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.
10. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.

### **Mixing Humulin L with Regular or Ultralente Human Insulin**

1. Lente human insulin should be mixed with regular or Ultralente human insulin only on the advice of your doctor.
2. Draw air into your syringe equal to the amount of Humulin L you are taking. Insert the needle into the Humulin L bottle and inject the air. Withdraw the needle.
3. Now inject air into your regular or Ultralente human insulin bottle in the same manner, but **do not** withdraw the needle.
4. Turn the bottle and syringe upside down.
5. Making sure the tip of the needle is in the insulin, withdraw the correct dose of regular or Ultralente insulin into the syringe.
6. Before removing the needle from the bottle, check your syringe for air bubbles which reduce the amount of insulin in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.
7. Remove the needle from the bottle of regular or Ultralente insulin and insert it into the bottle of Humulin L. Turn the bottle and syringe upside down. Hold the bottle and syringe firmly in **one** hand and shake gently. Making sure the tip of the needle is in the insulin, withdraw your dose of Humulin L.
8. Remove the needle and lay the syringe down so that the needle does not touch anything.

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

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 4

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

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

### **Injection**

Cleanse the skin with alcohol where the injection is to be made. Stabilize the skin by spreading it or pinching up a large area. Insert the needle as instructed by your doctor. Push the plunger in as far as it will go. Pull the needle out and apply gentle pressure over the injection site for several seconds. **Do not rub the area.** To avoid tissue damage, give the next injection at a site at least 1/2" from the previous site. Used needle should be placed in sharps containers (such as red biohazard containers), hard plastic containers (such as detergent bottles), or metal containers (such as an empty coffee can). Such containers should be sealed and disposed of properly.

### **DOSAGE**

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

Your usual insulin dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your insulin 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/urine frequently and call your doctor as instructed.

### **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, consult your doctor.

### **Medication**

Insulin requirements may be increased if you are taking other drugs with hyperglycemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy. Insulin requirements may be reduced in the presence of drugs with hypoglycemic activity, such as oral hypoglycemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants. 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 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 regimen to accommodate exercise.

### **Travel**

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

## **COMMON PROBLEMS OF DIABETES**

### **Hypoglycemia (Insulin Reaction)**

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. Taking too much insulin
2. Missing or delaying meals
3. Exercising or working more than usual

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 5

4. An infection or illness (especially 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 hypoglycemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

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

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, medications such as beta-blockers, change in insulin preparations, or intensified control (3 or more insulin 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 candy mints 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.

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

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

### **Hyperglycemia and Diabetic Acidosis**

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

NDA 19-377/S-036  
FDA revision (4/15/03)  
Page 6

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

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

### **Lipodystrophy**

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

### **Allergy to Insulin**

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

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

### **ADDITIONAL INFORMATION**

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

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

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

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

Text revised August 3, 2000

Literature issued XXX 2003

Manufactured by Lilly France S.A.S.  
F-67640 Fegersheim, France  
for Eli Lilly and Company  
Indianapolis, IN 46285, USA

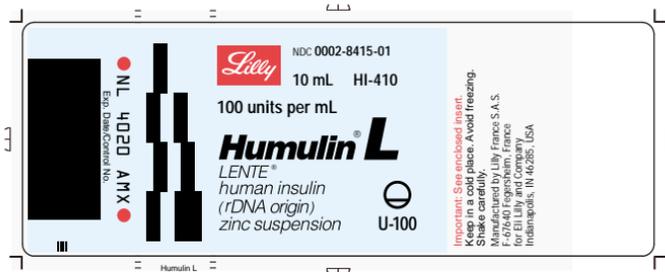
NL 4480 AMP

PRINTED IN USA

Copyright © 1997, 2003, Eli Lilly and Company. All rights reserved.

This label may not be the latest approved by FDA.  
For current labeling information, please visit <https://www.fda.gov/drugsatfda>

← 1 " →



← 1 " →

