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INFORMATION FOR THE PATIENT
10 mL Vial (1000 Units per vial)
3 mL Vial (300 Units per vial)

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HUMULIN[®] N
NPH
HUMAN INSULIN (rDNA ORIGIN)
ISOPHANE SUSPENSION
100 UNITS PER ML (U-100)

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WARNINGS

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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.

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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.

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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.

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DIABETES

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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.

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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.

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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.

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NPH HUMAN INSULIN

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Description

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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 N [Human insulin (rDNA origin) isophane suspension] is a crystalline suspension of human insulin with protamine and zinc providing an intermediate-acting insulin with a slower onset of action and a longer duration of activity (up to 24 hours) than that of Regular human insulin. The time course of action of any insulin may vary considerably in different individuals or at different times in the

49 same individual. As with all insulin preparations, the duration of action of Humulin N is
50 dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin N
51 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously
52 or intramuscularly. The concentration of Humulin N 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 N before withdrawing each dose.
61 Before each injection the Humulin N bottle must be carefully shaken or rotated several times to
62 completely mix the insulin. Humulin N suspension should look uniformly cloudy or milky after
63 mixing. If not, repeat the above steps until contents are mixed.

64 Do not use Humulin N:

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

69 If you see anything unusual in the appearance of Humulin N suspension in your bottle or notice
70 your insulin requirements changing, talk to your doctor.

71 **Storage**

72 **Not in-use (unopened):** Humulin N bottles not in-use should be stored in a refrigerator, but
73 not in the freezer.

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

76 **Do not use Humulin N after the expiration date stamped on the label or if it has been**
77 **frozen.**

78 **INSTRUCTIONS FOR INSULIN VIAL USE**

79 **NEVER SHARE NEEDLES AND SYRINGES.**

80 **Correct Syringe Type**

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

85 **Syringe Use**

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

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

90 **Preparing the Dose**

- 91 1. Wash your hands.
- 92 2. Carefully shake or rotate the bottle of insulin several times to completely mix the insulin.
- 93 3. Inspect the insulin. Humulin N suspension should look uniformly cloudy or milky. Do not
94 use Humulin N if you notice anything unusual in its appearance.
- 95 4. If using a new Humulin N bottle, flip off the plastic protective cap, but **do not** remove the
96 stopper. Wipe the top of the bottle with an alcohol swab.
- 97 5. If you are mixing insulins, refer to the "Mixing Humulin N and Regular Human Insulin"
98 section below.

- 99 6. Draw an amount of air into the syringe that is equal to the Humulin N dose. Put the needle
100 through rubber top of the Humulin N bottle and inject the air into the bottle.
101 7. Turn the Humulin N bottle and syringe upside down. Hold the bottle and syringe firmly in
102 one hand and shake gently.
103 8. Making sure the tip of the needle is in the Humulin N suspension, withdraw the correct
104 dose of Humulin N into the syringe.
105 9. Before removing the needle from the Humulin N bottle, check the syringe for air bubbles.
106 If bubbles are present, hold the syringe straight up and tap its side until the bubbles float
107 to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
108 10. Remove the needle from the bottle and lay the syringe down so that the needle does not
109 touch anything.
110 11. If you do not need to mix your Humulin N with Regular human insulin, go to the
111 “Injection Instructions” section below and follow the directions.

112 **Mixing Humulin N and Regular Human Insulin (Humulin R)**

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

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

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

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

138 **Injection Instructions**

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

149

DOSAGE

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

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

Illness

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

Pregnancy

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

Medication

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

Exercise

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

Travel

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

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COMMON PROBLEMS OF DIABETES**Hypoglycemia (Low Blood Sugar)**

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

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

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

- | | |
|-------------------|----------------------|
| 197 • sweating | • drowsiness |
| 198 • dizziness | • sleep disturbances |
| 199 • palpitation | • anxiety |

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

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

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

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

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

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

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

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

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

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

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

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

250 **Lipodystrophy**

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

255 **Allergy**

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

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

265 **ADDITIONAL INFORMATION**

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

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

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270 **10 mL Vials manufactured by**

271 **Eli Lilly and Company, Indianapolis, IN 46285, USA or**
272 **Lilly France, F-67640 Fegersheim, France**

273 **3 mL Vials manufactured by**

274 **Eli Lilly and Company, Indianapolis, IN 46285, USA**

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