

A1.0 NL 5691 AMP
A1.0 NL 5681 AMP
A2.0 NL 4460 AMP

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 rapidly and has a relatively short duration of activity (4 to 12 hours) as compared with other insulins. 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 R is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin R is a sterile solution and is for subcutaneous injection. It should not be used intramuscularly. The concentration of Humulin R is 100 units/mL (U-100).

Identification

Human insulin from Eli Lilly and Company has the trademark Humulin. 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.

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 prescribed by your doctor.

Always check the appearance of your bottle of Humulin R before withdrawing each dose. Humulin R is a clear and colorless liquid with a water-like appearance and consistency.

Do not use Humulin R:

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

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

Storage

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

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

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

INSTRUCTIONS FOR INSULIN VIAL USE

NEVER SHARE NEEDLES AND SYRINGES.

Correct Syringe Type

Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc). With Humulin R, 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 by placing the used needle in a puncture-resistant disposable container. Properly dispose of the puncture-resistant container as directed by your Health Care Professional.

Preparing the Dose

1. Wash your hands.
2. Inspect the insulin. Humulin R solution should look clear and colorless. Do not use Humulin R if it appears cloudy, thickened, or slightly colored, or if you see particles in the solution. Do not use Humulin R if you notice anything unusual in its appearance.

3. If using a new Humulin R bottle, flip off the plastic protective cap, but **do not** remove the stopper. Wipe the top of the bottle with an alcohol swab.
4. If you are mixing insulins, refer to the “Mixing Humulin R with Longer-Acting Human Insulins” section below.
5. Draw an amount of air into the syringe that is equal to the Humulin R dose. Put the needle through rubber top of the Humulin R bottle and inject the air into the bottle.
6. Turn the Humulin R bottle and syringe upside down. Hold the bottle and syringe firmly in one hand.
7. Making sure the tip of the needle is in the Humulin R solution, withdraw the correct dose of Humulin R into the syringe.
8. Before removing the needle from the Humulin R bottle, check the syringe for air bubbles. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
9. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.
10. If you do not need to mix your Humulin R with a longer-acting insulin, go to the “Injection Instructions” section below and follow the directions.

Mixing Humulin R with Longer-Acting Human Insulins

1. Humulin R should be mixed with longer-acting human insulins only on the advice of your doctor.
2. Draw an amount of air into the syringe that is equal to the amount of longer-acting insulin you are taking. Insert the needle into the longer-acting insulin bottle and inject the air. Withdraw the needle.
3. Draw an amount of air into the syringe that is equal to the amount of Humulin R you are taking. Insert the needle into the Humulin R bottle and inject the air, but **do not** withdraw the needle.
4. Turn the Humulin R bottle and syringe upside down.
5. Making sure the tip of the needle is in the Humulin R solution, withdraw the correct dose of Humulin R into the syringe.
6. Before removing the needle from the Humulin R bottle, check the syringe for air bubbles. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
7. Remove the syringe with the needle from the Humulin R bottle and insert it into the longer-acting insulin bottle. Turn the longer-acting insulin 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 longer-acting insulin, withdraw the correct dose of longer-acting insulin.
8. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.
9. Follow the directions under “Injection Instructions” section below.

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.

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 your doctor has prescribed.

Injection Instructions

1. To avoid tissue damage, choose a site for each injection that is at least 1/2 inch from the previous injection site. The usual sites of injection are abdomen, thighs, and arms.
2. Cleanse the skin with alcohol where the injection is to be made.
3. With one hand, stabilize the skin by spreading it or pinching up a large area.

4. Insert the needle as instructed by your doctor.
5. Push the plunger in as far as it will go.
6. Pull the needle out and apply gentle pressure over the injection site for several seconds.
Do not rub the area.
7. Place the used needle in a puncture-resistant disposable container and properly dispose of the puncture-resistant container as directed by your Health Care Professional.

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
- 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, use of medications such as beta-blockers, changing 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 hard candy 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 talk to your doctor to discuss possible changes in therapy, meal plans, and/or exercise programs to help you avoid hypoglycemia.

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

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

1. Omitting your insulin or taking less than your 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 type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in DKA (a life-threatening emergency). The first symptoms of DKA 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 DKA, blood and urine tests show large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, 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 (seen as an apparent depression of the skin) or lipohypertrophy (seen as a raised area of the skin). If you notice either of these conditions, talk to your doctor. A change in your injection technique may help alleviate the problem.

Allergy

Local Allergy — Patients occasionally experience redness, swelling, and itching at the site of injection. 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, talk to 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, call your doctor immediately.

ADDITIONAL INFORMATION

Information about diabetes may be obtained from your diabetes educator.

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

Patient Information issued/revised Month dd, yyyy

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INFORMATION FOR THE PATIENT

10 mL Vial (1000 Units per vial)

**HUMULIN[®] N
NPH
HUMAN INSULIN (rDNA ORIGIN)
ISOPHANE 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.

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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.

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.

NPH 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 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 same individual. As with all insulin preparations, the duration of action of Humulin N is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin N is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously or intramuscularly. The concentration of Humulin N is 100 units/mL (U-100).

Identification

Human insulin from Eli Lilly and Company has the trademark Humulin. 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.

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 prescribed by your doctor.

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

Do not use Humulin N:

- 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 Humulin N suspension in your bottle or notice your insulin requirements changing, talk to your doctor.

Storage

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

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

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

INSTRUCTIONS FOR INSULIN VIAL USE

NEVER SHARE NEEDLES AND SYRINGES.

Correct Syringe Type

Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc). With Humulin N, 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 by placing the used needle in a puncture-resistant disposable container. Properly dispose of the puncture-resistant container as directed by your Health Care Professional.

Preparing the Dose

1. Wash your hands.
2. Carefully shake or rotate the bottle of insulin several times to completely mix the insulin.
3. Inspect the insulin. Humulin N suspension should look uniformly cloudy or milky. Do not use Humulin N if you notice anything unusual in its appearance.
4. If using a new Humulin N bottle, flip off the plastic protective cap, but **do not** remove the stopper. Wipe the top of the bottle with an alcohol swab.
5. If you are mixing insulins, refer to the “Mixing Humulin N and Regular Human Insulin” section below.
6. Draw an amount of air into the syringe that is equal to the Humulin N dose. Put the needle through rubber top of the Humulin N bottle and inject the air into the bottle.
7. Turn the Humulin N 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 Humulin N suspension, withdraw the correct dose of Humulin N into the syringe.
9. Before removing the needle from the Humulin N bottle, check the syringe for air bubbles. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
10. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.
11. If you do not need to mix your Humulin N with Regular human insulin, go to the “Injection Instructions” section below and follow the directions.

Mixing Humulin N and Regular Human Insulin (Humulin R)

1. Humulin N should be mixed with Humulin R only on the advice of your doctor.
2. Draw an amount of air into the syringe that is equal to the amount of Humulin N you are taking. Insert the needle into the Humulin N bottle and inject the air. Withdraw the needle.
3. Draw an amount of air into the syringe that is equal to the amount of Humulin R you are taking. Insert the needle into the Humulin R bottle and inject the air, but **do not** withdraw the needle.
4. Turn the Humulin R bottle and syringe upside down.
5. Making sure the tip of the needle is in the Humulin R solution, withdraw the correct dose of Humulin R into the syringe.
6. Before removing the needle from the Humulin R bottle, check the syringe for air bubbles. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
7. Remove the syringe with the needle from the Humulin R bottle and insert it into the Humulin N bottle. Turn the Humulin R 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 Humulin N, withdraw the correct dose of Humulin N.
8. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.
9. Follow the directions under “Injection Instructions” section below.

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.

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 your doctor has prescribed.

Injection Instructions

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

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 N 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 N 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
- 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, use of medications such as beta-blockers, changing 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 hard candy 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 talk to your doctor to discuss possible changes in therapy, meal plans, and/or exercise programs to help you avoid hypoglycemia.

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

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

1. Omitting your insulin or taking less than your 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 type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in DKA (a life-threatening emergency). The first symptoms of DKA 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 DKA, blood and urine tests show large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, 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 (seen as an apparent depression of the skin) or lipohypertrophy (seen as a raised area of the skin). If you notice either of these conditions, talk to your doctor. A change in your injection technique may help alleviate the problem.

Allergy

Local Allergy — Patients occasionally experience redness, swelling, and itching at the site of injection. 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, talk to 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, call your doctor immediately.

ADDITIONAL INFORMATION

Information about diabetes may be obtained from your diabetes educator.

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

Patient Information issued/revised Month dd, yyyy

Vials manufactured by
Eli Lilly and Company, Indianapolis, IN 46285, USA or
Lilly France, F-67640 Fegersheim, France

for Eli Lilly and Company, Indianapolis, IN 46285, USA

A1.0 NL 5711 AMP
A1.0 NL 6792 AMP

PRINTED IN USA

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

A1.0 NL 3682 AMP
A6.0 PA 9134 FSAMP

INFORMATION FOR THE PATIENT
3 ML DISPOSABLE INSULIN DELIVERY DEVICE

HUMULIN[®] N Pen
NPH
HUMAN INSULIN
(rDNA ORIGIN) ISOPHANE 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, 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.

TO OBTAIN AN ACCURATE DOSE, CAREFULLY READ AND FOLLOW THE INSULIN DELIVERY DEVICE USER MANUAL AND THIS "INFORMATION FOR THE PATIENT" INSERT BEFORE USING THIS PRODUCT.

BEFORE EACH INJECTION, YOU SHOULD PRIME THE PEN, A NECESSARY STEP TO MAKE SURE THE PEN IS READY TO DOSE. PRIMING THE PEN IS IMPORTANT TO CONFIRM THAT INSULIN COMES OUT WHEN YOU PUSH THE INJECTION BUTTON AND TO REMOVE AIR THAT MAY COLLECT IN THE INSULIN CARTRIDGE DURING NORMAL USE. IF YOU DO NOT PRIME, YOU MAY RECEIVE TOO MUCH OR TOO LITTLE INSULIN (*see also* INSTRUCTIONS FOR INSULIN PEN USE section).

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

47 levels, you should also let your doctor know. Proper control of your diabetes requires close and
48 constant cooperation with your doctor. Despite diabetes, you can lead an active and healthy life
49 if you eat a balanced diet, exercise regularly, and take your insulin injections as prescribed by
50 your doctor.

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

NPH HUMAN INSULIN

Description

56 Humulin is synthesized in a special non-disease-producing laboratory strain of *Escherichia*
57 *coli* bacteria that has been genetically altered to produce human insulin. Humulin N [Human
58 insulin (rDNA origin) isophane suspension] is a crystalline suspension of human insulin with
59 protamine and zinc providing an intermediate-acting insulin with a slower onset of action and a
60 longer duration of activity (up to 24 hours) than that of Regular human insulin. The time course
61 of action of any insulin may vary considerably in different individuals or at different times in the
62 same individual. As with all insulin preparations, the duration of action of Humulin N is
63 dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin N
64 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously
65 or intramuscularly. The concentration of Humulin N is 100 units/mL (U-100).

Identification

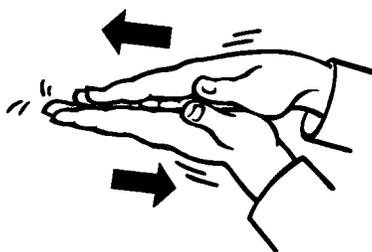
67 Human insulin from Eli Lilly and Company has the trademark Humulin. Your doctor has
68 prescribed the type of insulin that he/she believes is best for you.

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

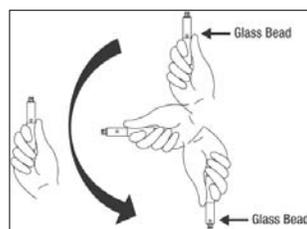
71 **The Humulin N Pen is available in boxes of 5 disposable insulin delivery devices ("insulin**
72 **Pens"). The Humulin N Pen is not designed to allow any other insulin to be mixed in its**
73 **cartridge, or for the cartridge to be removed.**

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

76 Always check the appearance of Humulin N suspension in your insulin Pen before using. A
77 cartridge of Humulin N contains a small glass bead to assist in mixing. Roll the Pen between the
78 palms 10 times (*see* Figure 1). Holding the Pen by one end, invert it 180° slowly 10 times to
79 allow the small glass bead to travel the full length with each inversion (*see* Figure 2).



80 Figure 1.



81 Figure 2.

82

82 Humulin N suspension should look uniformly cloudy or milky after mixing. If not, repeat the
83 above steps until contents are mixed. Pens containing Humulin N suspension should be
84 examined frequently.

85 Do not use Humulin N:

- 86 • if the insulin substance (the white material) remains visibly separated from the liquid
87 after mixing or

- 88 • if there are clumps in the insulin after mixing, or
- 89 • if solid white particles stick to the walls of the cartridge, giving a frosted appearance.

90 If you see anything unusual in the appearance of the Humulin N suspension in your Pen or
91 notice your insulin requirements changing, talk to your doctor.

92 Never attempt to remove the cartridge from the Humulin N Pen. Inspect the cartridge through
93 the clear cartridge holder.

94 **Storage**

95 **Not in-use (unopened):** Humulin N Pens not in-use should be stored in a refrigerator, but not
96 in the freezer.

97 **In-use (opened):** Humulin N Pens in-use should **NOT** be refrigerated but should be kept at
98 room temperature [below 86°F (30°C)] away from direct heat and light. The Humulin N Pen you
99 are currently using must be discarded **2 weeks** after the first use, even if it still contains Humulin
100 N.

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

103 **INSTRUCTIONS FOR INSULIN PEN USE**

104 **It is important to read, understand, and follow the instructions in the Insulin Delivery**
105 **Device User Manual before using. Failure to follow instructions may result in getting too**
106 **much or too little insulin. The needle must be changed and the Pen must be primed before**
107 **each injection to make sure the Pen is ready to dose. Performing these steps before each**
108 **injection is important to confirm that insulin comes out when you push the injection**
109 **button, and to remove air that may collect in the insulin cartridge during normal use.**

110 **Every time you inject:**

- 111 • **Use a new needle.**
- 112 • **Prime to make sure the Pen is ready to dose.**
- 113 • **Make sure you got your full dose.**

114 **NEVER SHARE INSULIN PENS, CARTRIDGES, OR NEEDLES.**

115 **PREPARING FOR INJECTION**

- 116 1. Wash your hands.
- 117 2. To avoid tissue damage, choose a site for each injection that is at least 1/2 inch from the
118 previous injection site. The usual sites of injection are abdomen, thighs, and arms.
- 119 3. Follow the instructions in your Insulin Delivery Device User Manual to prepare for
120 injection.
- 121 4. After injecting the dose, pull the needle out and apply gentle pressure over the injection
122 site for several seconds. **Do not rub the area.**
- 123 5. After the injection, remove the needle from the Humulin N Pen. **Do not reuse needles.**
- 124 6. Place the used needle in a puncture-resistant disposable container and properly dispose of
125 the puncture-resistant container as directed by your Health Care Professional.

126 **DOSAGE**

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

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

132 **Illness**

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

137 **Pregnancy**

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

141 **Medication**

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

149 **Exercise**

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

155 **Travel**

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

158 **COMMON PROBLEMS OF DIABETES**

159 **Hypoglycemia (Low Blood Sugar)**

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

- 162 1. **Missing or delaying meals.**
- 163 2. Taking too much insulin.
- 164 3. Exercising or working more than usual.
- 165 4. An infection or illness associated with diarrhea or vomiting.
- 166 5. A change in the body's need for insulin.
- 167 6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver
168 disease.
- 169 7. Interactions with certain drugs, such as oral antidiabetic agents, salicylates (for example,
170 aspirin), sulfa antibiotics, certain antidepressants and some kidney and blood pressure
171 medicines.
- 172 8. Consumption of alcoholic beverages.

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

- | | |
|--|-----------------------|
| 174 • sweating | • drowsiness |
| 175 • dizziness | • sleep disturbances |
| 176 • palpitation | • anxiety |
| 177 • tremor | • blurred vision |
| 178 • hunger | • slurred speech |
| 179 • restlessness | • depressed mood |
| 180 • tingling in the hands, feet, lips, or tongue | • irritability |
| 181 • lightheadedness | • abnormal behavior |
| 182 • inability to concentrate | • unsteady movement |
| 183 • headache | • personality changes |

184 Signs of severe hypoglycemia can include:

- | | |
|-----------------------|------------|
| 185 • disorientation | • seizures |
| 186 • unconsciousness | • death |

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

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

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

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

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

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

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

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

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

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

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

227 **Lipodystrophy**

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

232 **Allergy**

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

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

242 **ADDITIONAL INFORMATION**

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

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

246 Patient Information issued/revised Month dd, yyyy

247 **Pens manufactured by**

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

250 **for Eli Lilly and Company, Indianapolis, IN 46285, USA**

253 A1.0 NL 3682 AMP

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254 A6.0 PA 9134 FSAMP

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A1.0 NL 5721 AMP
A3.0 NL 3770 AMP

INFORMATION FOR THE PATIENT

10 mL Vial (1000 Units per vial)

**HUMULIN[®] 70/30
70% HUMAN INSULIN
ISOPHANE SUSPENSION
AND
30% HUMAN INSULIN INJECTION
(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.

70/30 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 70/30 is a mixture of 70% Human Insulin Isophane Suspension and 30% Human Insulin Injection (rDNA origin). It is an intermediate-acting insulin combined with the more rapid onset of action of Regular human insulin. The duration of activity may last up to 24 hours following injection. 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 70/30 is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin 70/30 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously or intramuscularly. The concentration of Humulin 70/30 is 100 units/mL (U-100).

Identification

Human insulin from Eli Lilly and Company has the trademark Humulin. 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.

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 prescribed by your doctor.

Always check the appearance of your bottle of Humulin 70/30 before withdrawing each dose. Before each injection the Humulin 70/30 bottle must be carefully shaken or rotated several times to completely mix the insulin. Humulin 70/30 suspension should look uniformly cloudy or milky after mixing. If not, repeat the above steps until contents are mixed.

Do not use Humulin 70/30:

- 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 Humulin 70/30 suspension in your bottle or notice your insulin requirements changing, talk to your doctor.

Storage

Not in-use (unopened): Humulin 70/30 bottles not in-use should be stored in a refrigerator, but not in the freezer.

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

Do not use Humulin 70/30 after the expiration date stamped on the label or if it has been frozen.

INSTRUCTIONS FOR INSULIN VIAL USE

NEVER SHARE NEEDLES AND SYRINGES

Correct Syringe Type

Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc). With Humulin 70/30, 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 by placing the used needle in a puncture-resistant disposable container. Properly dispose of the puncture-resistant container as directed by your Health Care Professional.

Preparing the Dose

1. Wash your hands.
2. Carefully shake or rotate the bottle of insulin several times to completely mix the insulin.
3. Inspect the insulin. Humulin 70/30 suspension should look uniformly cloudy or milky. Do not use Humulin 70/30 if you notice anything unusual in its appearance.
4. If using a new Humulin 70/30 bottle, flip off the plastic protective cap, but **do not** remove the stopper. Wipe the top of the bottle with an alcohol swab.
5. Draw an amount of air into the syringe that is equal to the Humulin 70/30 dose. Put the needle through rubber top of the Humulin 70/30 bottle and inject the air into the bottle.
6. Turn the Humulin 70/30 bottle and syringe upside down. Hold the bottle and syringe firmly in one hand and shake gently.
7. Making sure the tip of the needle is in the Humulin 70/30 suspension, withdraw the correct dose of Humulin 70/30 into the syringe.
8. Before removing the needle from the Humulin 70/30 bottle, check the syringe for air bubbles. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push the bubbles out with the plunger and then withdraw the correct dose.
9. Remove the needle from the bottle and lay the syringe down so that the needle does not touch anything.

Injection Instructions

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

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 70/30 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 70/30 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
- 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, use of medications such as beta-blockers, changing 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 hard candy 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 talk to your doctor to discuss possible changes in therapy, meal plans, and/or exercise programs to help you avoid hypoglycemia.

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

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

1. Omitting your insulin or taking less than your 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 type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in DKA (a life-threatening emergency). The first symptoms of DKA 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 DKA, blood and urine tests show large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, 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 (seen as an apparent depression of the skin) or lipohypertrophy (seen as a raised area of the skin). If you notice either of these conditions, talk to your doctor. A change in your injection technique may help alleviate the problem.

Allergy

Local Allergy — Patients occasionally experience redness, swelling, and itching at the site of injection. 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, talk to 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, call your doctor immediately.

ADDITIONAL INFORMATION

Information about diabetes may be obtained from your diabetes educator.

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

Patient Information issued/revised Month dd, yyyy

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for Eli Lilly and Company, Indianapolis, IN 46285, USA

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A1.0 NL 3672 AMP
A2.0 PA 9145 FSAMP

**INFORMATION FOR THE PATIENT
3 ML DISPOSABLE INSULIN DELIVERY DEVICE**

**HUMULIN[®] 70/30 Pen
70% HUMAN INSULIN
ISOPHANE SUSPENSION
AND
30% HUMAN INSULIN INJECTION
(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.

TO OBTAIN AN ACCURATE DOSE, CAREFULLY READ AND FOLLOW THE INSULIN DELIVERY DEVICE USER MANUAL AND THIS "INFORMATION FOR THE PATIENT" INSERT BEFORE USING THIS PRODUCT.

BEFORE EACH INJECTION, YOU SHOULD PRIME THE PEN, A NECESSARY STEP TO MAKE SURE THE PEN IS READY TO DOSE. PRIMING THE PEN IS IMPORTANT TO CONFIRM THAT INSULIN COMES OUT WHEN YOU PUSH THE INJECTION BUTTON AND TO REMOVE AIR THAT MAY COLLECT IN THE INSULIN CARTRIDGE DURING NORMAL USE. IF YOU DO NOT PRIME, YOU MAY RECEIVE TOO MUCH OR TOO LITTLE INSULIN (*see also* INSTRUCTIONS FOR INSULIN PEN USE section).

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.

70/30 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 70/30 is a mixture of 70% Human Insulin Isophane Suspension and 30% Human Insulin Injection, (rDNA origin). It is an intermediate-acting insulin combined with the more rapid onset of action of Regular human insulin. The duration of activity may last up to 24 hours following injection. 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 70/30 is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin 70/30 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously or intramuscularly. The concentration of Humulin 70/30 is 100 units/mL (U-100).

Identification

Human insulin from Eli Lilly and Company has the trademark Humulin.

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.

The Humulin 70/30 Pen is available in boxes of 5 disposable insulin delivery devices ("insulin Pens"). The Humulin 70/30 Pen is not designed to allow any other insulin to be mixed in its cartridge, or for the cartridge to be removed.

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

Always check the appearance of Humulin 70/30 suspension in your insulin Pen before using. A cartridge of Humulin 70/30 contains a small glass bead to assist in mixing. Roll the Pen between the palms 10 times (*see* Figure 1). Holding the Pen by one end, invert it 180° slowly 10 times to allow the small glass bead to travel the full length with each inversion (*see* Figure 2).

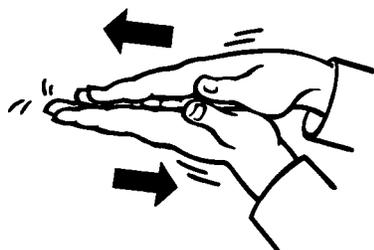


Figure 1.

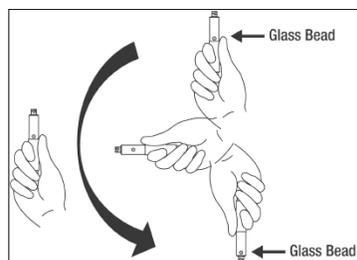


Figure 2.

Humulin 70/30 suspension should look uniformly cloudy or milky after mixing. If not, repeat the above steps until contents are mixed. Pens containing Humulin 70/30 suspension should be examined frequently.

Do not use Humulin 70/30:

- if the insulin substance (the white material) remains visibly separated from the liquid after mixing or
- if there are clumps in the insulin after mixing, or
- if solid white particles stick to the walls of the cartridge, giving a frosted appearance.

If you see anything unusual in the appearance of the Humulin 70/30 suspension in your Pen or notice your insulin requirements changing, talk to your doctor.

Never attempt to remove the cartridge from the Humulin 70/30 Pen. Inspect the cartridge through the clear cartridge holder.

Storage

Not in-use (unopened): Humulin 70/30 Pens not in-use should be stored in a refrigerator, but not in the freezer.

In-use (opened): Humulin 70/30 Pens in-use should **NOT** be refrigerated but should be kept at room temperature [below 86°F (30°C)] away from direct heat and light. The Humulin 70/30 Pen you are currently using must be discarded **10 days** after the first use, even if it still contains Humulin 70/30.

Do not use Humulin 70/30 after the expiration date stamped on the label or if it has been frozen.

INSTRUCTIONS FOR INSULIN PEN USE

It is important to read, understand, and follow the instructions in the Insulin Delivery Device User Manual before using. Failure to follow instructions may result in getting too much or too little insulin. The needle must be changed and the Pen must be primed before each injection to make sure the Pen is ready to dose. Performing these steps before each injection is important to confirm that insulin comes out when you push the injection button, and to remove air that may collect in the insulin cartridge during normal use.

Every time you inject:

- Use a new needle.
- Prime to make sure the Pen is ready to dose.
- Make sure you got your full dose.

NEVER SHARE INSULIN PENS, CARTRIDGES, OR NEEDLES.

PREPARING FOR INJECTION

1. Wash your hands.
2. To avoid tissue damage, choose a site for each injection that is at least 1/2 inch from the previous injection site. The usual sites of injection are abdomen, thighs, and arms.
3. Follow the instructions in your Insulin Delivery Device User Manual to prepare for injection.
4. After injecting the dose, pull the needle out and apply gentle pressure over the injection site for several seconds. **Do not rub the area.**
5. After the injection, remove the needle from the Humulin 70/30 Pen. **Do not reuse needles.**
6. Place the used needle in a puncture-resistant disposable container and properly dispose of the puncture-resistant container as directed by your Health Care Professional.

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 70/30 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 70/30 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
- dizziness
- palpitation
- tremor
- hunger
- restlessness
- tingling in the hands, feet, lips, or tongue
- lightheadedness
- drowsiness
- sleep disturbances
- anxiety
- blurred vision
- slurred speech
- depressed mood
- irritability
- abnormal behavior

- inability to concentrate
- headache
- 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, use of medications such as beta-blockers, changing 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 hard candy 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 talk to your doctor to discuss possible changes in therapy, meal plans, and/or exercise programs to help you avoid hypoglycemia.

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

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

1. Omitting your insulin or taking less than your 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 type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in DKA (a life-threatening emergency). The first symptoms of DKA 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 DKA, blood and urine tests show large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pain, dehydration, loss of consciousness, or death. Therefore, it is important that you obtain medical assistance immediately.

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

Patient Information issued/ revised Month dd, yyyy

Pens manufactured by
Eli Lilly and Company, Indianapolis, IN 46285, USA or
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for Eli Lilly and Company, Indianapolis, IN 46285, USA

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PRINTED IN USA

A2.0 PA 9145 FSAMP

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A1.0 NL 5701 AMP
A3.0 NL 4590 AMP

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

HUMULIN[®] 50/50
50% HUMAN INSULIN
ISOPHANE SUSPENSION
AND
50% HUMAN INSULIN INJECTION
(rDNA ORIGIN)
100 UNITS PER ML (U-100)

WARNINGS

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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.

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.

50/50 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 50/50 is a mixture of 50% Human Insulin Isophane Suspension and 50% Human Insulin Injection (rDNA origin). It is an intermediate-acting insulin combined with the more rapid onset of action of Regular human insulin. The duration of activity may last up to 24 hours following injection. 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 50/50 is dependent on dose, site of injection, blood supply, temperature, and physical activity. Humulin 50/50 is a sterile suspension and is for subcutaneous injection only. It should not be used intravenously or intramuscularly. The concentration of Humulin 50/50 is 100 units/mL (U-100).

Identification

Human insulin from Eli Lilly and Company has the trademark Humulin. 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.

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 prescribed by your doctor.

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

Do not use Humulin 50/50:

- 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 Humulin 50/50 suspension in your bottle or notice your insulin requirements changing, talk to your doctor.

Storage

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

In-use (opened): The Humulin 50/50 bottle you are currently using can be kept unrefrigerated as long as it is kept as cool as possible [below 86°F (30°C)] away from heat and light.

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

INSTRUCTIONS FOR INSULIN VIAL USE

NEVER SHARE NEEDLES AND SYRINGES.

Correct Syringe Type

Doses of insulin are measured in **units**. U-100 insulin contains 100 units/mL (1 mL=1 cc). With Humulin 50/50, 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 by placing the used needle in a puncture-resistant disposable container. Properly dispose of the puncture-resistant container as directed by your Health Care Professional.

98 **Preparing the Dose**

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

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

128 **DOSAGE**

129 Your doctor has told you which insulin to use, how much, and when and how often to inject it.
130 Because each patient's diabetes is different, this schedule has been individualized for you. Your
131 usual dose of Humulin 50/50 may be affected by changes in your diet, activity, or work schedule.
132 Carefully follow your doctor's instructions to allow for these changes. Other things that may
133 affect your Humulin 50/50 dose are:

134 **Illness**

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

139 **Pregnancy**

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

143 **Medication**

144 Insulin requirements may be increased if you are taking other drugs with blood-glucose-raising
145 activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy. Insulin
146 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 Healthcare Professional may be aware of other medications that may affect your diabetes control. Therefore, always discuss any medications you are taking with your doctor.

151 **Exercise**

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

157 **Travel**

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

160 **COMMON PROBLEMS OF DIABETES**

161 **Hypoglycemia (Low Blood Sugar)**

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

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

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

- 176 • sweating • drowsiness
177 • dizziness • sleep disturbances
178 • palpitation • anxiety
179 • tremor • blurred vision
180 • hunger • slurred speech
181 • restlessness • depressed mood
182 • tingling in the hands, feet, lips, or tongue • irritability
183 • lightheadedness • abnormal behavior
184 • inability to concentrate • unsteady movement
185 • headache • personality changes

186 Signs of severe hypoglycemia can include:

- 187 • disorientation • seizures
188 • unconsciousness • death

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

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

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

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

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

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

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

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

216 Hyperglycemia (too much glucose in the blood) may develop if your body has too little insulin.
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- 218 1. Omitting your insulin or taking less than your doctor has prescribed.
- 219 2. Eating significantly more than your meal plan suggests.
- 220 3. Developing a fever, infection, or other significant stressful situation.

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

229 **Lipodystrophy**

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

234 **Allergy**

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

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

244 **ADDITIONAL INFORMATION**

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

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

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