

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.

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.

Humulin N may cause serious side effects, including:

- **swelling of your hands and feet**
- **heart failure.** Taking certain diabetes pills called thiazolidinediones or "TZDs" with Humulin N may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with Humulin N. Your healthcare provider should monitor you closely while you are taking TZDs with Humulin N. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
 - shortness of breath
 - swelling of your ankles or feet
 - sudden weight gain

Treatment with TZDs and Humulin N may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.

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 healthcare provider.

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 N 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 healthcare provider.

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 healthcare provider may be aware of other medications that may affect your diabetes control. Therefore, always discuss any medications you are taking with your doctor.

Before you use Humulin N, tell your healthcare provider if you:

- take any other medicines, especially ones commonly called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with Humulin N.

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.

Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

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

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

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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.

THE PEN MUST BE PRIMED TO A STREAM OF INSULIN (NOT JUST A FEW DROPS) BEFORE EACH INJECTION TO MAKE SURE THE PEN IS READY TO DOSE. YOU MAY NEED TO PRIME A NEW PEN UP TO SIX TIMES BEFORE A STREAM OF INSULIN APPEARS.

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).

Humulin N may cause serious side effects, including:

- **swelling of your hands and feet**
- **heart failure.** Taking certain diabetes pills called thiazolidinediones or "TZDs" with Humulin N may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with Humulin N. Your healthcare provider should monitor you closely while you are taking TZDs with Humulin N. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
 - shortness of breath
 - swelling of your ankles or feet
 - sudden weight gain

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

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.

The Humulin N Pen is available in boxes of 5 prefilled insulin delivery devices ("insulin Pens"). The Humulin N 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.

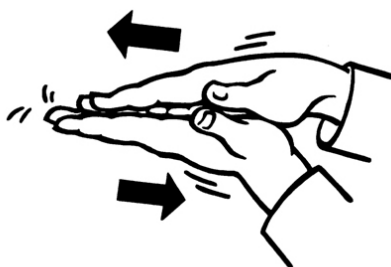


Figure 1.

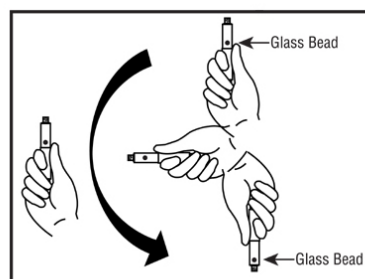


Figure 2.

Always check the appearance of Humulin N suspension in your insulin Pen before using. A cartridge of Humulin N contains a small glass bead to assist in mixing. Roll the Pen back and forth between the palms 10 times (*see* Figure 1). Gently turn the Pen up and down 10 times until the insulin is evenly mixed (*see* Figure 2). If not evenly mixed, repeat the above steps until contents are mixed. Pens containing Humulin N suspension should be examined frequently.

Do not use Humulin N:

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

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

Storage

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

In-use (opened): Humulin N 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 N Pen you are currently using must be discarded **2 weeks** after the first use, even if it still contains Humulin N.

Do not use Humulin N 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 to a stream of insulin (not just a few drops) before each injection to make sure the Pen is ready to dose. You may need to prime a new Pen up to six times before a stream of insulin appears. 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 a stream of insulin (not just a few drops) 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 N 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 healthcare provider.

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 healthcare provider may be aware of other medications that may affect your diabetes control. Therefore, always discuss any medications you are taking with your doctor.

Before you use Humulin N, tell your healthcare provider if you:

- take any other medicines, especially ones commonly called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with Humulin N.

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.

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Lilly

Prefilled Insulin Delivery Device
User Manual

Instructions for Use

Read and follow all of these instructions carefully. If you do not follow these instructions completely, you may get too much or too little insulin.

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 (see page 18)**



Also, read the “Patient Information” enclosed in your Pen box.

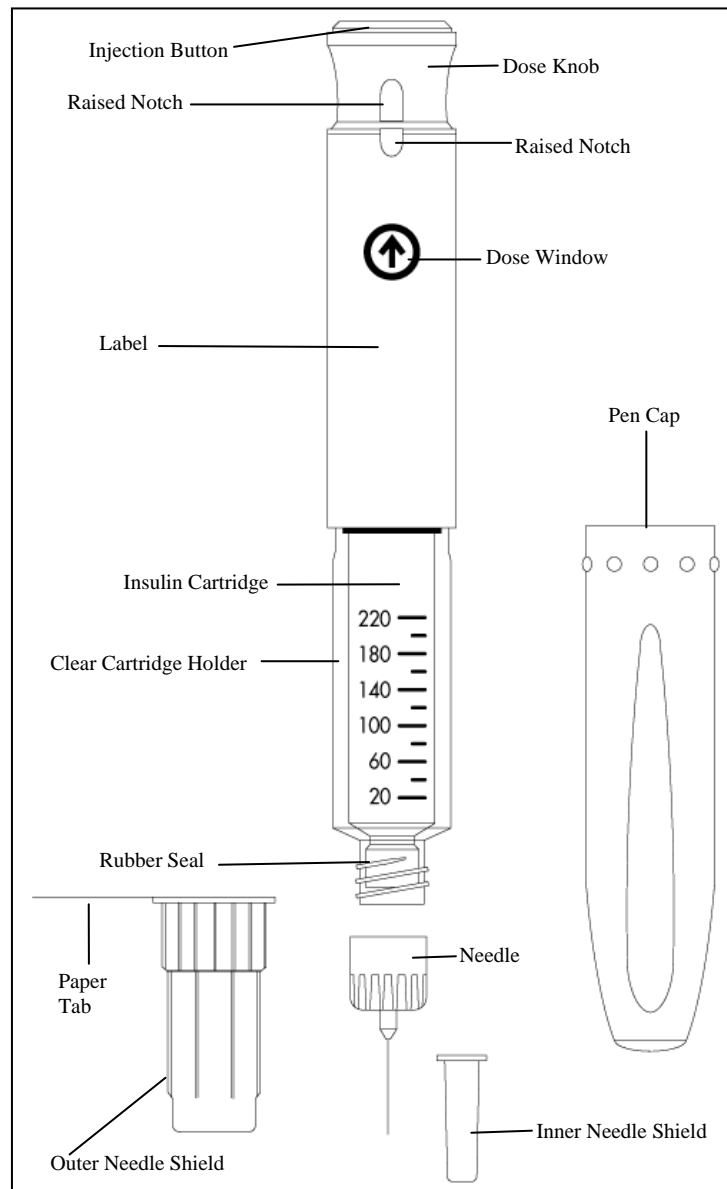
Pen Features

- A multiple dose, prefilled insulin delivery device (“insulin Pen”) containing 3 mL (300 units) of U-100 insulin
- Delivers up to 60 units per dose
- Doses can be dialed by single units

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Pen Parts



Important Notes

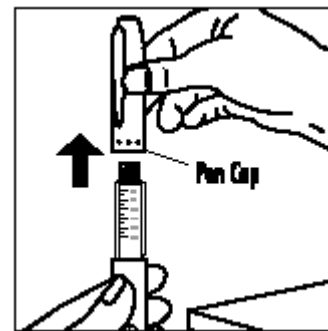
- Read and follow all of these instructions carefully. If you do not follow these instructions completely, you may get too much or too little insulin.
- Use a new needle for each injection.
 - Be sure a needle is completely attached to the Pen before priming, setting the dose and injecting your insulin.
- Prime every time.
 - The Pen must be primed before each injection to make sure the Pen is ready to dose. Performing the priming step 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. See Section III. “Priming the Pen”, pages 10-13.
 - If you do not prime, you may get too much or too little insulin.
- Make sure you get your full dose.
 - To make sure you get your full dose, you must push the injection button all the way down until you see a diamond (♦) or an arrow (➔) in the center of the dose window. See “Following an Injection”, page 18.
- The numbers on the clear cartridge holder give an estimate of the amount of insulin remaining in the cartridge. Do not use these numbers for measuring an insulin dose.
- Do not share your Pen or needles.
- Keep your Pen and needles out of the reach of children.
- Pens that have not been used should be stored in a refrigerator but not in a freezer. Do not use a Pen if it has been frozen. Refer to the “Patient Information” for complete storage instructions.

Important Notes (Continued)

- After a Pen is used for the first time, it should **NOT** be refrigerated but should be kept at room temperature [below 86°F (30°C)] and away from direct heat and light.
- An unrefrigerated Pen should be discarded according to the time specified in the “Patient Information”, even if it still contains insulin.
- Never use a Pen after the expiration date stamped on the label.
- Do not store your Pen with the needle attached. Doing so may allow insulin to leak from the Pen and air bubbles to form in the cartridge. Additionally, with suspension (cloudy) insulins, crystals may clog the needle.
- Always carry an extra Pen in case yours is lost or damaged.
- Follow your Health Care Professional’s instruction for safe handling of needles and disposal of empty pens.
- This Pen is not recommended for use by blind or visually impaired persons without the assistance of a person trained in the proper use of the product.
- The directions regarding needle handling are not intended to replace local, Health Care Professional, or institutional policies.
- **Any changes in insulin should be made cautiously and only under medical supervision.**

I. Preparing the Pen

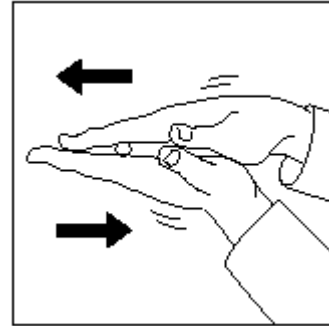
1. Before proceeding, refer to the “Patient Information” for instructions on checking the appearance of your insulin.
2. Check the label on the Pen to be sure the Pen contains the type of insulin that has been prescribed for you.
3. Always wash your hands before preparing your Pen for use.
4. Pull the Pen cap to remove.



I. Preparing the Pen (Continued)

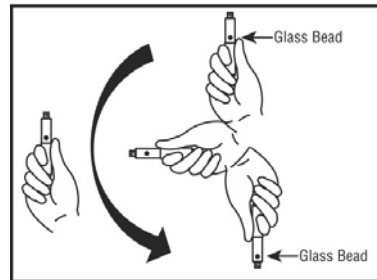
5. If your insulin is a suspension (cloudy):

- a. Roll the Pen back and forth 10 times then perform step b.

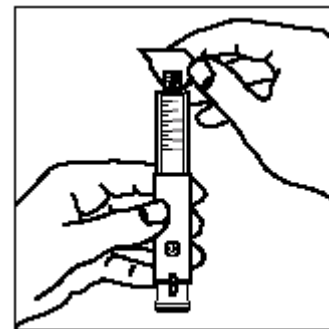


- b. Gently turn the Pen up and down 10 times until the insulin is evenly mixed.

Note: Suspension (cloudy) insulin cartridges contain a small glass bead to assist in mixing.



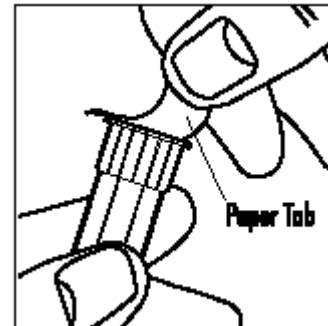
6. Use an alcohol swab to wipe the rubber seal on the end of the Pen.



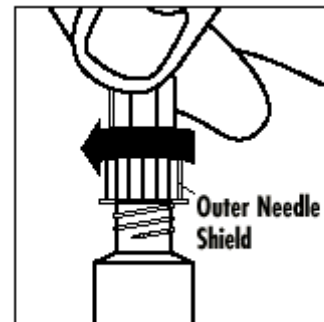
II. Attaching the Needle

This device is suitable for use with Becton Dickinson and Company's insulin pen needles.

1. Always use a new needle for each injection. Do not push injection button without a needle attached. Storing the Pen with the needle attached may allow insulin to leak from the Pen and air bubbles to form in the cartridge.
2. Remove the paper tab from the outer needle shield.

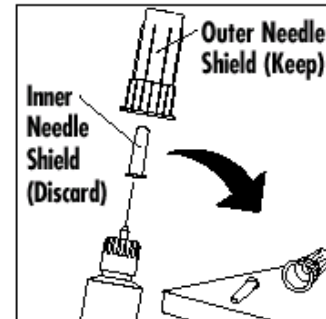


3. Attach the capped needle onto the end of the Pen by turning it clockwise until tight.



II. Attaching the Needle (Continued)

4. Hold the Pen with the needle pointing up and remove the **outer needle shield**. Keep it to use during needle removal.

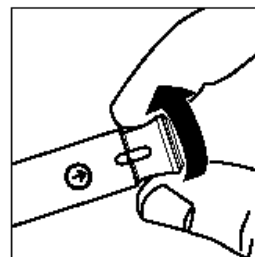


5. Remove the inner needle shield and discard.

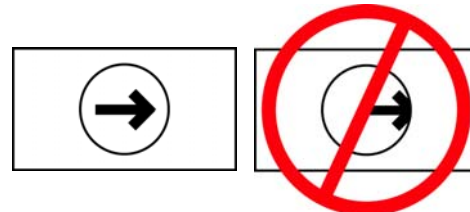
III. Priming the Pen

- **Prime every time.** The Pen must be primed to a stream of insulin (not just a few drops) before each injection to make sure the Pen is ready to dose.
- You may need to prime a new Pen up to six times before a stream of insulin appears.
- **If you do not prime, you may get too much or too little insulin.**
- **Always use a new needle for each injection.**

1. Make sure the arrow (→) is in the center of the dose window as shown.

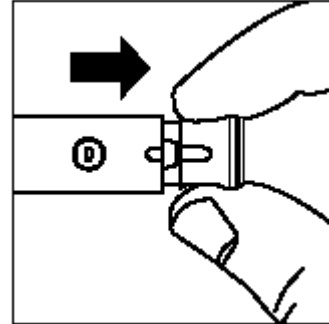


2. If you do not see the arrow in the center of the dose window, push in the injection button fully and turn the dose knob until the arrow is seen in the center of the dose window.

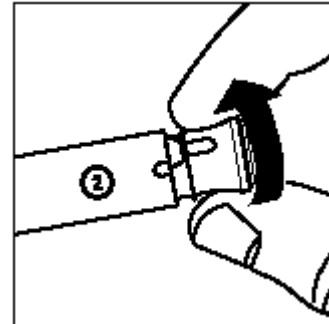


III. Priming the Pen (Continued)

3. With the arrow in the center of the dose window, pull the dose knob out in the direction of the arrow until a “0” is seen in the dose window.



4. Turn the dose knob clockwise until the number “2” is seen in the dose window. If the number you have dialed is too high, simply turn the dose knob backward until the number “2” is seen in the dose window.

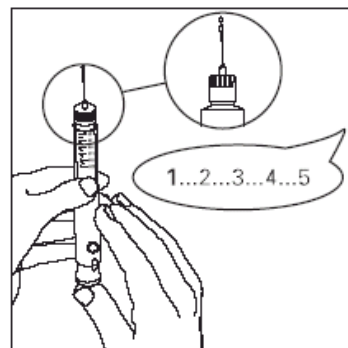


III. Priming the Pen (Continued)

5. Hold your Pen with the needle pointing straight up. Tap the clear cartridge holder gently with your finger so any air bubbles collect near the top.

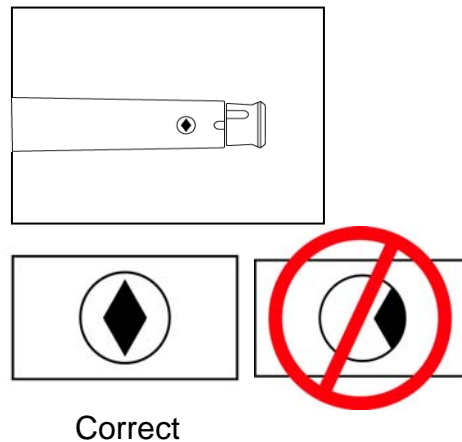
Using your thumb, if possible, push in the injection button completely. Keep pressing and continue to hold the injection button **firmly** while counting **slowly** to 5. You should see a stream of insulin come out of the tip of the needle.

If a stream of insulin does not come out of the tip of the needle, repeat steps 1 through 5. If after six attempts a stream of insulin does not come out of the tip of the needle, change the needle. Repeat steps 1 through 5 up to two more times. If you are still unable to get insulin flowing out of the needle, **do NOT use** the Pen. Contact your Health Care Professional or Lilly.



III. Priming the Pen (Continued)

6. At the completion of the priming step, a diamond (◆) must be seen in the center of the dose window. If a diamond (◆) is not seen in the center of the dose window, continue pushing on the injection button until you see a diamond (◆) in the center of the dose window.



Note: A small air bubble may remain in the cartridge after the completion of the priming step. If you have properly primed the Pen, this small air bubble will not affect your insulin dose.

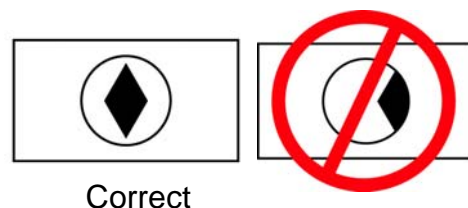
7. Now you are ready to set your dose. See next page.

IV. Setting a Dose

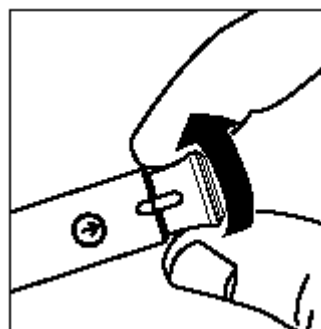
- **Always use a new needle for each injection. Storing the Pen with the needle attached may allow insulin to leak from the Pen and air bubbles to form in the cartridge.**
- **Caution: Do not push in the injection button while setting your dose. Failure to follow these instructions carefully may result in getting too much or too little insulin. If you accidentally push the injection button while setting your dose, you must prime the Pen again before injecting your dose. See Section III. “Priming the Pen”, pages 10-13.**

1. A diamond must be seen in the center of the dose window before setting your dose.

If you do not see a diamond in the center of the dose window, the Pen has not been primed correctly and you are not ready to set your dose. Before continuing, repeat the priming steps.

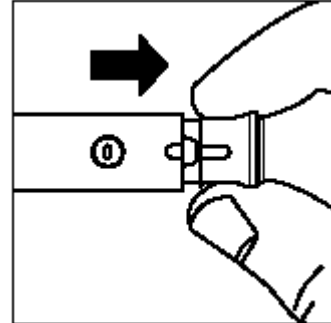


2. Turn the dose knob clockwise until the arrow (➡) is seen in the center of the dose window and the notches on the Pen and dose knob are in line.

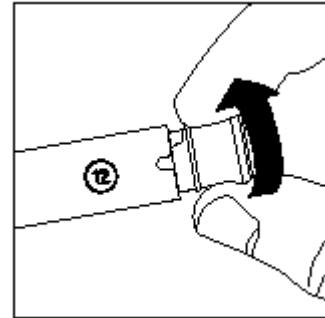


IV. Setting a Dose (Continued)

3. With the arrow (→) in the center of the dose window, pull the dose knob out in the direction of the arrow until a “0” is seen in the dose window. A dose cannot be dialed until the dose knob is pulled out.



4. Turn the dose knob clockwise until your dose is seen in the dose window. If the dose you have dialed is too high, simply turn the dose knob backward until the correct dose is seen in the dose window.



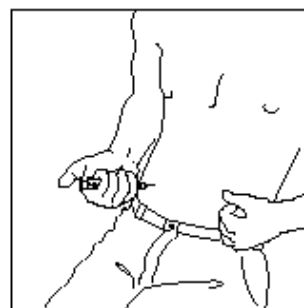
5. If you cannot dial your full dose, see the “Questions and Answers” section, Question 5, at the end of this manual.

V. Injecting a Dose

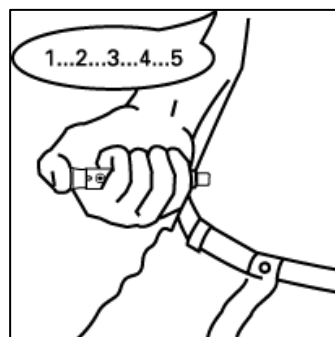
- **Always use a new needle for each injection. Storing the Pen with the needle attached may allow insulin to leak from the Pen and air bubbles to form in the cartridge.**
- **Caution: Do not attempt to change the dose after you begin to push in the injection button. Failure to follow these instructions carefully may result in getting too much or too little insulin.**
- **The effort needed to push in the injection button may increase while you are injecting your insulin dose. If you cannot completely push in the injection button, refer to the “Questions and Answers” section, Question 7, at the end of this manual.**
- **Do not inject a dose unless the Pen is primed, just before injection, or you may get too much or too little insulin.**
- **If you have set a dose and pushed in the injection button without a needle attached or if no insulin comes out of the needle, see the “Questions and Answers” section, Questions 1 and 2.**

V. Injecting a Dose (Continued)

1. Wash hands. Prepare the skin and use the injection technique recommended by your Health Care Professional.
2. Insert the needle into your skin. Inject the insulin by using your thumb, if possible, to push in the injection button completely.



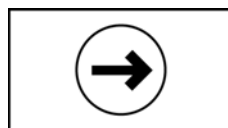
3. Keep pressing and continue to hold the injection button **firmly** while counting **slowly** to 5.



4. When the injection is done, a diamond (♦) or an arrow (➡) must be seen in the center of the dose window. This means your full dose has been delivered. **If you do not see a diamond or an arrow in the center of the dose window, you did not get your full dose. Contact your Health Care Professional for additional instructions.**



Correct

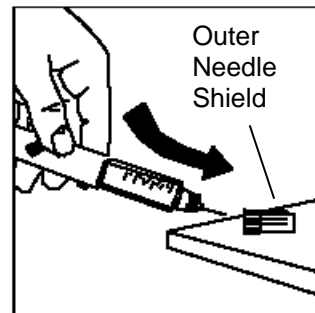
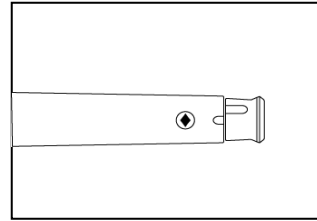


Correct



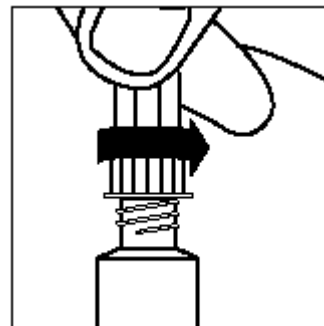
VI. Following an Injection

1. Make sure you got your full dose by checking that the injection button has been completely pushed in and you can see a diamond (◆) or an arrow (➡) in the center of the dose window. If you do not see a diamond (◆) or an arrow (➡) in the center of the dose window, you have not received your full dose. Contact your Health Care Professional for additional instructions.
2. Carefully replace the **outer needle shield** as instructed by your Health Care Professional.

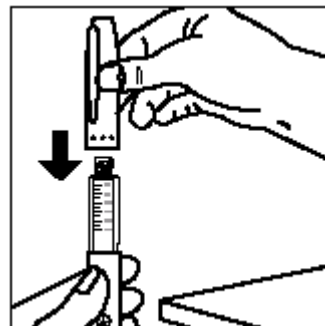


VI. Following an Injection (Continued)

3. Remove the capped needle by turning it counterclockwise. Place the used needle in a puncture-resistant disposable container and properly throw it away as directed by your Health Care Professional.



4. Replace the cap on the Pen.



5. The Pen that you are using should **NOT** be refrigerated but should be kept at room temperature [below 86°F (30°C)] and away from direct heat and light. It should be discarded according to the time specified in the “Patient Information”, even if it still contains insulin.

Do not store or dispose of the Pen with a needle attached. Storing the Pen with the needle attached may allow insulin to leak from the Pen and air bubbles to form in the cartridge.

Questions and Answers

Problem	Action
1. Dose dialed and injection button pushed in without a needle attached.	To obtain an accurate dose you must: 1) Attach a new needle. 2) Push in the injection button completely (even if a "0" is seen in the window) until a diamond (♦) or an arrow (➡) is seen in the center of the dose window. 3) Prime the Pen.
2. Insulin does not come out of the needle. Note: You may need to prime a new pen up to six times before a stream of insulin appears.	To obtain an accurate dose you must: 1) Attach a new needle. 2) Push in the injection button completely (even if a "0" is seen in the window) until a diamond (♦) or an arrow (➡) is seen in the center of the dose window. 3) Prime the Pen. See Section III. "Priming the Pen", pages 10-13.

Questions and Answers (Continued)

Problem	Action
3. Why do I need to prime a new pen up to six times?	The first time you use a new pen, priming up to six times may be needed to see a stream of insulin come out of the tip of the needle. If you do not prime until you see a stream of insulin, you may get too much or too little insulin.
4. Wrong dose (too high or too low) dialed.	If you have not pushed in the injection button, simply turn the dose knob backward or forward to correct the dose.
5. Not sure how much insulin remains in the cartridge.	Hold the Pen with the needle end pointing down. The scale (20 units between marks) on the clear cartridge holder shows an estimate of the number of units remaining. These numbers should not be used for measuring an insulin dose.

Questions and Answers (Continued)

Problem	Action
6. Full dose cannot be dialed.	The Pen will not allow you to dial a dose greater than the number of insulin units remaining in the cartridge. For example, if you need 31 units and only 25 units remain in the Pen, you will not be able to dial past 25. Do not attempt to dial past this point. (The insulin that remains is unusable and not part of the 300 units.) If a partial dose remains in the Pen you may either: 1) Give the partial dose and then give the remaining dose using a new Pen, or 2) Give the full dose with a new Pen.
7. A small amount of insulin remains in the cartridge but a dose cannot be dialed.	The Pen design prevents the cartridge from being completely emptied. The Pen has delivered 300 units of usable insulin.

Questions and Answers (Continued)

Problem	Action
8. Cannot completely push in the injection button when priming the Pen or injecting a dose.	<ol style="list-style-type: none">1) Needle is not attached or is clogged.<ol style="list-style-type: none">a. Attach a new needle.b. Push in the injection button completely (even if a “0” is seen in the window) until a diamond (♦) or an arrow (➔) is seen in the center of the dose window.c. Prime the Pen.2) If you are sure insulin is coming out of the needle, push in the injection button more slowly to reduce the effort needed and maintain a constant pressure until the injection button is completely pushed in.

**For additional information call,
1-800-LILLY-RX (1-800-545-5979),
or visit our website at www.Humalog.com**

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