HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use HUMULIN N safely and effectively. See full prescribing information for HUMULIN N.
HUMULIN® N (human insulin [rDNA origin]) isophane suspension), injectable suspension, for subcutaneous use
Initial U.S. Approval: 1982

---------- RECENT MAJOR CHANGES ----------

Warnings and Precautions (5.5) 03/2013

---------- INDICATIONS AND USAGE ----------

HUMULIN N is an intermediate-acting human insulin indicated to improve glycemic control in adult and pediatric patients with diabetes mellitus. (1)

---------- DOSAGE AND ADMINISTRATION ----------

- Only administer subcutaneously (in abdominal wall, thigh, upper arm, or buttocks). (2.2)
- Individualize and adjust dosage based on metabolic needs, blood glucose monitoring results and glycemic control goal. (2.3)
- See Full Prescribing Information for dosage adjustments due to drug interactions and patients with renal and hepatic impairment. (2.3, 2.4)
- May use with a meal-time insulin if indicated. (2.4)

---------- DOSAGE FORMS AND STRENGTHS ----------

Injectable suspension 100 units per mL (U-100) available as 10 mL vials or 3 mL prefilled pens. (3)

---------- CONTRAINDICATIONS ----------

- During episodes of hypoglycemia. (4)
- In patients with hypersensitivity to HUMULIN N or any of its excipients. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- *Changes in Insulin Regimen*: Carry out under close medical supervision and increase frequency of blood glucose monitoring. (5.1)
- *Hypoglycemia*: May be life-threatening. Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.2, 7, 8.6, 8.7)
- *Hypersensitivity Reactions*: May be life-threatening. Discontinue HUMULIN N, monitor and treat if indicated. (5.3)
- *Hypokalemia*: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated. (5.4)
- *Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs)*: Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs. (5.5)

---------- ADVERSE REACTIONS ----------

Adverse reactions observed with HUMULIN N include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, weight gain, and edema. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-LillyRx (1-800-545 5979) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- *Drugs that Affect Glucose Metabolism*: Adjustment of insulin dosage may be needed. (7.1, 7.2, 7.3)
- *Anti-Adrenergic Drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine)*: Signs and symptoms of hypoglycemia may be reduced or absent. (5.2, 7.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 11/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Important Administration Instructions
2.2 Route of Administration
2.3 Dosage Information
2.4 Dosage Adjustment due to Drug Interactions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Changes in Insulin Regimen
5.2 Hypoglycemia
5.3 Hypersensitivity Reactions
5.4 Hypokalemia
5.5 Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
7.1 Drugs That May Increase the Risk of Hypoglycemia
7.2 Drugs That May Decrease the Blood Glucose Lowering Effect of HUMULIN N
7.3 Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of HUMULIN N
7.4 Drugs That May Blunt Signs and Symptoms of Hypoglycemia
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
16.2 Storage and Handling
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

HUMULIN N is an intermediate-acting recombinant human insulin indicated to improve glycemic control in adults and pediatric patients with diabetes mellitus.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Inspect HUMULIN N visually before use. It should not contain particulate matter and should appear uniformly cloudy after mixing. Do not use HUMULIN N if particulate matter is seen.

2.2 Route of Administration

HUMULIN N should only be administered subcutaneously.

Administer in the subcutaneous tissue of the abdominal wall, thigh, upper arm, or buttocks. To reduce the risk of lipodystrophy, rotate the injection site within the same region from one injection to the next *[see Adverse Reactions (6)]*.

Do not administer HUMULIN N intravenously or intramuscularly and do not use HUMULIN N in an insulin infusion pump.

2.3 Dosage Information

Individualize and adjust the dosage of HUMULIN N based on the individual's metabolic needs, blood glucose monitoring results and glycemic control goal.

Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness *[see Warnings and Precautions (5.1, 5.2), and Use in Specific Populations (8.6, 8.7)]*.

2.4 Dosage Adjustment due to Drug Interactions

Dosage adjustment may be needed when HUMULIN N is coadministered with certain drugs *[see Drug Interactions (7)]*.

Dosage adjustment may be needed when switching from another insulin to HUMULIN N *[see Warnings and Precautions (5.1)]*.

Instructions for Mixing with Other Insulins

HUMULIN N may be used with a prandial insulin if indicated. HUMULIN N may be mixed with HUMULIN R or HUMALOG before injection.

- If HUMULIN N is mixed with HUMULIN R, HUMULIN R should be drawn into the syringe first. Injection should occur immediately after mixing.
- If HUMULIN N is mixed with HUMALOG, HUMALOG should be drawn into the syringe first. Injection should occur immediately after mixing.

3 DOSAGE FORMS AND STRENGTHS

HUMULIN N injectable suspension: 100 units per mL (U-100) is available as:

- 10 mL vials
- 3 mL prefilled pens

4 CONTRAINDICATIONS

HUMULIN N is contraindicated:

- During episodes of hypoglycemia *[see Warnings and Precautions (5.2)]*, and
- In patients who have had hypersensitivity reactions to HUMULIN N or any of its excipients *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Changes in Insulin Regimen

Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia *[see Warnings and Precautions (5.2)]* or hyperglycemia. These changes should be made cautiously and under close medical supervision and the frequency of blood glucose monitoring should be increased.

5.2 Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulins, including HUMULIN N. Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery).

Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) *[see Drug Interactions (7)]*, or in patients who experience recurrent hypoglycemia.

Risk Factors for Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of HUMULIN N may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature *[see Clinical Pharmacology (12.2)]*. Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication *[see Drug Interactions (7)]*. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia *[see Use in Specific Populations (8.6, 8.7)]*.

Risk Mitigation Strategies for Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

5.3 Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including HUMULIN N. If hypersensitivity reactions occur, discontinue HUMULIN N; treat per standard of care and monitor until symptoms and signs resolve *[see Adverse Reactions (6)]*. HUMULIN N is contraindicated in patients who have had hypersensitivity reactions to HUMULIN N or any of its excipients *[see Contraindications (4)]*.

5.4 Hypokalemia

All insulin products, including HUMULIN N, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

5.5 Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin, including HUMULIN N, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

6 ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere in the labeling:

- Hypoglycemia *[see Warnings and Precautions (5.2)]*.
- Hypokalemia *[see Warnings and Precautions (5.4)]*.

The following additional adverse reactions have been identified during post-approval use of HUMULIN N. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure.

Allergic Reactions

Some patients taking HUMULIN N have experienced erythema, local edema, and pruritus at the site of injection. These conditions were usually self-limiting. Severe cases of generalized allergy (anaphylaxis) have been reported *[see Warnings and Precautions (5.3)]*.

Peripheral Edema

Some patients taking HUMULIN N have experienced sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Lipodystrophy

Administration of insulin subcutaneously, including HUMULIN N, has resulted in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) *[see Dosage and Administration (2.2)]* in some patients.

Weight gain

Weight gain has occurred with some insulin therapies including HUMULIN N and has been attributed to the anabolic effects of insulin and the decrease in glycosuria.

Immunogenicity

Development of antibodies that react with human insulin have been observed with all insulin, including HUMULIN N.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase the Risk of Hypoglycemia

The risk of hypoglycemia associated with HUMULIN N use may be increased when co-administered with antidiabetic agents, salicylates, sulfonamide antibiotics, monoamine oxidase inhibitors, fluoxetine, disopyramide, fibrates, propoxyphene, pentoxifylline, ACE inhibitors, angiotensin II receptor blocking agents, and somatostatin analogs (e.g., octreotide). Dose adjustment and increased frequency of glucose monitoring may be required when HUMULIN N is co-administered with these drugs.

7.2 Drugs That May Decrease the Blood Glucose Lowering Effect of HUMULIN N

The glucose lowering effect of HUMULIN N may be decreased when co-administered with corticosteroids, isoniazid, niacin, estrogens, oral contraceptives, phenothiazines, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, albuterol, terbutaline), somatropin, atypical antipsychotics, glucagon, protease inhibitors, and thyroid hormones. Dose adjustment and increased frequency of glucose monitoring may be required when HUMULIN N is co-administered with these drugs.

7.3 Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of HUMULIN N

The glucose lowering effect of HUMULIN N may be increased or decreased when co-administered with beta-blockers, clonidine, lithium salts, and alcohol. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

Dose adjustment and increased frequency of glucose monitoring may be required when HUMULIN N is co-administered with these drugs.

7.4 Drugs That May Blunt Signs and Symptoms of Hypoglycemia

The signs and symptoms of hypoglycemia *[see Warnings and Precautions (5.2)]* may be blunted when beta-blockers, clonidine, guanethidine, and reserpine are co-administered with HUMULIN N.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

Risk Summary

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. This background risk is increased in pregnancies complicated by hyperglycemia and may be decreased with good metabolic control. It is essential for patients with diabetes or history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. In patients with diabetes or gestational diabetes, insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients. Therefore, female patients should be advised to tell their physicians if they intend to become, or if they become pregnant while taking HUMULIN N.

Human Data

While there are no adequate and well-controlled studies of HUMULIN N in pregnant women, evidence from published literature suggests that good glycemic control in patients with diabetes during pregnancy provides significant maternal and fetal benefits.

Animal Data

Reproduction and fertility toxicity studies were not performed in animals.

8.3 Nursing Mothers

Endogenous insulin is present in human milk; it is unknown whether HUMULIN N is present in human milk. Insulin orally ingested is degraded in the gastrointestinal tract. No adverse reactions associated with infant exposure to insulin through the consumption of human milk have been reported. Good glucose control supports lactation in patients with diabetes. Women with diabetes who are lactating may require adjustments in their insulin dose.

8.4 Pediatric Use

HUMULIN N has not been studied in pediatric patients. As in adults, the dosage of HUMULIN N in pediatric patients must be individualized based on metabolic needs, treatment goal and blood glucose monitoring results.

8.5 Geriatric Use

The effect of age on the pharmacokinetics and pharmacodynamics of HUMULIN N has not been studied *[see Clinical Pharmacology (12.3)]*. Patients with advanced age using any insulin, including HUMULIN N, may be at increased risk of hypoglycemia due to co-morbid disease and polypharmacy *[see Warnings and Precautions (5.2)]*.

8.6 Renal Impairment

The effect of renal impairment on the pharmacokinetics and pharmacodynamics of HUMULIN N has not been studied *[see Clinical Pharmacology (12.3)]*. Patients with renal impairment are at increased risk of hypoglycemia and may require more frequent HUMULIN N dose adjustment and more frequent blood glucose monitoring.

8.7 Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics and pharmacodynamics of HUMULIN N has not been studied *[see Clinical Pharmacology (12.3)]*. Patients with hepatic impairment are at increased risk of hypoglycemia and may require more frequent HUMULIN N dose adjustment and more frequent blood glucose monitoring.

10 OVERDOSAGE

Excess insulin administration may cause hypoglycemia and hypokalemia *[see Warnings and Precautions (5.2, 5.4)]*. Mild episodes of hypoglycemia can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or physical activity level may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

11 DESCRIPTION

HUMULIN N (human insulin [rDNA origin] isophane suspension) is a human insulin suspension. Human insulin is produced by recombinant DNA technology utilizing a non-pathogenic laboratory strain of *Escherichia coli*. HUMULIN N is a suspension of crystals produced from combining human insulin and protamine sulfate under appropriate conditions for crystal formation. The amino acid sequence of HUMULIN N is identical to human insulin and has the empirical formula $C_{257}H_{383}N_{65}O_{77}S_6$ with a molecular weight of 5808.

HUMULIN N is a sterile white suspension. Each milliliter of HUMULIN N contains 100 units of insulin human, 0.35 mg of protamine sulfate, 16 mg of glycerin, 3.78 mg of dibasic sodium phosphate, 1.6 mg of metacresol, 0.65 mg of phenol, zinc oxide

content adjusted to provide 0.025 mg zinc ion, and Water for Injection. The pH is 7.0 to 7.5. Sodium hydroxide and/or hydrochloric acid may be added during manufacture to adjust the pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

HUMULIN N lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulins inhibit lipolysis and proteolysis, and enhance protein synthesis.

12.2 Pharmacodynamics

HUMULIN N is an intermediate-acting insulin with a slower onset of action and a longer duration of activity than that of regular human insulin. In a study in which healthy subjects (n=16) received subcutaneous injections of HUMULIN N (0.4 unit/kg) on 4 occasions, the median maximum effect occurred at 6.5 hours (range: 2.8 to 13 hours). In this study, insulin activity was measured by the rate of glucose infusions.

The time course of action of insulin, such as HUMULIN N may vary in different individuals or within the same individual. The parameters of HUMULIN N activity (time of onset, peak time, and duration) as designated in Figure 1 should be considered only as general guidelines. The rate of insulin absorption and consequently the onset of activity is known to be affected by the site of injection, physical activity level, and other variables *[see Warnings and Precautions (5.2)]*.

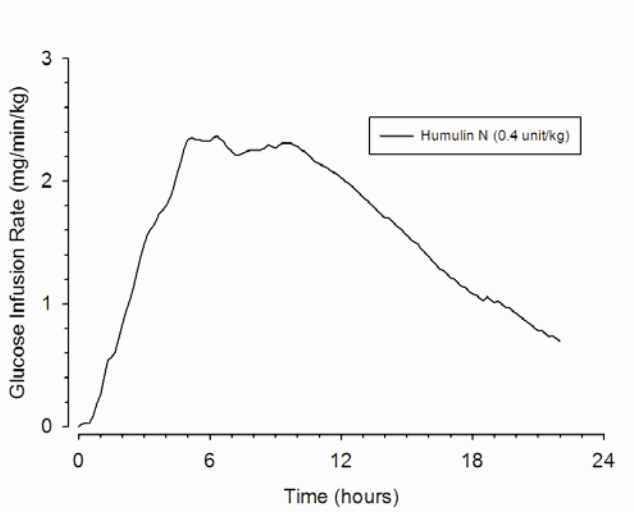

Figure 1: Mean Insulin Activity Versus Time Profile After Subcutaneous Injection of HUMULIN N (0.4 unit/kg) in Healthy Subjects.

12.3 Pharmacokinetics

Absorption — In healthy subjects given subcutaneous doses of HUMULIN N (0.4 unit/kg), median peak serum concentration of insulin occurred at approximately 4 hours (range: 1 to 12 hours) after dosing.

Metabolism — The uptake and degradation of insulin occurs predominantly in liver, kidney, muscle, and adipocytes, with the liver being the major organ involved in the clearance of insulin.

Elimination — Because of the absorption-rate limited kinetics of insulin mixtures, a true half-life cannot be accurately estimated from the terminal slope of the concentration versus time curve. In healthy subjects given subcutaneous doses of HUMULIN N (0.4 unit/kg), the mean apparent half-life was approximately 4.4 hours (range: 1-84 hours).

Specific Populations

The effects of age, gender, race, obesity, pregnancy, or smoking on the pharmacokinetics of HUMULIN N have not been studied.

Careful glucose monitoring and dose adjustments of insulin, including HUMULIN N, may be necessary in patients with renal or hepatic dysfunction *[see Use in Specific Populations (8.6, 8.7)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity and fertility studies were not performed in animals. Biosynthetic human insulin was not genotoxic in the *in vivo* sister chromatid exchange assay and the *in vitro* gradient plate and unscheduled DNA synthesis assays.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

HUMULIN N 100 units per mL (U-100) is available as:

10 mL vials	NDC 0002-8315-01 (HI-310)
5 x 3 mL prefilled pen	NDC 0002-8730-59 (HP-8730)

16.2 Storage and Handling

Protect from heat and light. Do not freeze. Do not use after the expiration date.

Not In-Use (Unopened) HUMULIN N Vials

Refrigerated

Store in a refrigerator (36° to 46°F [2° to 8°C]), but not in the freezer. Do not use if it has been frozen.

Room Temperature

If stored at room temperature, below 86°F (30°C) the vial must be discarded after 31days.

In-Use (Opened) HUMULIN N Vials

Refrigerated

Store in a refrigerator (36° to 46°F [2° to 8°C]), but not in the freezer. Do not use if it has been frozen. Vials must be used within 31 days or be discarded, even if they still contain HUMULIN N.

Room Temperature

If stored at room temperature, below 86°F (30°C) the vial must be discarded after 31 days, even if the vial still contains HUMULIN N.

Not In-Use (Unopened) HUMULIN N Pen

Refrigerated

Store in a refrigerator (36° to 46°F [2° to 8°C]), but not in the freezer. Do not use if it has been frozen.

Room Temperature

If stored at room temperature, below 86°F (30°C) the pen must be discarded after 14 days.

In-Use (Opened) HUMULIN N Pen

Refrigerated

Do NOT store in a refrigerator.

Room Temperature

Store at room temperature, below 86°F (30°C) and the pen must be discarded after 14 days, even if the pen still contains HUMULIN N. See storage table below:

	Not In-Use (Unopened) Refrigerated	**Not In-Use (Unopened) Room Temperature**	**In-Use (Opened)**
10 mL vial	Until expiration date	31 days	31 days, refrigerated/room temperature
3 mL pen	Until expiration date	14 days	14 days, room temperature. **Do not refrigerate.**

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Hypoglycemia

Instruct patients on self-management procedures including glucose monitoring, proper injection technique, and management of hypoglycemia and hyperglycemia especially at initiation of HUMULIN N therapy. Instruct patients on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, and skipped meals. Instruct patients on the management of hypoglycemia.

Inform patients that their ability to concentrate and react may be impaired as a result of hypoglycemia. Advise patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery *[see Warnings and Precautions (5.2)]*.

Inform patients that accidental mix-ups between HUMULIN N and other insulins have been reported. Instruct patients to always carefully check that they are administering the correct insulin (e.g., by checking the insulin label before each injection) to avoid medication errors between HUMULIN N and other insulins.

Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with HUMULIN N. Inform patients on the symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.3)]*.

Females with Reproductive Potential

Advise females of reproductive potential with diabetes to inform their doctor if they are pregnant or are contemplating pregnancy *[see Use in Specific Populations (8.1)]*.

Visual Inspection Prior to Use

Instruct patients to visually inspect HUMULIN N before use and to use HUMULIN N only if it contains no particulate matter and appears uniformly cloudy after mixing *[see Dosage and Administration (2.1)]*.

Expiration Date

Instruct patients not to use HUMULIN N after the printed expiration date.

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

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PATIENT INFORMATION
HUMULIN® (HU-mu-lin) N
(human insulin [rDNA origin] isophane suspension)

What is HUMULIN N?

- HUMULIN N is a man-made insulin that is used to control high blood sugar in adults and children with diabetes mellitus.

Who should not use HUMULIN N?
Do not use HUMULIN N if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to HUMULIN N or any of the ingredients in HUMULIN N.

Before using HUMULIN N, tell your healthcare provider about all your medical conditions including, if you:

- **have liver or kidney problems.**
- 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.
- are pregnant, planning to become pregnant, or are breastfeeding.
- are taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

Before you start using HUMULIN N, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use HUMULIN N?

- Read the **Instructions for Use** that come with your HUMULIN N.
- Use HUMULIN N exactly as your healthcare provider tells you to.
- Know the type and strength of insulin you use. **Do not** change the type of insulin you use unless your healthcare provider tells you to. The amount of insulin and the best time for you to take your insulin may need to change if you use different types of insulin.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.

Your HUMULIN N dose may need to change because of:

- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet.

What should I avoid while using HUMULIN N?
While using HUMULIN N do not:

- Drive or operate heavy machinery, until you know how HUMULIN N affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of HUMULIN N?
HUMULIN N may cause serious side effects that can lead to death, including:

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability, or mood changes, hunger.
- **serious allergic reaction (whole body reaction). Get medical help right away, if you have any of these symptoms of an allergic reaction:**
  - a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **low potassium in your blood (hypokalemia).**
- **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.

Get emergency medical help if you have:

- trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of HUMULIN N include:

- low blood sugar (hypoglycemia), allergic reactions including reactions at the injection site, skin thickening or pits at the injection site (lipodystrophy), itching, rash, weight gain, and swelling of your hands and feet.

These are not all the possible side effects of HUMULIN N. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of HUMULIN N:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about HUMULIN N that is written for health professionals. Do not use HUMULIN N for a condition for which it was not prescribed. Do not give HUMULIN N to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in HUMULIN N?

Active Ingredient: insulin human (rDNA origin)

Inactive Ingredients: protamine sulfate, glycerin, dibasic sodium phosphate, metacresol, phenol, zinc oxide, water for injection, hydrochloric acid or sodium hydroxide

For more information, call 1-800-545-5979 or go to www.humulin.com.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: Month DD, YYYY

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

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Instructions for Use

HUMULIN® (HU-mu-lin) N

(human insulin [rDNA origin] isophane suspension)

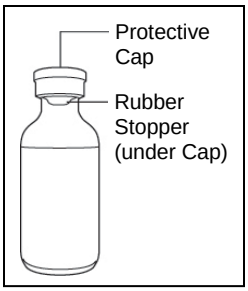
vial (100 Units/mL, U-100)

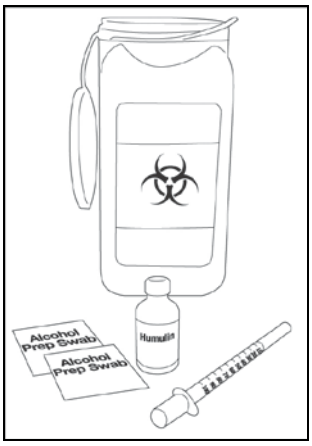
Read the Instructions for Use before you start taking HUMULIN N and each time you get a new HUMULIN N vial. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Do not share your syringes or needles with anyone else. You may give an infection to them or get an infection from them.

Supplies needed to give your injection:

- a HUMULIN N vial
- a U-100 insulin syringe and needle
- 2 alcohol swabs
- 1 sharps container for throwing away used needles and syringes. See **"Disposing of used needles and syringes"** at the end of these instructions.

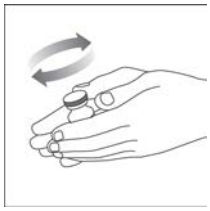
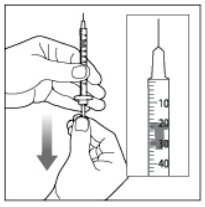


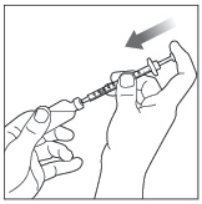
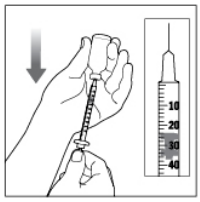
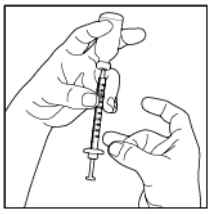
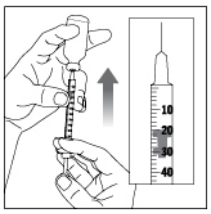
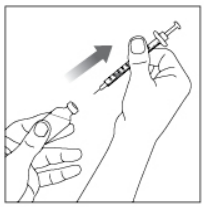


Preparing your HUMULIN N dose:

- Wash your hands with soap and water.
- **Check the HUMULIN N label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.**
- **Do not** use HUMULIN N past the expiration date printed on the label or 31 days after you first use it.

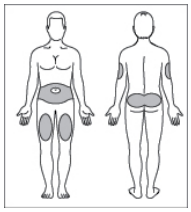
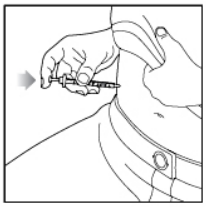
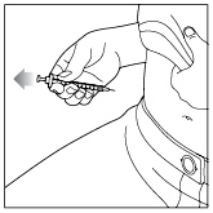
- **Always use a new needle for each injection** to help ensure sterility and prevent blocked needles.

Step 1: Gently roll the vial between the palms of your hands at least 10 times.	
Step 2: Invert the vial at least 10 times. Do not shake. **Mixing is important** to make sure you get the right dose. Humulin N should look white and cloudy after mixing. **Do not** use it if it looks clear or contains any lumps or particles.	
Step 3: If you are using a new vial, pull off the plastic Protective Cap, but **do not** remove the Rubber Stopper.	
Step 4: Wipe the Rubber Stopper with an alcohol swab.	
Step 5: Hold the syringe with the needle pointing up. Pull down on the Plunger until the tip of the Plunger reaches the line for the number of units for your prescribed dose.	 (Example Dose: 20 units shown)
Step 6: Push the needle through the Rubber Stopper of the vial.	

Step 7: Push the plunger all the way in. This puts air into the vial.	
Step 8: Turn the vial and syringe upside down and slowly pull the Plunger down until the tip is a few units past the line for your prescribed dose. If there are air bubbles, tap the syringe gently a few times to let any air bubbles rise to the top.	 (Example Dose: 20 units Plunger is shown at 24 units) 
Step 9: Slowly push the Plunger up until the tip reaches the line for your prescribed dose. Check the syringe to make sure that you have the right dose.	 (Example Dose: 20 units shown)
Step 10: Pull the syringe out of the vial's Rubber Stopper.	

Giving your HUMULIN N injection:

- Inject your insulin exactly as your healthcare provider has shown you.
- Change (rotate) your injection site for each injection.

Step 11: Choose your injection site. HUMULIN N is injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs or upper arms. Wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose.	
Step 12: Insert the needle into your skin.	
Step 13: Push down on the Plunger to inject your dose. The needle should stay in your skin for at least 5 seconds to make sure you have injected all of your insulin dose.	
Step 14: Pull the needle out of your skin. • If you see blood after you take the needle out of your skin, press the injection site with a piece of gauze or an alcohol swab. **Do not** rub the area. • **Do not** recap the needle. Recapping the needle can lead to a needle stick injury.	

Disposing of used needles and syringes:

- Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic,
    - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    - upright and stable during use,

- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal
- Do not recycle the container.

How should I store HUMULIN N?

All unopened HUMULIN N vials:

- Store all unopened vials in the refrigerator.
- **Do not** freeze. **Do not** use if it has been frozen.
- Keep away from heat and out of direct light.
- Unopened vials can be used until the expiration date on the carton and label, if they have been stored in the refrigerator.
- Unopened vials should be thrown away after 31 days, if they are stored at room temperature.

After HUMULIN N vials have been opened:

- Store opened vials in the refrigerator or at room temperature below 86°F (30°C) for up to 31 days.
- Keep away from heat and out of direct light.
- Throw away all opened vials after 31 days of use, even if there is still insulin left in the vial.

General information about the safe and effective use of HUMULIN N.

Keep HUMULIN N vials, syringes, needles, and all medicines out of the reach of children.

If you have any questions or problems with your HUMULIN, contact Lilly at 1-800-Lilly-Rx (1-800-545-5979) or call your healthcare provider for help. For more information on HUMULIN and insulin, go to www.humulin.com.

Scan this code to launch the humulin.com website

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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

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Revised: 11/2013

Instructions for Use

HUMULIN® N KwikPen™

(human insulin [rDNA origin] isophane suspension)

Read the Instructions for Use before you start taking HUMULIN N and each time you get another HUMULIN® N KwikPen™. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

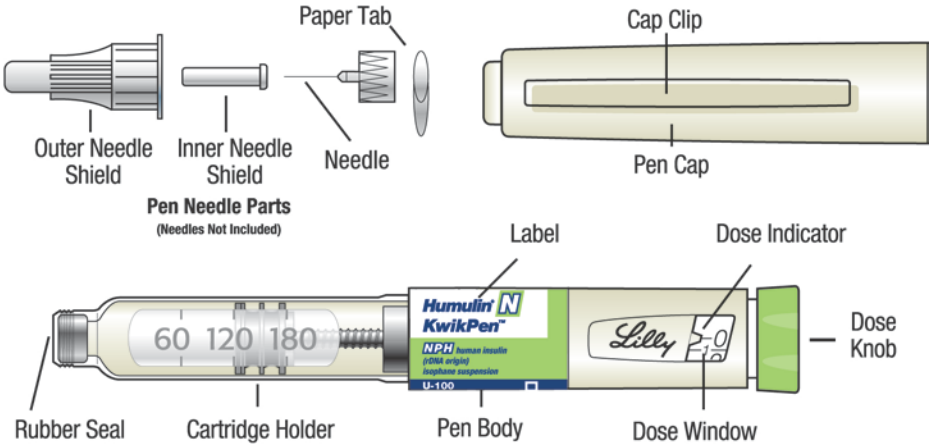
HUMULIN N KwikPen ("Pen") is a disposable pen containing 3 mL (300 units) of U-100 HUMULIN® N (human insulin isophane suspension [rDNA origin]) insulin. You can inject from 1 to 60 units in a single injection.

HUMULIN N KwikPen has a blue and light green Label with a matching light green Dose Knob (See the KwikPen Parts diagram below).

Do not share your HUMULIN N KwikPen or needles with another person. You may give an infection to them or get an infection from them.

This Pen is not recommended for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product.

KwikPen Parts

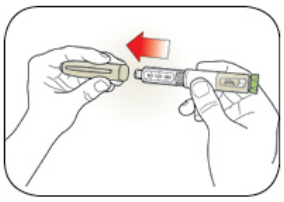
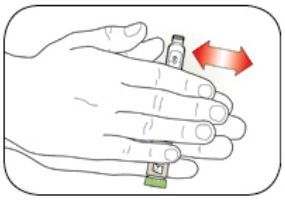
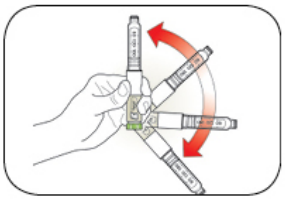


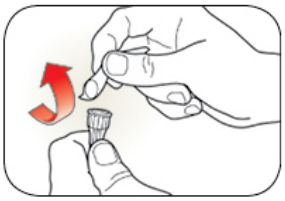
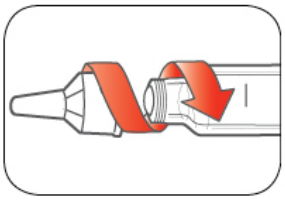
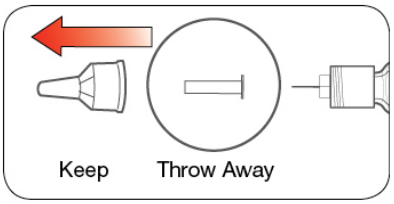
Supplies you will need to give your HUMULIN N injection:

- HUMULIN N KwikPen
- KwikPen compatible Needle (Becton, Dickinson and Company Pen Needles recommended)
- alcohol swab

Preparing HUMULIN N KwikPen:

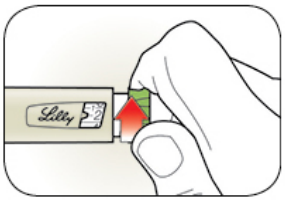
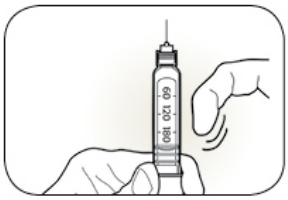
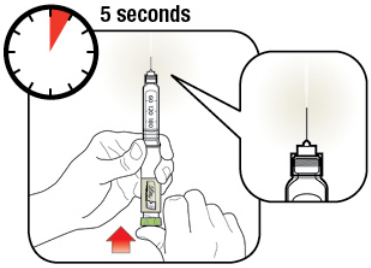
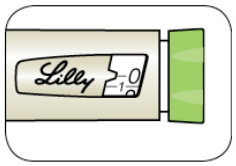
- Wash your hands with soap and water.
- **Check the HUMULIN N KwikPen Label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.**
- **Do not** use HUMULIN N past the expiration date printed on the Label or 14 days after you start using the Pen.
- **Always use a new needle for each injection to help ensure sterility and prevent blocked needles.**

Step 1: • Pull the Pen Cap straight off. • Wipe the Rubber Seal with an alcohol swab. - **Do not** twist the cap. - **Do not** remove the HUMULIN N KwikPen Label. - **Do not** attach the Needle before mixing.	
Step 2: • Gently roll the Pen between your hands 10 times.	
Step 3: • Move the Pen up and down (invert) the Pen 10 times. **Mixing by rolling and inverting the Pen is important** to make sure you get the right dose. **Step 4:** • **Check the liquid in the Pen**. HUMULIN N should look white and cloudy after mixing. **Do not** use if it looks clear or has any lumps or particles in it.	

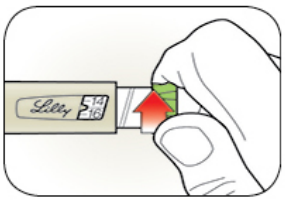
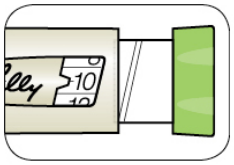
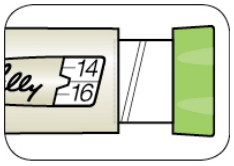
Step 5: • **Select a new Needle.** • Pull off the Paper Tab from the Outer Needle Shield.	
Step 6: • Push the capped Needle straight onto the Pen and twist the Needle on until it is tight.	
Step 7: • Pull off the Outer Needle Shield. **Do not** throw it away. • Pull off the Inner Needle Shield and throw it away.	

Priming the HUMULIN N KwikPen:

Prime the HUMULIN N KwikPen before each injection. Priming ensures the Pen is ready to dose and removes air that may collect in the cartridge during normal use. If you do not prime before each injection, you may get too much or too little insulin.

Step 8: • Turn the Dose Knob to select 2 units.	
Step 9: • Hold the Pen with the Needle pointing up. Tap the Cartridge Holder gently to collect air bubbles at the top.	
Step 10: • Hold the Pen with Needle pointing up. Push the Dose Knob in until it stops, and “0” is seen in the Dose Window. • **Hold the Dose Knob in and count to 5 slowly**. A stream of insulin should be seen from the needle. - If you **do not** see a stream of insulin, repeat steps 8 to 10, no more than 4 times. - If you **still do not** see a stream of insulin, change the needle and repeat steps 8 to 10.	 

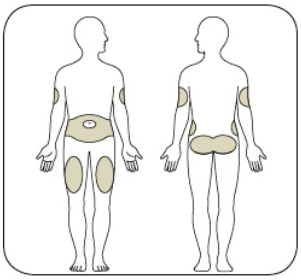
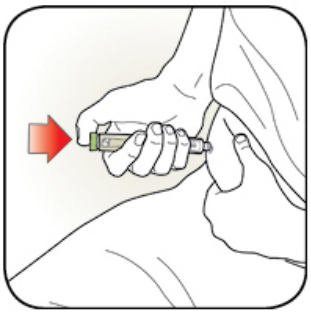
Selecting your dose:

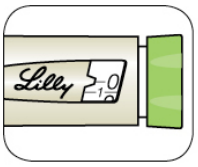
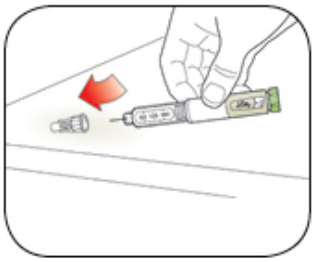
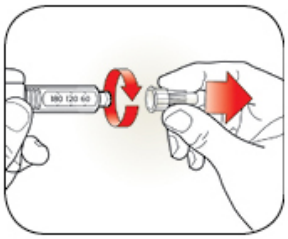
Step 11: • Turn the Dose Knob to select the number of units you need to inject. The Dose Indicator should line up with your dose. The dose can be corrected by turning the Dose Knob in either direction until the correct dose lines up with the Dose Indicator. - The **even** numbers are printed on the dial. - The **odd** numbers, after the number 1, are shown as full lines.	  (Example: 10 units shown)  (Example: 15 units shown)

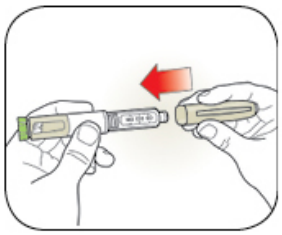
- The HUMULIN N KwikPen will not let you dial more than the number of units left in the Pen.
- If your dose is more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose, **or**
  - get a new Pen and inject the full dose.
- The Pen is designed to deliver a total of 300 units of insulin. The cartridge contains an additional small amount of insulin that cannot be delivered.

Giving your HUMULIN N injection:

- Inject your HUMULIN N exactly as your healthcare provider has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting HUMULIN N.

Step 12: • Choose your injection site. HUMULIN N is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms. • Wipe the skin with an alcohol swab, and let the injection site dry before you inject your dose.	
Step 13: • Insert the Needle into your skin.	
Step 14: • Put your **thumb** on the Dose Knob and push the Dose Knob in until it stops. • **Hold the Dose Knob in and slowly count to 5.** 	

Step 15: • Pull the Needle out of your skin. You should see “0” in the Dose Window. If you do not see “0” in the Dose Window, you did not receive your full dose. - If you see blood after you take the Needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. **Do not** rub the area. - A drop of insulin at the needle tip is normal. It will not affect your dose. - **If you do not think you received your full dose, do not take another dose.** Call Lilly at 1-800-LillyRx (1-800-545-5979) or your healthcare provider for help.	
Step 16: • Carefully replace the Outer Needle Shield.	
Step 17: • Unscrew the capped Needle and throw it away. • **Do not** store the Pen with the Needle attached to prevent leaking, blocking of the Needle, and air from entering the Pen.	

Step 18: • Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.	

After your injection:

- Put your used needles and pens in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and pens in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal

How should I store my HUMULIN N KwikPen?

- Store unused HUMULIN N KwikPens in the refrigerator at 36°F to 46°F (2°C to 8°C). The Pen you are currently using should be stored at room temperature, below 86°F (30°C).
- **Do not** freeze HUMULIN N. **Do not** use HUMULIN N if it has been frozen.
- Unused Pens may be used until the expiration date printed on the Label, if kept in the refrigerator.
- The HUMULIN N Pen you are using should be thrown away after 14 days, even if it still has insulin left in it.
- Keep HUMULIN N away from heat and out of the light.

General information about the safe and effective use of HUMULIN N KwikPen.

- **Keep HUMULIN N KwikPen and needles out of the reach of children.**
- **Do not** use the Pen if any part looks broken or damaged.
- Always carry an extra Pen in case yours is lost or damaged.
- If you cannot remove the Pen Cap, gently twist the Pen Cap back and forth, and then pull the Pen Cap straight off.
- If it is hard to push the Dose Knob or the Pen is not working the right way:
  - Your Needle may be blocked. Put on a new Needle and prime the Pen.
  - You may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new one.
  - It may help to push the Dose Knob more slowly during your injection.
- Use the space below to keep track of how long you should use each HUMULIN N KwikPen.
  - Write down the date you start using your HUMULIN N KwikPen. Count forward 14 days.
  - Write down the date you should throw it away.

Example:

First used on _____ + 14 days = Throw out on _____

Date Date

Pen 1 - First used on _____ Throw out on _____

Date Date

Pen 2 - First used on _____ Throw out on _____

Date Date

Pen 3 - First used on _____ Throw out on _____

Date Date

Pen 4 - First used on _____ Throw out on _____

Date Date

Pen 5 - First used on _____ Throw out on _____

Date Date

If you have any questions or problems with your HUMULIN N KwikPen, contact Lilly at 1-800-LillyRx (1-800-545-5979) or call your healthcare provider for help. For more information on HUMULIN N KwikPen and insulin, go to www.lilly.com.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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HUMULIN N KwikPen meets the current dose accuracy and functional requirements of ISO 11608-1:2000.

Issued: Month Day, Year