

Novo Nordisk

Insulin Information For The Patient Using

Novolin® N FlexPen[®]

NPH, Human Insulin Isophane ([recombinant DNA origin](#))

Suspension ([recombinant DNA origin](#))

in a 3 mL Prefilled [Insulin](#) Syringe

100 units/mL ([U-100](#))

Please read both sides of this leaflet carefully before using this product.

Novolin® N FlexPen™

~~prefilled insulin syringe~~ is for single-person use only.

See Important Notes section.

WARNING

ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY UNDER MEDICAL SUPERVISION. CHANGES IN PURITY, STRENGTH, BRAND (MANUFACTURER), TYPE (REGULAR, NPH, LENTE®, ETC.), SPECIES (BEEF, PORK, BEEF-PORK, HUMAN), AND/OR METHOD OF MANUFACTURE (RECOMBINANT DNA VERSUS ANIMAL-SOURCE INSULIN) MAY RESULT IN THE NEED FOR A CHANGE IN DOSAGE.

SPECIAL CARE SHOULD BE TAKEN WHEN THE TRANSFER IS FROM A STANDARD BEEF OR MIXED SPECIES INSULIN TO A PURIFIED PORK OR HUMAN INSULIN. IF A DOSAGE ADJUSTMENT IS NEEDED, IT WILL USUALLY BECOME APPARENT EITHER IN THE FIRST FEW DAYS OR OVER A PERIOD OF SEVERAL WEEKS. ANY CHANGE IN TREATMENT SHOULD BE CAREFULLY MONITORED. PLEASE READ THE SECTIONS “INSULIN REACTION AND SHOCK” AND “DIABETIC KETOACIDOSIS AND COMA” FOR SYMPTOMS OF HYPOGLYCEMIA (LOW BLOOD GLUCOSE) AND HYPERGLYCEMIA (HIGH BLOOD GLUCOSE).

INSULIN USE IN DIABETES

Your physician has explained that you have diabetes and that your treatment involves injections of insulin or insulin therapy combined with an oral antidiabetic medicine. Insulin is normally produced by the pancreas, a gland that lies behind the stomach. Without insulin, glucose (a simple sugar made from digested food) is trapped in the bloodstream and cannot enter the cells of the body. Some patients who don't make enough of their own insulin, or who cannot use the insulin they do make properly, must take insulin by injection in order to control their blood glucose levels.

Each case of diabetes is different and requires direct and continued medical supervision. Your physician has told you the type, strength and amount of insulin you should use and the time(s) at which you should inject it, and has also discussed with you a diet and exercise schedule. You

should contact your physician if you experience any difficulties or if you have questions.

TYPES OF INSULINS

Standard and purified animal insulins as well as human insulins are available. Standard and purified insulins differ in their degree of purification and content of noninsulin material. Standard and purified insulins also vary in species source; they may be of beef, pork, or mixed beef and pork origin. Human insulin is identical in structure to the insulin produced by the human pancreas, and thus differs from animal insulins. Insulins vary in time of action; see **PRODUCT DESCRIPTION** for additional information.

Your physician has prescribed the insulin that is right for you; be sure you have purchased the correct insulin and check it carefully before you use it.

PRODUCT DESCRIPTION

This package contains five (5) Novolin® N FlexPen™ ~~prefilled insulin syringes~~. Novolin® N is commonly known as NPH, Human Insulin Isophane Suspension (recombinant DNA origin). The concentration of this product is 100 units of insulin per milliliter. It is a cloudy or milky suspension of human insulin with protamine and zinc. The insulin substance (the cloudy material) settles at the bottom of the insulin reservoir, therefore, the ~~syringe~~ Novolin N FlexPen must be rotated up and down so that the contents are uniformly mixed before a dose is given. Novolin® N has an intermediate duration of action. The effect of Novolin® N begins approximately 1½ hours after injection. The effect is maximal between 4 and 12 hours. The full duration of action may last up to 24 hours after injection.

The time course of action of any insulin may vary considerably in different individuals, or at different times in the same individual. Because of this variation, the time periods listed here should be considered as general guidelines only.

This human insulin (recombinant DNA origin) is structurally identical to the insulin produced by the human pancreas. This human insulin is produced by recombinant DNA technology utilizing *Saccharomyces cerevisiae* (bakers' yeast) as the production organism.

STORAGE

Novolin® N FlexPen™ ~~prefilled insulin syringes~~ should be stored in a cold (2° - 8°C [36° - 46°F]) place, preferably in a refrigerator, but not in the freezer. **Do not let it freeze.** Keep Novolin® N FlexPen™ ~~prefilled insulin syringes~~ in the carton so that they will stay clean and protected from light. The Novolin N FlexPen ~~prefilled insulin syringe~~ that you are currently using can be kept unrefrigerated for 14 days, as long as it is kept as cool as possible (below 86°F [30°C]). Unrefrigerated Novolin® N FlexPen ~~prefilled insulin syringes~~ must be used within this time period or discarded after 14 days even if it still contains Novolin N. Be sure to protect Novolin® N FlexPen™ ~~prefilled insulin syringes~~ from

sunlight and extreme heat or cold. **Never use insulin after the expiration date printed on the label and carton.**

Never use any Novolin® N FlexPen™ ~~prefilled insulin syringes~~ if the precipitate (the white deposit) has become lumpy or granular in appearance or has formed a deposit of solid particles on the wall of the insulin reservoir. This insulin should not be used if the liquid in the insulin reservoir remains clear after it has been mixed.

~~Never use insulin after the expiration date printed on the label and carton.~~

IMPORTANT

Failure to comply with the following antiseptic measures may lead to infections at the injection site.

- Disposable needles are not to be re-used; they should be used only once and destroyed.
- Clean your hands and the injection site with soap and water or with alcohol.
- Wipe the rubber stopper on the insulin cartridge with an alcohol swab.

PREPARING THE INJECTION

Never place a single-use disposable needle on your Novolin® N FlexPen™ ~~prefilled insulin syringe~~ until you are ready to give an injection, and remove the needle immediately after each injection. If the needle is not removed some liquid may be expelled from the cartridge causing a change in the insulin concentration (strength). The cloudy material in an insulin suspension will settle to the bottom of the insulin reservoir, so the contents must be mixed before injection. FlexPen ~~prefilled insulin syringes~~ contain a glass ball to aid mixing. Rotate the FlexPen ~~prefilled insulin syringe~~ up and down so that the contents are uniformly mixed before the dose is given. Follow the directions for use of this syringe on the reverse side of this insert.

~~Insulin prefilled syringes~~ Novolin® N FlexPen™ may contain a small amount of air. To prevent an injection of air and make certain insulin is delivered, an air shot must be done before each injection. Directions for performing an air shot are provided on the reverse side of this insert.

GIVING THE INJECTION

1. The following areas are suitable for subcutaneous insulin injection: thighs, upper arms, buttocks, abdomen. Do not change areas without consulting your physician. The actual point of injection should be changed each time; injection sites should be about an inch apart.
2. The injection site should be clean and dry. Pinch up skin area to be injected and hold it firmly.
3. Hold the device upright and push the needle quickly and firmly into the pinched-up area. Release the skin and push the push-button all the way in to inject insulin beneath the skin. To ensure that all the insulin is injected keep the needle in the skin for several seconds after injection with your thumb on the push-button.
4. Do not inject into a muscle unless your physician has advised it. You should never inject insulin into a vein.

5. Remove the needle. If slight bleeding occurs, press lightly with a dry cotton swab for a few seconds – **do not rub.**

For additional information see **GIVING THE INJECTION** on the reverse side of this insert.

USAGE IN PREGNANCY

It is particularly important to maintain good control of your diabetes during pregnancy and special attention must be paid to your diet, exercise and insulin regimens. If you are pregnant or nursing a baby, consult your physician or nurse educator.

INSULIN REACTION AND SHOCK

Insulin reaction (hypoglycemia) occurs when the blood glucose falls very low. This can happen if you take too much insulin, miss or delay a meal, exercise more than usual or work too hard without eating, or become ill (especially with vomiting or fever). Hypoglycemia can also happen if you combine insulin therapy and other medications that lower blood glucose, such as oral antidiabetic agents or other prescription and over-the-counter drugs. The first symptoms of an insulin reaction usually come on suddenly. They may include a cold sweat, fatigue, nervousness or shakiness, rapid heartbeat, or nausea. Personality change or confusion may also occur. If you drink or eat something right away (a glass of milk or orange juice, or several sugar candies), you can often stop the progression of symptoms. If symptoms persist, call your physician - an insulin reaction can lead to unconsciousness. If a reaction results in loss of consciousness, emergency medical care should be obtained immediately. If you have had repeated reactions or if an insulin reaction has led to a loss of consciousness, contact your physician. Severe hypoglycemia can result in temporary or permanent impairment of brain function and death.

In certain cases, the nature and intensity of the warning symptoms of hypoglycemia may change. A few patients have reported that after being transferred to human insulin, the early warning symptoms of hypoglycemia were less pronounced than they had been with animal-source insulin.

DIABETIC KETOACIDOSIS AND COMA

Diabetic ketoacidosis may develop if your body has too little insulin. The most common causes are acute illness or infection or failure to take enough insulin by injection. If you are ill you should check your urine for ketones. The symptoms of diabetic ketoacidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst and loss of appetite. Notify your physician right away if the urine test is positive for ketones (acetone) or if you have any of these symptoms. Fast, heavy breathing and rapid pulse are more severe symptoms and you should have medical attention right away. Severe, sustained hyperglycemia may result in diabetic coma and death.

ADVERSE REACTIONS

A few people with diabetes develop red, swollen and itchy skin where the insulin has been injected. This is called a “local reaction” and it may occur if the injection is not properly made, if the skin is sensitive to the cleansing solution, or if you are allergic to the insulin being used. If you have a local reaction, tell your physician.

Generalized insulin allergy occurs rarely, but when it does it may cause a serious reaction, including skin rash over the body, shortness of breath, fast pulse, sweating, and a drop in blood pressure. If any of these symptoms develop, you should seek emergency medical care.

If severe allergic reactions to insulin have occurred (i.e., generalized rash, swelling or breathing difficulties) you should be skin-tested with **each** new insulin preparation before it is used.

IMPORTANT NOTES

1. A change in the type, strength, species or purity of insulin could require a dosage adjustment. Any change in insulin should be made under medical supervision.
2. To avoid possible transmission of disease, **Novolin® N FlexPen®** ~~prefilled insulin syringe~~ is for single-person use only.
3. You may have learned how to test your urine or your blood for glucose. It is important to do these tests regularly and to record the results for review with your physician or nurse educator.
4. If you have an acute illness, especially with vomiting or fever, continue taking your insulin. If possible, stay on your regular diet. If you have trouble eating, drink fruit juices, regular soft drinks, or clear soups; if you can, eat small amounts of bland foods. Test your urine for glucose and ketones and, if possible, test your blood glucose. Note the results and contact your physician for possible insulin dose adjustment. If you have severe and prolonged vomiting, seek emergency medical care.
5. You should always carry identification which states that you have diabetes.
6. Always ask your physician or pharmacist before taking any drug.

Always consult your physician if you have any questions about your condition or the use of insulin.

Helpful information for people with diabetes is published by American Diabetes Association, 1660 Duke Street, Alexandria, VA 22314

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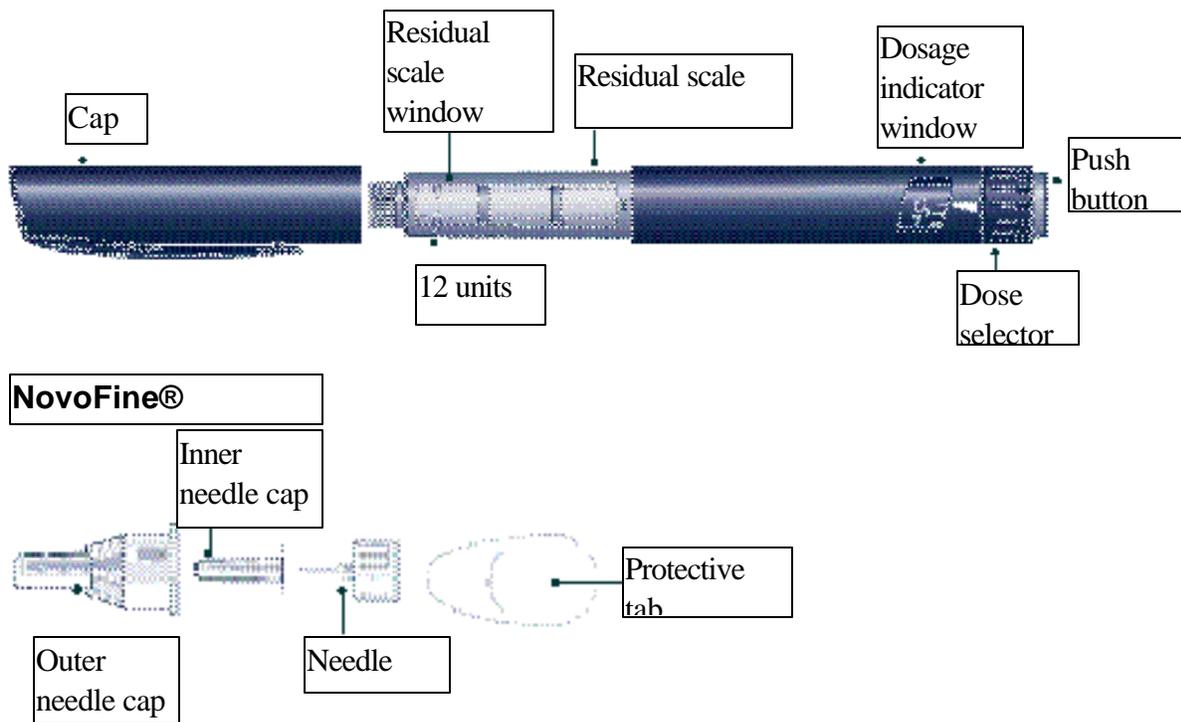
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FlexPen^ä prefilled insulin syringe directions for use

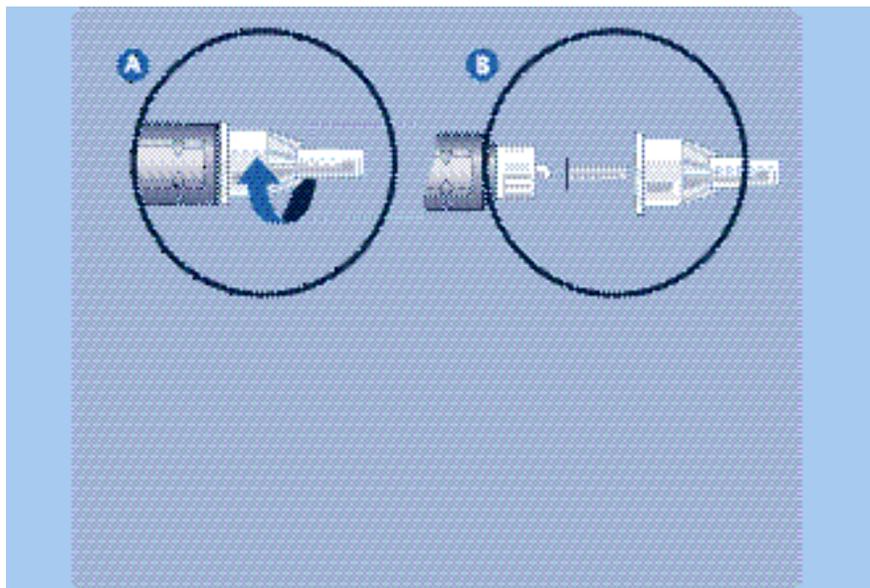
Novolin® N FlexPen™ prefilled insulin syringe is a disposable dial-a-dose insulin delivery system able to deliver 1 to a maximum of 60 units. The dose can be adjusted in increments of 1 unit. Novolin N FlexPen prefilled insulin syringe is designed for use with NovoFine® single use needles or other products specifically recommended by Novo Nordisk. Novolin N FlexPen prefilled insulin syringe is not recommended for the blind or severely visually impaired without the assistance of a sighted individual trained in the proper use of the product.

Please read these instructions completely before using this device.



1. PREPARING THE FLEXPEN: ~~PREFILLED INSULIN SYRINGE~~

- a Pull off the cap.
- b Wipe the rubber stopper with an alcohol swab.

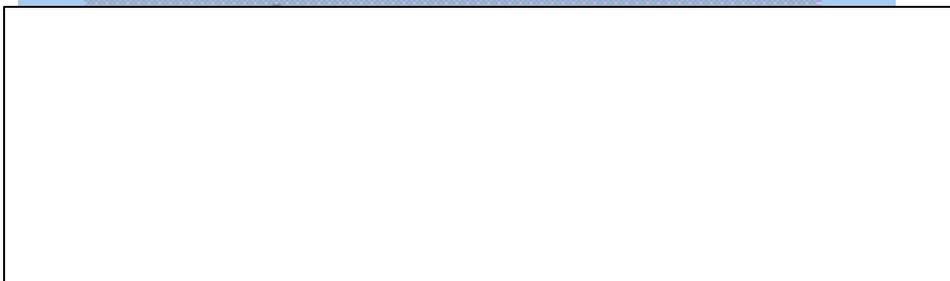
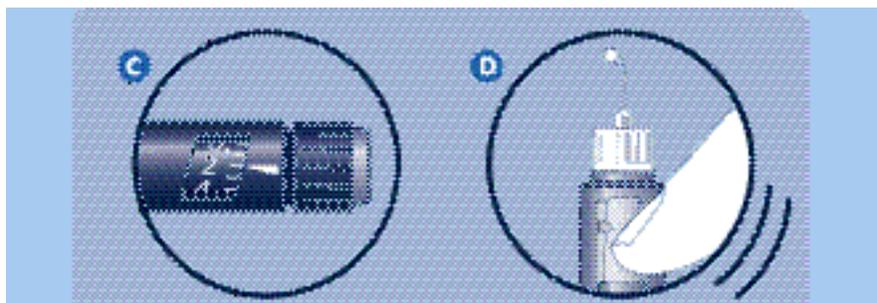


- c ~~A.~~ Remove the protective tab from the disposable needle and screw the needle onto the FlexPen. Never place a disposable needle on your FlexPen until you are ready to give an injection. Remove the needle right after use. If the needle is not removed, some liquid may leak from the FlexPen.
- d ~~B.~~ Pull off the outer and inner needle caps. Do not discard the outer needle cap.

Giving The Airshot Before Each Injection:

Small amounts of air may collect in the needle and insulin reservoir during normal use.

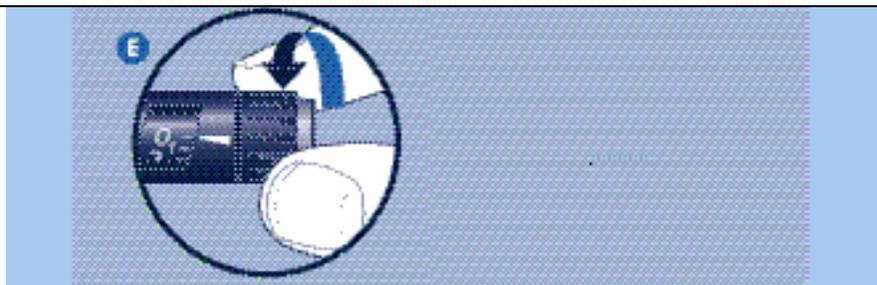
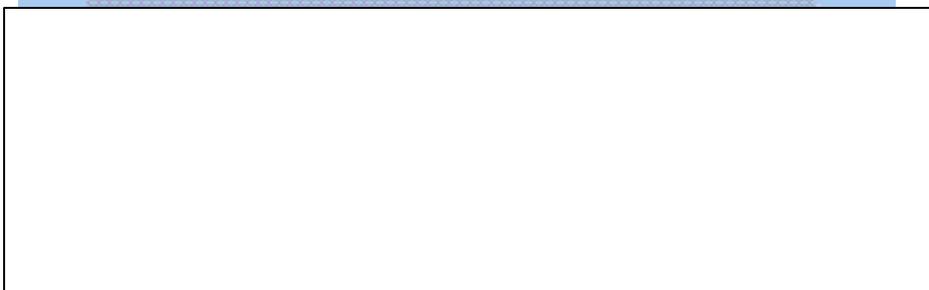
To avoid injecting air and to ensure proper dosing, hold the syringe with the needle pointing up and tap the syringe gently with your finger so any air bubbles collect in the top of the reservoir. Remove both the plastic outer cap and the needle cap.



e ~~C.~~ Dial 2 units.

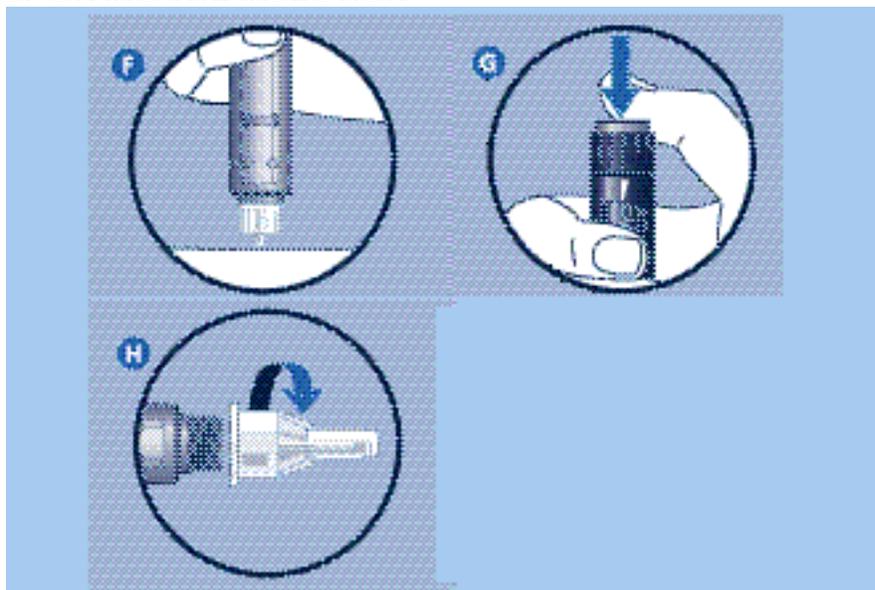
f ~~D.~~ Holding the syringe with the needle pointing up, tap the reservoir gently with your finger a few times. Still with the needle pointing up, press the push button as far as it will go and see if a drop of insulin appears at the needle tip. If not, repeat the procedure until insulin appears. Before the first use of each Novolin N FlexPen ~~prefilled insulin syringe~~ you may need to perform up to 6 airshots to get a droplet of insulin at the needle tip. If you need to make more than 6 airshots, do not use the syringe, and return the product to Novo Nordisk. A small air bubble may remain but it will not be injected because the operating mechanism prevents the reservoir from being completely emptied.

2. SETTING THE DOSE



g E. Check that the dose selector is set at **0**. Dial the number of units you need to inject. The dose can be corrected either up or down by turning the dose selector in either direction. When dialing back be careful not to push the push button as insulin will come out. You cannot set a dose larger than the number of units left in the reservoir.

3. GIVING THE INJECTION



Use the injection technique recommended by your doctor.

h F. Deliver the dose by pressing the push button all the way in. Be careful only to push the push button when injecting.

i G. After the injection the needle should remain under the skin for several seconds. Keep the push button fully depressed until the needle is withdrawn from the skin. This will ensure that the full dose has been delivered.

j H. Replace the outer needle cap, unscrew the needle, and throw it away appropriately.

It is important that you use a new needle for each injection. Health care professionals, relatives and other care givers should follow general precautionary measures for removal and disposal of needles to eliminate the risk of unintended needle penetration.

For more information see **GIVING THE INJECTION** on the reverse side of this insert.

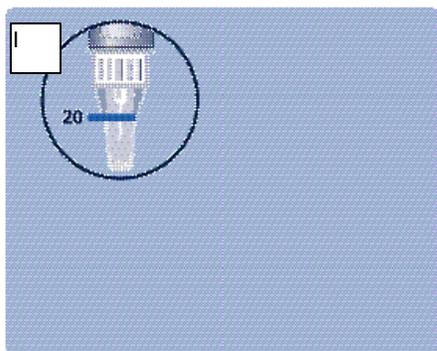
4. SUBSEQUENT INJECTIONS

It is important that you use a new needle for each injection. Follow the directions in steps 1 – 3.

The numbers on the insulin reservoir can be used to estimate the amount of insulin left in the syringe. Do not use these numbers to measure the insulin dose.

You cannot set a dose greater than the number of units remaining in the reservoir.

5. FUNCTION CHECK



If your Novolin N FlexPen ~~prefilled insulin syringe~~ is not working properly, follow this procedure:

- Screw on a new NovoFine needle
- Give an airshot as described in sections ~~C to D~~ e to f
- Put the outer needle cap onto the needle
- Dispense 20 units into the outer needle cap, holding the pen with the needle pointing downwards.

The insulin should fill the lower part of the cap (as shown in figure I). If Novolin N FlexPen ~~prefilled insulin syringe~~ has released too much or too little insulin, repeat the test. If it happens again, contact Novo Nordisk and do not use your Novolin N FlexPen ~~prefilled insulin syringe~~.

Dispose of the used Novolin N FlexPen ~~prefilled insulin syringe~~ carefully without the needle attached.

6. IMPORTANT NOTES

- If you need to perform more than 6 airshots before the first use of Novolin N FlexPen ~~prefilled insulin syringe~~ to get a droplet of insulin at the needle tip, do not use the FlexPen.
- Remember to perform an air shot before each injection. See figures ~~C and D~~ e and f.
- Take care not to drop the FlexPen.
- Remember to keep the Novolin N FlexPen ~~prefilled insulin syringe~~ with you; don't leave it in a car or other location where extremes of temperature can occur.
- Novolin N FlexPen ~~prefilled insulin syringe~~ is designed for use with NovoFine disposable needles or other products specifically recommended by Novo Nordisk.
- Never place a disposable needle on this syringe until you are ready to use it. Remove the needle immediately after use.
- **Throw away used needles in a responsible manner, so others will not be harmed.**
- Throw away the used syringe, without the needle attached.
- Always carry a spare Novolin N FlexPen ~~prefilled insulin syringe~~ with you in case your FlexPen is damaged or lost.

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- Novo Nordisk cannot be held responsible for adverse reactions occurring as a consequence of using this insulin delivery system with products that are not recommended by Novo Nordisk.
- Keep this syringe out of the reach of children.

Call 800-727-6500 for additional information.

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this page is the manifestation of the electronic signature.**

/s/

David Orloff
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