

**PATIENT PACKAGE LEAFLET IN ACCORDANCE WITH THE PHARMACISTS'  
REGULATIONS (PREPARATIONS) - 1986**

**This medicine is dispensed with a doctor's prescription only**

**NovoMix® 50 FlexPen**

**100 units/ml**

**Suspension for injection in a pre-filled pen**

**Active ingredients:** 50% soluble insulin aspart and 50% insulin aspart crystallized with protamine.

**Inactive ingredients and allergens in the medicine:** See section 2 under "Important information about some of this medicine's ingredients" and section 6 – "Further Information".

**Read the entire leaflet carefully before you start using this medicine.** This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours..

**1. What is this medicine intended for?**

NovoMix 50 is used to treat diabetes in adults.

**Therapeutic group:** Diabetes medicines. Insulins and analogs for injection, with a combination of an intermediate-acting or long-acting insulin with rapid-acting insulin.

NovoMix 50 is a modern insulin (insulin analog) with both a rapid-acting and an intermediate-acting effect, in the ratio 50/50. Modern insulin products are improved versions of human insulin.

Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. NovoMix 50 may be used in combination with metformin.

NovoMix 50 is used to reduce the high blood sugar level in patients with diabetes mellitus (diabetes).

NovoMix 50 will start to lower your blood sugar 10–20 minutes after you inject it; the maximum effect occurs between 1 and 4 hours after the injection, and the effect lasts for up to 14-24 hours.

**2. Before using this medicine**

### **Do not use this medicine:**

- ▶ If you are sensitive (allergic) to insulin aspart or to any of the other ingredients in this medicine (see section 6, "Further information").
- ▶ If you suspect hypoglycemia (low blood sugar) is starting, see section 4, item (a) "Summary of serious and very common side effects".
- ▶ In insulin infusion pumps.
- ▶ If FlexPen is dropped, damaged or crushed.
- ▶ If it has not been stored correctly or if it has been frozen, see section 5, "How to store the medicine".
- ▶ If the resuspended insulin does not appear uniformly white, cloudy and aqueous.
- ▶ If after resuspension, clumps of material are present or if solid white particles stick to the bottom or the wall of the cartridge.

If any of these apply, do not use NovoMix 50. Talk to your doctor, nurse or pharmacist for advice.

### **Before using NovoMix 50**

- ▶ Check the label to make sure it is the right type of insulin.
- ▶ Always use a new needle for each injection to prevent contamination.
- ▶ Needles and NovoMix 50 FlexPen must not be shared.
- ▶ NovoMix 50 FlexPen is only suitable for injecting under the skin. Speak to your doctor if you need to inject your insulin by another method.

### **Special warnings regarding the use of this medicine**

Some conditions and activities can affect your need for insulin. Consult your doctor if:

- ▶ you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
- ▶ you exercise more than usual or if you want to change your usual diet, as this may affect your blood sugar level.
- ▶ you are ill, carry on taking your insulin and consult your doctor.
- ▶ you are going abroad, travelling over time zones may affect your insulin needs and the timing of your injections.

### **Skin changes at the injection site**

The injection site should be rotated to help prevent changes to the fatty tissue under the skin, such as skin thickening, skin shrinking or lumps under the skin. The insulin may not work very well if you inject into a lumpy, shrunken or thickened area (see section 3, "How to use this medicine"). Tell your doctor if you notice any skin changes at the injection site. Tell your doctor if you are currently injecting into these affected areas before you start injecting in a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or other antidiabetic medications dose.

### **Other medicines and NovoMix 50**

**If you are taking or have recently taken other medicines, including non-prescription medications and nutritional supplements, tell your doctor or pharmacist.** Some medicines affect your blood sugar level and this may mean that your

insulin dose has to change. Listed below are the most common medicines which may affect your insulin treatment.

Your blood sugar level may fall (hypoglycemia) if you take:

- Other medicines for the treatment of diabetes
- Monoamine oxidase inhibitors (MAOI) (used to treat depression)
- Beta-blockers (used to treat high blood pressure)
- Angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure)
- Salicylates (used to relieve pain and lower fever)
- Anabolic steroids (such as testosterone)
- Sulfonamides (used to treat infections).

Your blood sugar level may rise (hyperglycemia) if you take:

- Oral contraceptives (birth control pills)
- Thiazides (used to treat high blood pressure or excessive fluid retention)
- Glucocorticoids (such as 'cortisone' used to treat inflammation)
- Thyroid hormones (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], salbutamol or terbutaline used to treat asthma)
- Growth hormone (medicine for stimulating skeletal and somatic growth which has a pronounced influence on the body's metabolic processes)
- Danazol (medicine that affects ovulation).

Octreotide and lanreotide (used for treatment of acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults, caused by the pituitary gland producing excess growth hormone) may either increase or decrease your blood sugar level.

Beta-blockers (used to treat high blood pressure) may weaken or suppress entirely the first warning signs which help you to recognize low blood sugar.

Pioglitazone (tablets used for the treatment of type 2 diabetes)

Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone and insulin developed heart failure. Inform your doctor as soon as possible if you experience signs of heart failure, such as unusual shortness of breath or rapid increase in weight or localized swelling (edema).

If you have taken any of the medicines listed here, tell your doctor, nurse or pharmacist.

**Using this medicine and alcohol consumption**

If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. Careful monitoring of blood sugar level is recommended.

**Pregnancy and breastfeeding**

- ▶ If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. There is limited clinical experience with insulin aspart in pregnancy. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes, particularly prevention of hypoglycemia, is important for the health of your baby.
- ▶ There are no restrictions on treatment with NovoMix 50 during breastfeeding.

Ask your doctor, nurse or pharmacist for advice before taking any medicine while pregnant or breastfeeding.

### **Driving and using machines**

- ▶ Please ask your doctor whether you can drive a car or operate a machine if:
  - you have frequent hypoglycemia.
  - you find it hard to recognize hypoglycemia.

If your blood sugar is low or high, it might affect your concentration and ability to react and therefore also your ability to drive or operate a machine. Bear in mind that you could endanger yourself or others.

### **Important information about some of the ingredients in this medicine**

NovoMix 50 contains less than 1 mmol sodium (23 mg) per dose, which means that NovoMix 50 is essentially 'sodium-free'.

## **3. How to use this medicine?**

### **Dose and when to take your insulin**

Always use this medicine according to your doctor's instructions. Only your doctor will determine your dose and how you should take this medicine. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. **Do not exceed the recommended dose.**

NovoMix 50 is generally taken immediately before a meal. Eat a meal or snack within 10 minutes of the injection to avoid low blood sugar. When necessary, NovoMix® 50 can be given soon after a meal. See "How and where to inject" below for further information.

When NovoMix 50 is used in combination with metformin, the dose should be adjusted. **Do not exceed the recommended dose.**

Do not change your insulin unless your doctor tells you to. If your doctor has switched you from one type or brand of insulin to another, your dose may have to be adjusted by your doctor.

### **Use in children and adolescents**

No clinical studies with NovoMix 50 have been carried out in children and adolescents under the age of 18 years.

### **Use in special patient groups**

If you have reduced kidney or liver function, or if you are above 65 years of age, you need to check your blood sugar more regularly and discuss changes in your insulin dose with your doctor.

### **How and where to inject**

NovoMix 50 is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein (intravenously) or muscle (intramuscularly). NovoMix® 50 FlexPen® is only suitable for injecting under the skin. Speak to your doctor if you need to inject your insulin by another method.

With each injection, change the area of skin where you inject. This may reduce the risk of developing lumps or skin pitting (see section 4, “Side effects”). The best places to give yourself an injection are: the front of your waist (abdomen); your buttocks; the front of your thighs or upper arms. The insulin will work more quickly if you inject around the waist (abdomen). You should always measure your blood sugar regularly.

### **How to handle NovoMix 50 FlexPen**

NovoMix 50 FlexPen is a pre-filled, color-coded, disposable pen containing a mixture of rapid-acting and intermediate-acting insulin aspart in the ratio 50/50.

Carefully read the instructions for use included in this package leaflet. You must use the injection pen as described in the Instructions for use.

Always ensure you use the correct injection pen before you inject your insulin.

### **If you accidentally took a higher dose**

If you accidentally inject too much insulin, your blood sugar will get too low (hypoglycemia). See section 4 item (a) “Summary of serious and very common side effects”.

If a child has accidentally taken some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

### **If you forget to take the medicine**

If you forget to take your insulin, your blood sugar may get too high (hyperglycemia). See section 4 item (c) “Effects from diabetes”.

Do not take a double dose. Take the next dose at the usual time and consult your doctor.

Adhere to the treatment as recommended by your doctor.

### **If you stop taking the medicine**

Even if your health improves, do not stop taking this medicine without speaking with a doctor who will tell you what needs to be done. Stopping this treatment could lead to very high blood sugar (severe hyperglycemia) and ketoacidosis. See section 4 item (c) “Effects from diabetes”.

**Do not take medicines in the dark! Check the label and dose each time you take the medicine. Wear glasses if you need them.**

**If you have any further questions about using this medicine, consult your doctor or pharmacist.**

#### 4. Side effects

As with any medicine, the use of NovoMix 50 may cause side effects in some people. Do not be alarmed when reading the list of side effects. You may not experience any of them.

##### a) Summary of serious and very common side effects

**Low blood sugar (hypoglycemia)** is a very common side effect. It may affect more than 1 in 10 users.

##### Low blood sugar may occur if you:

- Inject too much insulin.
- Eat too little or miss a meal.
- Exercise more than usual.
- Drink alcohol (see “Using this medicine and alcohol consumption” in section 2).

##### Signs of low blood sugar:

Cold sweat; cool pale skin; headache; rapid heartbeat; nausea; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If prolonged severe low blood sugar is not treated, it can cause brain damage (temporary or permanent) and even death. You may recover more quickly from unconsciousness with an injection of the hormone glucagon given by someone who knows how to use it. If you are given glucagon, you will need glucose or a sugar snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital.

##### What to do if you experience low blood sugar:

- ▶ If you experience low blood sugar, eat glucose tablets or another high sugar snack (e.g. sweets, biscuits, fruit juice). Measure your blood sugar if possible and rest. Always carry glucose tablets or high sugar snacks with you, just in case.
- ▶ When the symptoms of low blood sugar have disappeared or when your blood sugar level is stabilized, continue insulin treatment as usual.
- ▶ If you have such low blood sugar that it makes you pass out, if you have had the need for an injection of glucagon, or if you have experienced many incidents of low blood sugar, talk to a doctor. Your amount or timing of insulin, food or exercise may need to be adjusted.

Tell relevant people that you have diabetes and what the consequences may be, including the risk of passing out (becoming unconscious) due to low blood sugar. Let them know that if you pass out, they must turn you on your side and get medical help straight away. They must not give you any food or drink because you may choke.

**Serious allergic reactions** to NovoMix 50 or one of its ingredients (called systemic allergic reactions) are a very rare side effect, but they are potentially life-threatening. They may affect less than 1 in 10,000 users.

**Seek medical advice immediately if:**

- signs of allergy spread to other parts of your body.
- you suddenly feel unwell, and you: start sweating; start vomiting; have difficulty in breathing; have rapid heartbeat; feel dizzy.
- ▶ you notice any of these signs, seek medical advice immediately.

**Skin changes at the injection site:** If you inject insulin in the same place, the fatty tissue may shrink (lipoatrophy) or thicken (lipohypertrophy) (may affect less than 1 in 100 users). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis; how often this occurs is not known). The insulin may not work very well if you inject into a lumpy, shrunken or thickened area. Change the injection site with each injection to help prevent these skin changes.

**b) List of other side effects****Uncommon side effects**

May affect less than 1 in 100 users.

Signs of allergy: Local allergic injection-site reactions (pain, redness, hives, inflammation, bruising, swelling and itching) may occur. These usually disappear after a few weeks of taking your insulin. If they do not disappear, see your doctor.

Vision problems: When you first start your insulin treatment, it may disturb your vision, but the disturbance is usually temporary.

Swollen joints: When you start taking insulin, water retention may cause swelling around your ankles and other joints. Normally, this soon disappears. If not, contact your doctor.

Diabetic retinopathy (an eye disease related to diabetes which can lead to loss of vision): If you have diabetic retinopathy and your blood sugar level improves very fast, the retinopathy may get worse. Ask your doctor about this.

**Rare side effects**

May affect less than 1 in 1,000 users.

Painful neuropathy (pain due to nerve damage): If your blood sugar level improves very fast, you may get nerve related pain. This is called acute painful neuropathy and is usually transient.

**c) Effects from diabetes****High blood sugar (hyperglycemia)**

High blood sugar may occur if you:

- Have not injected enough insulin.
- Forget to take your insulin or stop taking insulin.
- Repeatedly take less insulin than you need.

- Get an infection and/or a fever.
- Eat more than usual.
- Exercise less than usual.

Warning signs of high blood sugar:

The warning signs appear gradually. They include: increased urination; feeling thirsty; losing your appetite; having nausea or vomiting; feeling drowsy or tired; flushing; dry skin; dry mouth and fruity (acetone) smelling breath.

What to do if you experience high blood sugar:

- ▶ If you notice any of the above signs: test your blood sugar level, test your urine for ketones if you can, then seek medical advice immediately.
- ▶ These may be signs of a very serious condition called diabetic ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). If you do not treat it, this could lead to diabetic coma and eventually death.

**If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.**

**Reporting side effects**

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page ([www.health.gov.il](http://www.health.gov.il)) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

**5. How to store the medicine?**

- Avoid poisoning! This medicine, and any other medicine, must be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not cause vomiting without explicit instruction from the doctor.
- Do not use this medicine after the expiry date (exp. date), which is stated on the FlexPen label and carton. The expiry date refers to the last day of that month.
- Always keep the pen cap on your FlexPen when you are not using it, in order to protect it from light. NovoMix 50 must be protected from excessive heat and light.
- **Before opening:** NovoMix 50 FlexPen that is not being used must be stored in the refrigerator at 2°C to 8°C, away from the cooling element. Do not freeze. Before you use NovoMix 50 FlexPen, remove it from the refrigerator. It is recommended to resuspend the insulin as instructed every time you use a new pen. See Instructions for use below.
- **During use or when carried as a spare:** NovoMix 50 FlexPen that is being used or carried as a spare should not be kept in the refrigerator. You can carry it with you and keep it at room temperature (below 30°C) for up to 4 weeks.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

**6. Further information**

**What NovoMix 50 contains**



- 1 ml of solution contains 100 units of insulin aspart. Each pre-filled pen contains 300 units of insulin aspart in 3 ml suspension for injection.
- **In addition to the active substances this medicine also contains:** glycerol, sodium hydroxide, metacresol, hydrochloric acid, phenol, disodium phosphate dihydrate, sodium chloride, protamine sulphate, zinc and water for injection.

**What the medicine looks like and contents of the package**

NovoMix 50 is presented as a suspension for injection in a pre-filled pen. The cartridge contains a glass ball to facilitate resuspension. After resuspension, the liquid should appear uniformly white, cloudy and aqueous. Do not use the insulin, if it does not look uniformly white, cloudy and aqueous after resuspension.

This medicine is available in a pack of 5 pre-filled pens of 3 ml.

**Registration holder name and address:**

Novo Nordisk Ltd.  
1 Atir Yeda St.  
Kfar-Saba 4464301

**Manufacturer name and address:**

Novo Nordisk A/S,  
Novo Allé, DK-2880 Bagsværd,  
Denmark

This leaflet was revised in November 2020.

Registration number of the medicine in the Ministry of Health National Drug Registry:  
138-75-31773

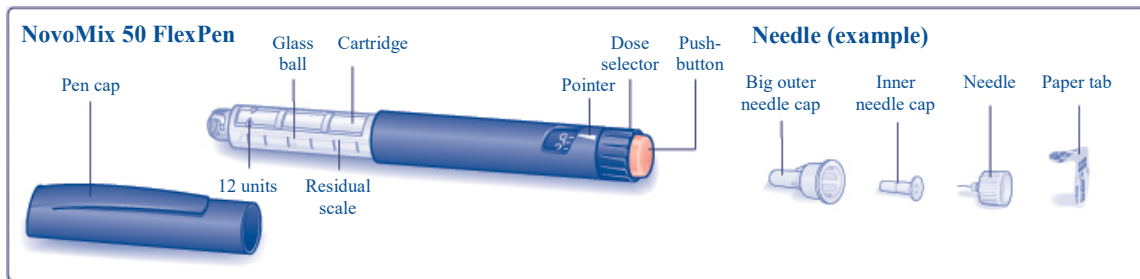
**Now turn over for information on how to use your FlexPen.**

**Instructions on how to use NovoMix 50 suspension for injection in FlexPen.**

**Read the instructions carefully before using your FlexPen.** If you do not follow the instructions carefully, you may get too little or too much insulin, which can lead to too high or too low blood sugar level.

Your FlexPen is a pre-filled dial-a-dose insulin pen.

- ▶ You can select doses from 1 to 60 units in increments of 1 unit.
- ▶ FlexPen is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.
- ▶ Always carry a spare insulin injection pen in case your FlexPen is lost or damaged.



## Caring for your pen

- ▶ Your FlexPen must be handled with care. If it is dropped, damaged or crushed, there is a risk of insulin leakage. This may cause inaccurate dosing, which can lead to too high or too low blood sugar level.
- ▶ You can clean the exterior of your FlexPen by wiping it with a medical swab. Do not soak, wash or lubricate your pen as this may damage it.
- ▶ **Do not refill your FlexPen.**

## Resuspending your insulin

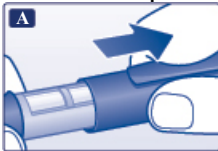
### A

**Check the name and colored label of your pen** to make sure that it contains the correct type of insulin. This is especially important if you take more than one type of insulin. If you take the wrong type of insulin, your blood sugar level may get too high or too low.

### Every time you use a new pen

Let the insulin reach room temperature before you use it.  
This makes it easier to resuspend.

Pull off the pen cap.



### B

**Before your first injection with a new FlexPen, you must resuspend the insulin:**  
Roll the pen between your palms 10 times – it is important that the pen is kept **horizontal** (level with the ground).



### C

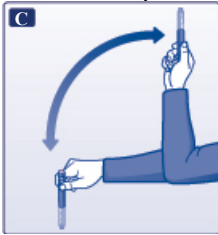
Then move the pen up and down 10 times between the two positions as shown, so the **glass ball moves** from one end of the cartridge to the other.

Repeat rolling and moving the pen until the liquid inside appears uniformly white, cloudy and aqueous.

### For every following injection

Move the pen up and down between the two positions at least 10 times until the liquid inside appears uniformly white, cloudy and aqueous. If the moving procedure alone is not enough to give a uniformly white, cloudy and aqueous liquid, repeat the rolling and moving procedures (see B and C) until the liquid does appear uniformly white, cloudy and aqueous.

- ▶ Always make sure that you have resuspended the insulin prior to each injection. This reduces the risk of too high or too low blood sugar level. After you have resuspended the insulin, complete the following steps of injection without delay.



- ⚠ Always check there are at least **12 units of insulin** left in the cartridge to allow resuspension. If there are less than 12 units left, use a new FlexPen. 12 units are marked on the residual scale. See the big picture on top of this instruction.

- ⚠ Do not use the pen if the **resuspended** insulin does not look **uniformly white, cloudy and aqueous**.

### Attaching a needle

### D

Take a new needle and tear off the paper seal. Screw the needle straight and tightly onto your FlexPen.



### E

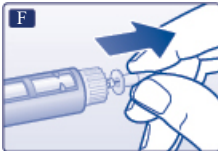
Pull off the big outer needle cap and keep it for later.



**F**

Pull off the inner needle cap and dispose of it.

Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.



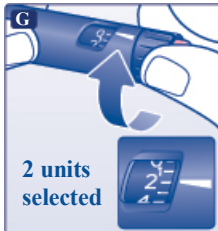
- ⚠ Always use a new needle for each injection.  
This reduces the risk of infection, contamination, leakage of insulin, blocked needles and inaccurate dosing.
- ⚠ Be careful not to bend or damage the needle before use.

### Checking the insulin flow

**Prior to each injection, small amounts of air may collect in the cartridge during normal use. To avoid injection of air and ensure proper dosing:**

**G**

Turn the dose selector to select 2 units.



**H**

Hold your FlexPen with the needle pointing upwards and tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge.

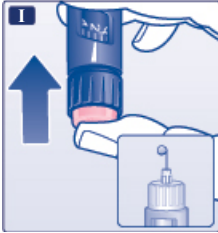


**I**

Keeping the needle upwards, press the push-button all the way in. The dose selector returns to 0.

A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

If a drop of insulin still does not appear, the pen is defective, and you must use a new one.



- ⚠ Always make sure that a drop appears at the needle tip before you inject. This makes sure that the insulin flows.  
If no drop appears you will not inject any insulin, even though the dose selector may move. This may indicate a blocked or damaged needle.
- ⚠ Always check the flow before you inject. If you do not check the flow, you may get too little insulin or no insulin at all. This may lead to too high blood sugar level.

## Selecting your dose

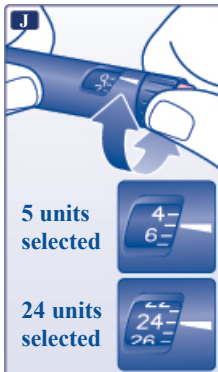
**Check that the dose selector is set at 0.**

### J

Turn the dose selector to select 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 until the correct dose lines up with the pointer. When turning the dose selector, be careful not to push the push-button as insulin will come out.

You cannot select a dose larger than the number of units left in the cartridge.



- ⚠ Always use the dose selector and the pointer to see how many units you have selected before injecting the insulin.

- ⚠ Do not count the pen clicks. If you select and inject the wrong dose, your blood sugar level may get too high or too low. Do not use the residual scale; it only shows approximately how much insulin is left in your pen.

## Making the injection

**Insert the needle into your skin. Use the injection technique you were shown by your doctor or nurse.**

### K

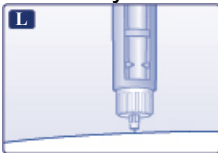
Inject the dose by pressing the push-button all the way in until 0 lines up with the pointer. Be careful only to push the push-button when injecting.

Turning the dose selector will not inject insulin.



### L

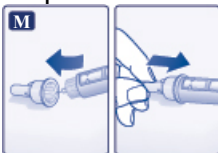
- ▶ Keep the **push-button fully depressed** and let the needle remain under the skin for **at least 6 seconds**. This will make sure you get the full dose.
- ▶ Withdraw the needle from the skin, then release the pressure on the push-button.
- ▶ Always make sure that the dose selector returns to 0 after the injection. If the dose selector stops before it returns to 0, the full dose has not been delivered, which may result in too high blood sugar level.



### M

Lead the needle into the big outer needle cap without touching it. When the needle is covered, carefully push the big outer needle cap completely on and then unscrew the needle.

Dispose of it carefully and put the pen cap back on your FlexPen.



- ⚠ Always remove the needle after each injection and store your FlexPen without the needle attached. This reduces the risk of infection, contamination, leakage of insulin, blocked needles and inaccurate dosing.

### **Further important information**

- ⚠ Caregivers must be very careful when handling used needles to reduce the risk of needle sticks and infections.
- ⚠ Dispose of the used FlexPen carefully without the needle attached.
- ⚠ Never share your pen or your needles with other people. It might lead to infections.
- ⚠ Never share your pen with other people. Your medicine might be harmful to their health.
- ⚠ Always keep your pen and needles out of sight and reach of others, especially children.