

Package leaflet: Information for the user

NovoMix® 30 FlexPen®

100 units/ml suspension for injection in a pre-filled pen

30% soluble insulin aspart and 70% insulin aspart crystallised with protamine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. *What NovoMix® 30 is and what it is used for*
2. *What you need to know before you use NovoMix® 30*
3. *How to use NovoMix® 30*
4. *Possible side effects*
5. *How to store NovoMix® 30*
6. *Contents of the pack and other information*

1. *What NovoMix® 30 is and what it is used for*

NovoMix® 30 is a modern insulin (insulin analogue) with both a rapid-acting and an intermediate-acting effect, in the ratio 30/70. Modern insulin products are improved versions of human insulin.

NovoMix® 30 is used **to reduce the high blood sugar level** in adults, adolescents and children aged 10 years and above with diabetes mellitus (diabetes). Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. NovoMix® 30 may be used in combination with tablets for diabetes.

NovoMix® 30 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 24 hours.

2. *What you need to know before you use NovoMix® 30*

Do not use NovoMix® 30

- ▶ If you are allergic to insulin aspart or any of the other ingredients in this medicine (see section 6, *Contents of the pack and other information*).
- ▶ If you suspect hypoglycaemia (low blood sugar) is starting, see a) *Summary of serious and very common side effects* in section 4.
- ▶ 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 NovoMix® 30*.
- ▶ 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® 30**. Talk to your doctor, nurse or pharmacist for advice.

Before using NovoMix® 30

- ▶ 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® 30 FlexPen® must not be shared.
- ▶ NovoMix® 30 FlexPen® is only suitable for injecting under the skin. Speak to your doctor if you need to inject your insulin by another method.

Warnings and precautions

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.
- ▶ If you exercise more than usual or if you want to change your usual diet, as this may affect your blood sugar level.
- ▶ If you are ill, carry on taking your insulin and consult your doctor.
- ▶ If you are going abroad, travelling over time zones may affect your insulin needs and the timing hereof.

Children and adolescents

- NovoMix® 30 can be used in adolescents and children aged 10 years and above.
- There is limited experience with NovoMix® 30 in children aged 6–9 years.
- No data are available for NovoMix® 30 in children below 6 years of age.

Other medicines and NovoMix® 30

Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. 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 (hypoglycaemia) 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 (hyperglycaemia) 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 stimulation of skeletal and somatic growth and pronounced influence on the body’s metabolic processes)
- Danazol (medicine acting on 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 symptoms which help you to recognise 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 experienced the development of 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 localised swelling (oedema).

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

Drinking alcohol and taking NovoMix® 30

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

Pregnancy and breast-feeding

- ▶ 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 hypoglycaemia, is important for the health of your baby.
- ▶ There are no restrictions on treatment with NovoMix® 30 during breast-feeding.

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

Driving and using machines

- ▶ Please ask your doctor whether you can drive a car or operate a machine:
 - If you have frequent hypoglycaemia.
 - If you find it hard to recognise hypoglycaemia.

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 NovoMix® 30

NovoMix® 30 contains less than 1 mmol sodium (23 mg) per dose, i.e. NovoMix® 30 is essentially 'sodium-free'.

3. *How to use NovoMix® 30*

Dose and when to take your insulin

Always use your insulin and adjust your dose exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

NovoMix® 30 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® 30 can be given soon after a meal. See *How and where to inject*, below for information.

When NovoMix® 30 is used in combination with tablets for diabetes, the dose should be adjusted.

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

NovoMix® 30 can be used in adolescents and children aged 10 years and above when premixed insulin is preferred. Limited clinical data exists for children aged 6–9 years. No data are available for NovoMix® 30 in children below 6 years of age.

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® 30 is for **injection under the skin** (subcutaneously). Never inject your insulin directly into a vein (intravenously) or muscle (intramuscularly). NovoMix® 30 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 injection site within the particular area of skin that you use. This may reduce the risk of developing lumps or skin pitting (see section 4, *Possible 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. You should always measure your blood sugar regularly.

How to handle NovoMix® 30 FlexPen®

NovoMix® 30 FlexPen® is a pre-filled, colour-coded, disposable pen containing a mixture of rapid-acting and intermediate-acting insulin aspart in the ratio 30/70.

Read carefully the instructions for use included in this package leaflet. You must use the pen as described in the Instructions for use.

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

If you take more insulin than you should

If you take too much insulin, your blood sugar gets too low (hypoglycaemia). See a) *Summary of serious and very common side effects* in section 4.

If you forget to take your insulin

If you forget to take your insulin, your blood sugar may get too high (hyperglycaemia). See c) *Effects from diabetes* in section 4.

If you stop taking your insulin

Do not stop taking your insulin without speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis. See c) *Effects from diabetes* in section 4.

If you have any further questions on the use of this medicine, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

a) Summary of serious and very common side effects

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

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 *Drinking alcohol and taking NovoMix® 30* in section 2).

Signs of low blood sugar: Cold sweat; cool pale skin; headache; rapid heartbeat; feeling sick; 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 stabilised, 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. The 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® 30 or one of its ingredients (called a systemic allergic reaction) is a very rare side effect, but it can potentially be life-threatening. It may affect less than 1 in 10,000 people.

Seek medical advice immediately:

- If signs of allergy spread to other parts of your body.
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heartbeat; feel dizzy.

- ▶ If you notice any of these signs, seek medical advice immediately.

b) List of other side effects

Uncommon side effects

May affect less than 1 in 100 people.

Signs of allergy: Local allergic reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site 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.

Changes at the injection site (lipodystrophy): The fatty tissue under the skin at the injection site may shrink (lipoatrophy) or thicken (lipohypertrophy). Changing the site with each injection reduces the risk of developing such skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor or nurse. These reactions can become more severe, or they may change the absorption of your insulin, if you inject in such a site.

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 people.

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.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

Ireland

HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2

Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie

United Kingdom

Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

c) Effects from diabetes

High blood sugar (hyperglycaemia)

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; feeling sick (nausea or vomiting); feeling drowsy or tired; flushed; dry skin; dry mouth and a fruity (acetone) smell of the breath.

What to do if you experience high blood sugar:

- ▶ If you get 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.

5. How to store NovoMix® 30

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the FlexPen® label and carton after 'EXP'. 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® 30 must be protected from excessive heat and light.

Before opening: NovoMix® 30 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® 30 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.

During use or when carried as a spare: NovoMix® 30 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. Contents of the pack and other information

What NovoMix® 30 contains

- The active substance is insulin aspart. NovoMix® 30 is a mixture consisting of 30% soluble insulin aspart and 70% insulin aspart crystallised with protamine. 1 ml contains 100 units of insulin aspart. Each pre-filled pen contains 300 units of insulin aspart in 3 ml suspension for injection.
- The other ingredients are glycerol, phenol, metacresol, zinc chloride, disodium phosphate dihydrate, sodium chloride, protamine sulfate, hydrochloric acid, sodium hydroxide and water for injections.

What NovoMix® 30 looks like and contents of the pack

NovoMix® 30 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.

Pack sizes of 1 (with or without needles), 5 (without needles) and 10 (without needles) pre-filled pens of 3 ml. Not all pack sizes may be marketed.

The suspension is cloudy, white and aqueous.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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

Manufacturer

The manufacturer can be identified by the batch number printed on the slip of the carton and on the label:

- If the second and third characters are S6, P5, K7, R7, VG, FG or ZF, the manufacturer is Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
- If the second and third characters are H7 or T6, the manufacturer is Novo Nordisk Production SAS, 45 Avenue d'Orléans, F-28000 Chartres, France.

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

This leaflet was last revised in 04/2018

Other sources of information

Detailed information on this medicine is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

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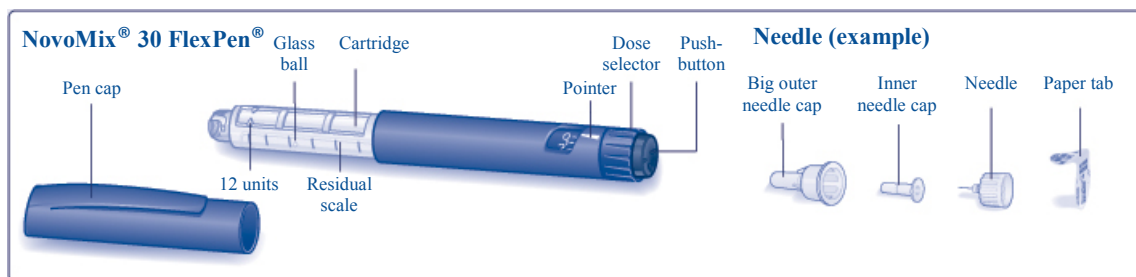
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Instruction on how to use NovoMix® 30 suspension for injection in FlexPen®.

Read the following 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 delivery device 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 medicinal swab. Do not soak, wash or lubricate it as it may damage the pen.
- ▶ **Do not refill your FlexPen®.**

Resuspending your insulin

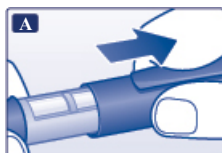
A

Check the name and coloured 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.

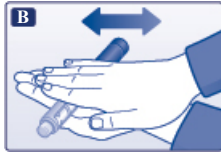
Pull off the pen cap.



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

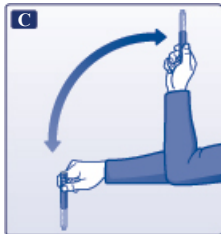
Then move the pen up and down 10 times between the two positions as shown, so the **glass ball moves** from one end of the cartridge to the other.

Repeat rolling and moving the pen until the liquid does appear 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 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 all 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 tab.

Screw the needle straight and tightly onto your FlexPen®.



E

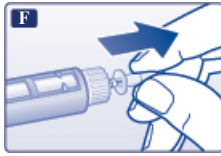
Pull off the big outer needle cap and keep it for later.



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 contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

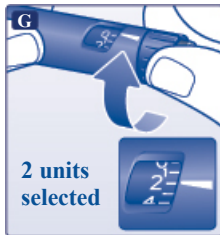
⚠ Be careful not to bend or damage the needle before use.

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 shown by your doctor or nurse.

K

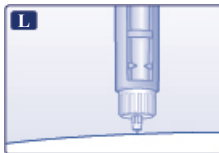
Inject the dose by pressing the push-button all the way in until 0 lines up with the pointer. Be careful only to push the push-button when injecting.

Turning the dose selector will not inject insulin.



L

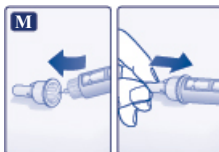
- ▶ Keep the **push-button fully depressed** and let the needle remain under the skin for **at least 6 seconds**. This will make sure you get the full dose.
- ▶ Withdraw the needle from the skin, then release the pressure on the push-button.
- ▶ Always make sure that the dose selector returns to 0 after 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 contamination, infection, 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 cross-infection.
- ⚠ Dispose of the used FlexPen® carefully without the needle attached.
- ⚠ Never share your pen or your needles with other people. It might lead to cross-infection.
- ⚠ 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.