

**Patient leaflet in accordance with the Pharmacists' Regulations
(Preparations) - 1986**

This medicine is dispensed with a doctor's prescription only

Mixtard 30 Vial

100 IU/ml

Suspension for injection in vial

Active ingredient: human insulin, 100 international units/ml

Inactive ingredients and allergens in this medicine: See section 6 Additional 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 for 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?

Mixtard 30 Vial is used to treat diabetes.

Therapeutic group: diabetes medicines, medium- or long-acting insulins and analogs for injection with fast-acting insulins, human insulin.

Mixtard 30 is human insulin composed of a mix of both a fast-acting and a long-acting insulin. It is used to reduce the high blood sugar level in patients with diabetes.

Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. Treatment with Mixtard 30 helps to prevent complications from your diabetes.

Mixtard 30 will start to lower your blood sugar about 30 minutes after you inject it, and the effect will last for approximately 24 hours.

2. Before using this medicine

Do not use this medicine:

- ▶ if you are sensitive (allergic) to human insulin or any of the other ingredients in this medicine (see section 6, 'Additional information')

- ▶ if you suspect your hypoglycemia (low blood sugar) is starting, (see section 4 under 'Summary of serious and very common side effects')
- ▶ in insulin infusion pumps
- ▶ if the protective cap is loose or missing. Each vial has a protective, resistant plastic cap. If the protective cap is defective when you buy the vial, return the vial to your supplier.
- ▶ if the vial has not been stored correctly or if it has frozen - see section 5
- ▶ if the resuspended insulin does not appear uniformly white and cloudy.

If any of these apply, do not use Mixtard 30. Ask your doctor, pharmacist, nurse or for advice.

Before using this medicine

- ▶ Check the label to make sure it is the right type of insulin.
- ▶ Remove the protective cap.
- ▶ Always use a new needle for each injection to prevent contamination.
- ▶ Needles and syringes must not be shared.

Special warnings about using this medicine

Some conditions and activities can affect your need for insulin. **Before starting treatment with Mixtard 30, tell 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, because these changes 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). 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 dose of insulin or other antidiabetic medications.

Use in special patient groups

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

Use in children and adolescents

Mixtard 30 can be used in children and in adolescents.

Other medicines and Mixtard 30 Vial

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Some medicines affect your blood sugar levels 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 problems 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 to treat 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 entirely suppress the first warning symptoms which help you recognize low blood sugar.

Pioglitazone (tablets used to treat type 2 diabetes)

Some patients with long-standing type 2 diabetes and who in addition have heart disease or previous stroke and 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, pharmacist or nurse.

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 is recommended.

Pregnancy, breastfeeding, and fertility

- ▶ 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. Mixtard 30 can be used during 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 Mixtard 30 during breastfeeding.

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

Driving and using machines

- ▶ 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 machines. Bear in mind that you could endanger yourself or others.

Important information about some of this medicine's ingredients

Mixtard 30 contains less than 1 mmol sodium (23 mg) per dose, which means that Mixtard 30 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. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

Do not exceed the recommended dose.

Eat a meal or snack containing carbohydrates within 30 minutes of the injection to avoid low blood sugar.

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

How and where to inject

Mixtard 30 is for injection under the skin (subcutaneously). Never inject directly into a vein (intravenously) or muscle (intramuscularly).

With each injection, change the injection site within the particular area of skin that you use. This may reduce your risk of developing lumps or skin pitting - see section 4. 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). Be careful to always measure your blood sugar regularly.

How to take Mixtard 30

Mixtard 30 vials are designed to be used with syringes marked with a unit scale for insulin.

1. Roll the vial between your hands until the liquid is uniformly white and cloudy. Resuspension is easier when the insulin has reached room temperature.
2. Draw into the syringe the same amount of air as the dose of insulin you are going to inject. Inject the air into the vial.
3. Turn the vial and syringe upside down so that the vial is on top, and draw the correct insulin dose into the syringe. Pull the needle out of the vial. Then expel the air from the syringe and check that the dose is correct.

How to inject Mixtard 30

- ▶ Inject the insulin under your skin. Use the injection technique that your doctor or nurse advised.
- ▶ Keep the needle under your skin for at least 6 seconds to make sure that you have injected all the insulin.

- ▶ After each injection, discard the needle and syringe.

If you have accidentally taken a higher dose

If you take too much insulin your blood sugar will get too low (hypoglycemia). See 'List of serious and very common side effects' in section 4.

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 your medicine

If you forget to take your insulin, your blood sugar may get too high (hyperglycemia), See 'Effects from diabetes' in section 4. If you forget to take the medicine at the scheduled time, do not take a double dose.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine

Do not stop taking your insulin without consulting 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 'Effects from diabetes' in section 4.

Do not take medicines in the dark! Check the label and dose every time you take 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

Like with all medicines, using Mixtard 30 may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

List of serious and very common side effects

Low blood sugar (hypoglycemia) is a very common side effect. It may affect more than one in ten 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; irritability or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If severe low blood sugar continues for long without being 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 a glucagon injection, 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 (such as candy, cookies, 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 has stabilized, continue insulin treatment as usual.
- ▶ If you have such low blood sugar that it makes you pass out, if you have needed 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 reaction to Mixtard 30 or any of its ingredients (called a systemic allergic reaction) is a very rare side effect, but it can be life-threatening. It 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 breathing, have a rapid heartbeat, feel dizzy
- ▶ If 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). Also, lumps under the skin may 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.

List of other side effects

Uncommon side effects - may affect less than one in 100 users.

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, or if they spread throughout your body, talk to your doctor immediately. See also 'Serious allergic reaction', above.

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.

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

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

Very rare side effects - may affect less than 1 in 10,000 users.

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

Effects from diabetes

High blood sugar (hyperglycemia)

High blood sugar may occur if:

- you have not injected enough insulin
- you forget to take your insulin or stop taking insulin
- you repeatedly inject less insulin than you need
- you get an infection and/or a fever
- you eat more than usual
- you exercise less than usual

Warning signs of high blood sugar:

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

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the vial label and on the carton. The expiry date refers to the last day of that month.

Storage conditions

- **Before opening:** Store in a refrigerator at 2°C to 8°C. Keep away from the cooling system wall. Do not freeze.
- **During use or when a vial is carried as a spare:** Do not refrigerate or freeze. You can carry it with you and keep it at room temperature (below 25°C) for up to 6 weeks.
- Always keep the vial in the outer carton when you are not using it, in order to protect it from light.
- Discard the needle and syringe after each injection.
- 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. Additional information

What Mixtard 30 contains:

Mixtard 30 is a mixture consisting of 30% soluble human insulin and 70% isophane human insulin. Each ml contains 100 IU of human insulin.

Each cartridge contains 1,000 IU of human insulin in 10 ml suspension for injection.

In addition to the active ingredients, this medicine also contains:

glycerol, disodium phosphate dihydrate, hydrochloric acid, metacresol, phenol, sodium hydroxide, protamine sulphate, zinc, water for injections.

What the medicine looks like and contents of the pack:

Mixtard 30 is a suspension for injection. After resuspension, the liquid should appear uniformly white and cloudy.

Pack size: a 10 ml vial.

The suspension is cloudy, white, and aqueous.

Registration holder's name and address

Novo Nordisk Ltd.
1 Atir Yeda Street
Kfar Saba 4464301

Manufacturer's name and address

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

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049-85-26012