

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

This medicine is dispensed with a doctor's prescription only

Actrapid Vial

100 IU/ml

Solution 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?

Actrapid is used for treatment of diabetes.

Therapeutic group: diabetes medicines, insulins and analogues for injection, fast-acting. Human insulin.

Actrapid is a fast-acting human insulin. It is used to reduce 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 Actrapid helps to prevent complications from your diabetes.

Actrapid will start to lower your blood sugar about half an hour after you inject it, and the effect will last for approximately 8 hours. Actrapid is often given in combination with intermediate-acting or long-acting insulin preparations.

2. Before using this medicine

Do not use this medicine:

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| <p>▶ if you are sensitive (allergic) to human insulin or any of the other ingredients in this medicine - see section 6</p> |
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- ▶ if you suspect hypoglycaemia (low blood sugar) is starting (see "List of serious and very common side effects" in section 4)
 - ▶ in insulin infusion pumps
 - ▶ if the protective cap is loose or missing. Each vial has a protective, tamper-proof plastic cap. If it is not in perfect condition when you buy the vial, return the vial to your supplier.

- ▶ if the cartridge has not been stored correctly or if it has frozen - see section 5
- ▶ if the insulin does not appear clear and colourless.

If any of the above applies to you, do not use Actrapid. Ask your doctor, pharmacist, or nurse 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 Actrapid, 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 insulin or other antidiabetic medications dose.

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.

Children and adolescents

Actrapid can be used in children and adolescents.

Interactions with other medicines

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

Some medicines affect your blood sugar level and your insulin dose may need to be changed. Listed below are the most common medicines which may affect your insulin treatment.

Your blood sugar level may fall (hypoglycaemia) if you are taking:

- 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 (hyperglycaemia) if you are taking:

- 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 hormone (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 and is 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 (oedema).

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. Actrapid 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 hypoglycaemia, is important for the health of your baby.
- ▶ There are no restrictions on treatment with Actrapid 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 hypoglycaemia
 - you find it hard to recognize 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 a car or operate a machine. Bear in mind that you could endanger yourself or others.

Important information about some of this medicine's ingredients

Actrapid contains less than 1 mmol sodium (23 mg) per dose, which means that Actrapid 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

Actrapid is given by injection under the skin (subcutaneously). You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). If necessary, Actrapid can be injected directly into a vein, but this must only be done by healthcare professionals.

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. 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 take Actrapid

Actrapid vials are for use with insulin syringes with a unit scale for insulin.

If you only use one type of insulin

1. 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.
2. Turn the vial and syringe upside down so that the vial is on top and draw the accurate 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.

If you have to mix two types of insulin

1. Just before use, roll the vial of intermediate or long-acting (cloudy) insulin between your hands until the liquid is uniformly white and cloudy.
2. Draw into the syringe the same amount of air as the dose of intermediate or long-acting insulin. Inject the air into the vial containing intermediate or long-acting insulin and pull out the needle.
3. Draw into the syringe the same amount of air as the dose of Actrapid. Inject the air into the vial containing Actrapid. Turn the vial and syringe upside down so that the vial is on top and draw up your prescribed dose of Actrapid. Expel any air from the syringe and check that the dose is correct.
4. Push the needle into the vial of intermediate or long-acting insulin, turn the vial and syringe upside down so that the vial is on top and draw out the dose you have been prescribed. Expel any air from the syringe and check that the dose is correct. Inject the mixture immediately.
5. Always mix Actrapid and intermediate or long-acting insulin in the same order.

How to inject Actrapid

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

If you have accidentally taken a higher dose

If you take too much insulin, your blood sugar will get too low (hypoglycaemia). 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 (hyperglycaemia). See “Effects of 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 first consulting your doctor who will tell you what needs to be done. Stopping this treatment could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis. See “Effects of 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 Actrapid 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 (hypoglycaemia) 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 section 2 “Using this medicine and alcohol consumption”.

Signs of low blood sugar: cold sweat; cool, pale skin; headache; rapid heartbeat; feeling sick (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 severe low blood sugar continues 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 inject 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 (such as 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 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 Actrapid or any 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 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 additional side effects

Uncommon side effects - may affect less than 1 in 100 users.

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

Vision problems: When you first start your insulin treatment, it may disturb your vision, but these disturbances are usually temporary.

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 - affect less than 1 in 10,000 users.

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.

Effects of 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 inject 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 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 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) 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 this 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 the refrigerator at 2°C to 8°C. Keep away from the cooling element. 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 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 Actrapid contains:

Each ml contains 100 IU of human insulin. Each vial contains 1000 IU of human insulin in 10 ml solution for injection.

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

Glycerol, metacresol, sodium hydroxide, hydrochloric acid, zinc chloride and water for injections.

What the medicine looks like and contents of the pack:

Actrapid is a solution for injection.

Pack size: One 10 ml vial.

The solution is clear and colourless.

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.

This leaflet was revised in December 2020.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 049-86-26015.