

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
The dispensing of this medicine requires a doctor's prescription

NovoRapid®

Vial 100 units/ml

Solution for injection in a vial

Active substance: Insulin aspart 100 units/ml

Inactive substances and allergens in this medicine: see section 2 "Important information about some of this medicine's ingredients" and section 6 "Additional information".

Read all of this 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 only. 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.
- This medicine is intended for adults, adolescents, and children over two years old.

1. What is this medicine intended for?

NovoRapid® is used to reduce the high blood sugar level in adults, adolescents, and children aged 2 years and above with diabetes.

Therapeutic group: Medicines for the treatment of diabetes. Fast-acting insulins and insulin analogs for injection.

NovoRapid® is a modern insulin (insulin analog) with a rapid-acting effect. 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. Treatment with NovoRapid® helps to prevent complications from your diabetes.

NovoRapid® will start to lower your blood sugar 10–20 minutes after you inject it, a maximum effect occurs between 1 and 3 hours after the injection and the effect lasts for 3–5 hours. Due to this short action NovoRapid® should normally be taken in combination with intermediate-acting or long-acting insulin preparations. NovoRapid® can also be used for continuous infusion in a pump system.

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 that this medicine contains (see section 6, "Additional information").

- ▶ You suspect hypoglycemia (low blood sugar) is starting (see section 4 item (a) "Summary of serious and very common side effects" in section 4).
- ▶ 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 purchase the vial, return the vial to your supplier.
- ▶ The vial has not been stored correctly or if it has frozen (see section 5, "How to store the medicine?").
- ▶ The insulin does not appear clear and colorless.

If any of these apply, do not use NovoRapid®. Talk with your doctor, nurse or pharmacist for advice.

Before using NovoRapid®

- ▶ 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. 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 these things 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 your other antidiabetic medications dose.

Children and adolescents

Do not give this medicine to children under two years old.

Interactions with other medicines

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. You must particularly tell your doctor if you are using any of the medicines, listed below, which affect your blood sugar level. Some medicines affect your blood sugar level and this means that your insulin dose may be affected. 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 (a medicine that stimulates skeletal and somatic growth and which has a pronounced effect on the body's metabolic processes)
- Danazol (a 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 suppress entirely the first warning symptoms which help you to recognize low blood sugar.

Pioglitazone (tablets used to treat 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. Tell 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 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. NovoRapid® 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 NovoRapid® during breastfeeding.

Ask your doctor, nurse or pharmacist 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 your concentration and ability to react might be affected and, therefore, also your ability to drive or operate a machine. Bear in mind that you could endanger yourself or others.

NovoRapid® has a rapid onset of effect therefore if hypoglycemia occurs, you may experience it earlier after an injection when compared to soluble human insulin.

Important information about some of this medicine's ingredients

NovoRapid® contains less than 1 mmol sodium (23 mg) per dose, which means that NovoRapid® is considered 'sodium-free'.

3. How to use this medicine?

Dose and when to take your insulin

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

NovoRapid® 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, NovoRapid® can be injected soon after a meal. See the section below "How and where to inject" for information about injecting.

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.

Do not exceed the recommended dose.

Use in children and adolescents

NovoRapid® can be given to adolescents and children aged 2 years and up instead of soluble human insulin when a rapid onset of effect is preferred. For example, when it is difficult to dose the child in relation to meals.

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

NovoRapid® is for injection under the skin (subcutaneously) or for continuous infusion in a pump system. Administration in a pump system will require comprehensive instruction by your healthcare professional. You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). If necessary NovoRapid® can be given directly into a vein but this must only be done by a doctor or other healthcare professional.

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, "Side effects"). The best places to give yourself an injection are the front of your waist (abdomen), the upper arm or the front of your thighs. The insulin will work more quickly if injected into the front of your waist. You should always measure your blood sugar regularly.

NPH (Neutral Protamine Hagedorn) insulin is the only type of insulin that can be mixed with NovoRapid® and the mixture must be injected immediately under your skin (subcutaneously). NovoRapid® should be drawn into the syringe before you draw your NPH insulin.

How to take NovoRapid®

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 with the vial end up 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.

If you have to mix two types of insulin

1. Just before use, roll the NPH 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 the NPH insulin. Inject the air into the vial containing the NPH insulin and pull out the needle.
3. Draw into the syringe the same amount of air as the dose of NovoRapid®. Inject the air into the vial containing NovoRapid®. Turn the vial and syringe upside down with the vial end up and draw up the prescribed dose of NovoRapid®. Expel the air from the syringe and check that the dose is correct.
4. Push the needle into the vial of the NPH insulin, turn the vial and syringe upside down with the vial end up, and draw out the dose you have been prescribed. Expel the air from the syringe and check the dose. Inject the mixture immediately.
5. Always mix NovoRapid® and the NPH insulin in the same sequence.

How to inject NovoRapid®

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

Use in an infusion pump system

NovoRapid® should never be mixed with any other insulin when used in a pump.

Follow the instructions and recommendations from your doctor regarding the use of NovoRapid® in a pump. Before using NovoRapid® in the pump system, you must receive comprehensive instruction in its use and information about any actions to be taken in case of illness, too high or too low blood sugar or failure of the pump system.

- Before inserting the needle, use soap and water to clean your hands and the skin where the needle is inserted to avoid any infection at the infusion site.
- When you fill a new reservoir, be certain not to leave large air bubbles in either the syringe or the tubing.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information leaflet supplied with the infusion set.
- Change the injection site every 3 days. Change the insulin in the reservoir at least every 6 days, even if you have not used up all the insulin.

To get the benefit of insulin infusion, and to detect possible malfunction of the insulin pump, it is advisable to measure your blood sugar level regularly.

What to do in case of pump system failure

You should always have an alternative delivery method for your insulin available for injection under the skin in case of pump system failure.

If you have accidentally taken a higher dose

If you take too much insulin your blood sugar gets too low (hypoglycemia). See item (a) "Summary 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 item (c) "Effects from diabetes" in section 4. If you forget to take this 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 speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycemia) and ketoacidosis. See item (c) "Effects from diabetes" in section 4.

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, ask your doctor or pharmacist.

4. Side effects

Like all medicines, using NovoRapid® may cause side effects in some users. Do not be alarmed by this 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; 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 by someone who

NovoRapid Vial IL PIL FEB-2021-NOTIFICATION

knows how to inject it. If you are given glucagon you will need glucose or a sugary 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 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. The amount or timing of your 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 NovoRapid® or one of its ingredients (called a systemic allergic reaction) are very rare side effects but can potentially be 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 a rapid heartbeat; feel dizzy
- ▶ you notice any of these signs, seek medical advice immediately.

Skin changes at the injection site: If you inject insulin at the same place, the fatty tissue may shrink (lipoatrophy) or thicken (lipohypertrophy) (may affect less than 1 in 100 people). 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 reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site may occur. These usually disappear after a few weeks of taking insulin. If they do not disappear, or if they spread throughout your body, talk to your doctor immediately. See also "Serious allergic reactions" above.

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, talk to 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.

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 Medication” 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>

(c) Effects from diabetes

High blood sugar (hyperglycemia)

High blood sugar may occur if you:

- Have not injected enough insulin.
- Forget to inject 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 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 the medicine?

- Prevent poisoning! To prevent poisoning, keep this medicine and all other medicines, in a closed place out of 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 which is stated on the vial label and on the carton, after "EXP" (short for expiry date). The expiry date refers to the last day of that month.
- Keep the vial in the outer carton in order to protect it from light.

Storage conditions

- **Before opening:** Store in a refrigerator at 2°C – 8°C. Keep away from the cooling element. Do not freeze.
- **During use or when carried as a spare:** The product may be stored for a maximum of 4 weeks. Store below 30°C. Do not refrigerate or freeze.
- Remove and discard the needle 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 NovoRapid® contains:

- Each ml contains 100 units of insulin aspart. Each vial contains 1,000 units of insulin aspart in 10 ml solution for injection.
- In addition to the active ingredient this medicine also contains:

Glycerol, sodium hydroxide, metacresol, hydrochloric acid, phenol, disodium phosphate dihydrate, sodium chloride, zinc, and water for injections.

What the medicine looks like and what are the contents of the package

NovoRapid® is presented as a solution for injection.

Each pack contains 1 vial of 10 ml.

The solution is clear and colorless.

Registration holder name and address

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

Manufacturer name and address

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This leaflet was revised in February 2021 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health National Drug Registry: 118-94-29983