**Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986**
**This medicine is dispensed with a doctor's prescription only**

**Levemir**
**100 units/ml**
**Solution for injection in cartridge (Penfill)**
**Active ingredient:** insulin detemir 100 units/ml
**Inactive ingredients and allergens in this medicine:** See section 2 under **'Important information about some of this medicine's ingredients'** and 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 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.

## 1. What is this medicine intended for?

Levemir is used to treat diabetes in adults, adolescents, and children aged 2 years and older.
**Therapeutic group:** Diabetes medicines. Long-acting insulins and analogs for injection.
Levemir is a modern insulin (insulin analog) with a long-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.

Levemir can be used with rapid acting insulin medicines that are taken close to meals.
In treatment of type 2 diabetes, Levemir may also be used in combination with medicines for diabetes taken by mouth and/or with injectable diabetes medicines, other than insulin.

Levemir has a long and steady blood-sugar-lowering effect within 3 to 4 hours after injection. Levemir provides sufficient basal insulin for up to 24 hours.

## 2. Before using this medicine

**Do not use this medicine:**

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

- If you suspect hypoglycemia (low blood sugar) is starting, see a) 'Summary of serious and very common side effects' in section 4.
- If you use insulin infusion pumps.
- If the cartridge or the device containing the cartridge is dropped, damaged or crushed.
- If it has not been stored correctly or has frozen, see section 5, 'How to store the medicine?'
- If the insulin does not appear water clear, colorless, and aqueous.

If any of the above happen, do not use Levemir. Ask your doctor, nurse or pharmacist for advice.

**Before using Levemir**
- Check the label to make sure it is the right type of insulin.
- Always check the cartridge, including the rubber plunger at the bottom of the cartridge. Do not use the cartridge if any damage is seen or if there is a gap between the rubber plunger and the white label band at the bottom of the cartridge. This could be the result of an insulin leakage. If you suspect that the cartridge is damaged, take it back to the pharmacy that supplied you with the medicine. See your delivery system manual for further instructions.

- Always use a new needle for each injection to prevent contamination.
- Needles and Levemir Penfill must not be shared.
- Levemir Penfill is only suitable for injecting under the skin using a reusable pen. Speak to your doctor if you need to inject your insulin by another method.

**Special warnings about using this medicine**
Some activities and conditions can affect your need for insulin.
**Before starting treatment with Levemir, 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, 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
- If you have very low albumin, you need to carefully monitor your blood sugar level. Discuss this with your doctor.

**Skin changes at the injection site**
Rotate the injection site 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.

**Children and adolescents**
Levemir can be used in adolescents and children aged 2 years and above.
The safety and efficacy of Levemir in children under two years old have not been established.

**Other medicines and Levemir**

**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 level. This may mean that your insulin dose has to change. Listed below are the most common medicines which may affect your insulin treatment.

<u>Your blood sugar level may fall (hypoglycemia) if you take:</u>
- 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).

<u>Your blood sugar level may rise (hyperglycemia) if you take:</u>
- 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 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 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 who have had a stroke and were treated with pioglitazone and insulin developed heart failure. Inform your doctor straight away 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. 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.
- If you are breastfeeding, consult your doctor as you may require adjustments in your insulin doses.

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

## 3. How to use this medicine?

**Insulin dose and when to take it**
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.

Levemir can be used with other medicines that contain rapid acting insulin and that are taken close to meals.
In treatment of type 2 diabetes, Levemir may also be used in combination with medicines for diabetes taken by mouth and/or with injectable diabetes medicines, other than insulin.
Do not change your insulin unless your doctor tells you to.
**Do not exceed the recommended dose.**
Your doctor may need to adjust your dose if:
- your doctor has switched you from one type or brand of insulin to another, or
- your doctor has added another medicine for the treatment of diabetes, in addition to your Levemir treatment.

**Use in children and adolescents**
Levemir can be used in adolescents and children aged 2 years and above.
There is no experience with the use of Levemir in children below the age of two years.

**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.

**How often to inject**
When Levemir is used in combination with diabetes medicines that are taken by mouth and/or in combination with injectable diabetes medicines, other than insulin, Levemir should be injected once a day. When Levemir is used as part of a basal-bolus insulin regimen Levemir should be injected once or twice daily depending on patients' needs. The dose of Levemir must be adjusted individually. The injection can be given at any time during the day, but at the same time each day. Patients who require treatment twice a day for optimal blood sugar control, can be given the evening dose in the evening or at bedtime.

**How and where to inject**
Levemir is for injection under the skin (subcutaneously). You must never inject Levemir directly into a vein (intravenously) or muscle (intramuscularly). Levemir Penfill is only suitable for injecting under the skin using a reusable injection pen. 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, 'Side effects'). The best places to give yourself an injection are: the front of your thighs, the front of your waist (abdomen), or the upper arm. Be careful to measure your blood sugar regularly.

- Do not refill the cartridge.
- Levemir Penfill cartridges are designed to be used with Novo Nordisk insulin delivery systems and NovoFine or NovoTwist needles.
- If you are treated with Levemir Penfill cartridges in addition to cartridges of another product, you should use a separate pen for each type of insulin.
- Always carry a spare insulin cartridge in case of loss or damage.

**How to inject Levemir**
- Inject the insulin under your skin. Use the injection technique advised by your doctor or nurse and as described in your insulin delivery system manual.
- Keep the needle under your skin for at least 6 seconds. Keep the injection-button fully depressed until the needle has been withdrawn from the skin. This will ensure correct delivery and limit possible flow of blood into the needle or insulin reservoir.
- After each injection be sure to remove and discard the needle and store Levemir without the needle attached. Otherwise the liquid may leak out which can cause inaccurate dosing.

**If you have accidentally taken a higher dose**
If you have accidentally taken a higher dose, your blood sugar will get too low (hypoglycemia). See item a) in 'Summary of serious and very common side effects' in section 4. If you have taken an overdose, or if a child has accidentally swallowed 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 medicine, your blood sugar may get too high (hyperglycemia). See item c) 'Effects from diabetes' in section 4. Do not take a double dose to make up for a missed dose. Adhere to the treatment as recommended by your doctor.

**If you stop taking this medicine**
Even if your health improves, do not stop your insulin treatment without consulting your 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 <u>every time</u> 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 Levemir 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; 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 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 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 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 signs 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 your doctor. The amount or timing of insulin injections, 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 Levemir 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.

**Consult your doctor 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; get a fast 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.

**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 reactions 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 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 swelling soon disappears. If it does 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; 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, and 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 cartridge label and on the package. The expiry date refers to the last day of that month.
- Always keep the cartridge in the outer package when you are not using it in order to protect it from light.
- Levemir must be protected from excessive heat and light.

**Storage conditions**

- **Before opening:** Levemir Penfill that is not being used must be stored in the refrigerator at 2°C to 8°C, away from the cooling system. Do not freeze.
- **During use or when Levemir Penfill is carried as a spare:** Do not keep Levemir Penfill in the refrigerator during use or when carried as a spare. You can carry the cartridge with you and keep it at room temperature (below 30°C) for up to 6 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. Additional information

**What Levemir contains:**

- The active ingredient is insulin detemir. Each ml contains 100 units of insulin detemir. Each cartridge contains 300 units of insulin detemir in 3 ml of solution for injection. One unit of insulin detemir corresponds to one international unit of human insulin.
- **In addition to the active ingredient, this medicine also contains:**
  glycerol, metacresol, phenol, sodium chloride, disodium phosphate dihydrate, zinc, hydrochloric acid, sodium hydroxide, and water for injections.

**What the medicine looks like and contents of the pack:**
Levemir is supplied as a solution for injection.
Each package contains 5 cartridges of 3 ml.

**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 Alle, DK-2880, Bagsværd
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This leaflet was revised in December 2020.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 132-40-31119.