Package leaflet: Information for the user

Levemir®
100 units/ml solution for injection in cartridge
insulin detemir

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 Levemir® is and what it is used for

Levemir® is a modern insulin (insulin analogue) with a long-acting effect. Modern insulin products are improved versions of human insulin.

Levemir® is used to **reduce the high blood sugar level** in adults, adolescents and children aged 1 year 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.

Levemir® can be used with meal-related rapid acting insulin medicines.
In treatment of type 2 diabetes mellitus, Levemir® may also be used in combination with tablets for diabetes and/or with injectable anti-diabetic products, other than insulin.

Levemir® has a long and steady blood-sugar-lowering action within 3 to 4 hours after injection. Levemir® provides up to 24 hours of basal insulin coverage.

2. What you need to know before you use Levemir®

Do not use Levemir®

- ► If you are allergic to insulin detemir 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 the cartridge or the device containing the cartridge is dropped, damaged or crushed.
- ► If it has not been stored correctly or been frozen, see section 5, *How to store Levemir®*.
- ► If the insulin does not appear water clear, colourless and aqueous.

If any of these applies, **do not use Levemir®**. Talk to 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 it if any damage is seen or if the rubber plunger has been drawn above 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 your supplier. See your pen 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.

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 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

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 Levemir®). 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

Levemir® can be used in adolescents and children aged 1 year and above.

The safety and efficacy of Levemir® in children below 1 year of age have not been established.
No data are available.

Other medicines and Levemir®

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)
- Sulphonamides (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], or salbutamol, 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 Levemir®

► 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. 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.
► If you are breast-feeding 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 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 a car or operate a machine. Bear in mind that you could

endanger yourself or others.

Important information about some of the ingredients in Levemir®

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

3. How to use Levemir®

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.

Levemir® can be used with meal-related rapid acting insulin medicines.
In treatment of type 2 diabetes mellitus, Levemir® may also be used in combination with tablets for diabetes and/or with injectable anti-diabetic products, other than insulin.

Do not change your insulin unless your doctor tells you to.
Your dose may have to be adjusted by your doctor 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 1 year and above.

There is no experience with the use of Levemir® in children below the age of 1 year.

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 often to inject

When Levemir® is used in combination with tablets for diabetes and/or in combination with injectable anti-diabetic products, other than insulin, Levemir® should be administered once a day. When Levemir® is used as part of a basal-bolus insulin regimen Levemir® should be administered once or twice daily depending on patients' needs. Dose of Levemir® should be adjusted individually. The injection can be given at any time during the day, but at the same time each day. For patients who require twice daily dosing to optimise blood sugar control, the evening dose can be administered 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 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, *Possible 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. You should always **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® and another insulin Penfill® cartridge, you should use two insulin delivery systems, one for each type of insulin.
- ► Always carry a spare Penfill® cartridge in case the one in use is lost or damaged.

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 pen manual.
- ► Keep the needle under your skin for at least 6 seconds. Keep the push-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 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 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 section 2 *Drinking alcohol and taking Levemir*®).

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 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 reaction to Levemir® or one of its ingredients (called a systemic allergic reaction) is a very rare side effect but 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.

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 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, 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 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

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.

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

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 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 Levemir®

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 cartridge label and carton after 'EXP'. The expiry date refers to the last day of that month.
Always keep the cartridge in the outer carton when you are not using it in order to protect it from light.

Levemir® must be protected from excessive heat and light.

Before opening: Levemir® Penfill® that is not being used is to be stored in the refrigerator at 2°C to 8°C, away from the cooling element. Do not freeze.

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

What Levemir® contains

- The active substance is insulin detemir. Each ml contains 100 units of insulin detemir. Each cartridge contains 300 units of insulin detemir in 3 ml solution for injection. 1 unit insulin detemir corresponds to 1 international unit of human insulin.
- The other ingredients are glycerol, phenol, metacresol, zinc acetate, disodium phosphate dihydrate, sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

What Levemir® looks like and contents of the pack

Levemir® is presented as a solution for injection.

Pack sizes of 1, 5 and 10 cartridges of 3 ml. Not all pack sizes may be marketed.

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.

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Other sources of information

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

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