PROFESSIONAL INFORMATION

Scheduling status

S3

1. Name of the medicine

Levemir® solution for injection.

2. Qualitative and quantitative composition

Contains insulin detemir 100 U/mL (produced by recombinant DNA technology in *Saccharomyces cerevisiae*). One unit (U) of insulin detemir contains 0,142 mg salt-free anhydrous insulin detemir. One unit (U) of insulin detemir corresponds to one IU of human insulin.

Excipients with known effect:

Preservatives:
Phenol 0,18 % *m/v*
Metacresol 0,206 % *m/v*
Sugar free.

For the full list of excipients, see section 6 .1.

3. Pharmaceutical form

Solution for injection.

Levemir® is a clear colourless liquid, free from turbidity and foreign matter.

4. Clinical particulars

4.1 Therapeutic indications

Levemir® is indicated for the treatment of diabetes mellitus in adults and children aged 1 year and older.

4.2 Posology and method of administration

The dosage of Levemir® should be adjusted individually.

Levemir® should be administered once or twice daily depending on patients' needs.

Levemir® can be used alone as the basal insulin or in combination with bolus insulin. It can also be used in combination with oral antidiabetic medicines and/or (glucagon-like peptide-1) GLP-1 receptor agonists treatment.

When Levemir® is used in combination with oral antidiabetic medicines or when added to GLP-1 receptor agonists, it is recommended to use Levemir® once daily, initially at a dose of 0,1 – 0,2 U/kg or of 10 U in adult patients. The injection can be given at any time during the day, but at the same time each day. The dose of Levemir® should be titrated based on the individual patients' needs.

When a GLP-1 receptor agonist is added to Levemir®, it is recommended to reduce the dose of Levemir® by 20 % to minimise the risk of hypoglycaemia. Subsequently, dosage should be adjusted individually.

For individual dose adjustments, the following titration guideline is recommended:

Average pre-breakfast SMPG*	**Levemir® dose adjustment**
> 10,0 mmol/L (180 mg/dL)	+8 U
9,1 – 10,0 mmol/L (163 – 180 mg/dL)	+6 U
8,1 – 9,0 mmol/L (145 – 162 mg/dL)	+4 U
7,1 – 8,0 mmol/L (127 – 144 mg/dL)	+2 U
6,1 – 7,0 mmol/L (109 – 126 mg/dL)	+2 U
4,1 – 6,0 mmol/L (73 – 108 mg/dL)	no change (target)
If one SMPG measurement:	
3,1 – 4,0 mmol/L (56 - 72 mg/dL)	-2 U
< 3,1 mmol/L (< 56 mg/dL)	-4 U
**Self Monitored Plasma Glucose*	

Levemir® is a long-acting insulin analogue used as a basal insulin. Levemir® is for subcutaneous administration only.
Levemir® must not be administered intravenously, as it may result in severe hypoglycaemia. Intramuscular administration should also be avoided. Levemir® is not to be used in insulin infusion pumps (see section 4.4).

Levemir® is administered subcutaneously by injection in the thigh, abdominal wall, the upper arm, the deltoid region or the gluteal region. Injection sites should be alternated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8). The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.

For patients who require twice daily dosing to optimise the blood glucose control, the evening dose can be administered either with the evening meal, at bedtime or 12 hours after the morning dose.

Transferring patients from intermediate or long-acting insulins to Levemir® may require adjustment of dose and timing of administration. Close glucose monitoring is recommended during the transition and in the initial weeks thereafter (see section 4.4.).

Concomitant antidiabetic treatment may need to be adjusted (dose and/or timing of concurrent short/rapid-acting insulins or the dose of oral antidiabetic medicines).

Adjustment of dosage may also be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness.
When adjusting dose in order to improve glucose control, patients should be advised to be aware of signs of hypoglycaemia.

Special populations
In elderly patients and in patients with renal or hepatic impairment, glucose monitoring should be intensified and insulin detemir dosage adjusted on an individual basis.

Paediatric population
Levemir® can be used in adolescents and children from the age of 1 year (see section 5.1). When changing basal insulin to Levemir®, dose reduction of basal and bolus insulin needs to be considered on an individual basis, in order to minimise the risk of hypoglycaemia (see section 4.4).

In children and adolescents, glucose monitoring should be intensified and the Levemir® dose adjusted on an individual basis.

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

Instructions for use and handling of Penfills:

Levemir® Penfill®: The cartridges are designed to be used with Novo Nordisk delivery systems (durable devices for repeated use) and NovoFine® or NovoTwist® needles.

Always ensure that the injection device is assembled according to the manufacturer's directions. Please refer to the instructions for use included with the relevant device.
Levemir® Penfill® is for use by one person only. The cartridge must not be refilled.

Instructions for use and handling are reflected in the attached Instructions for Use.

To avoid possible transmission of disease, FlexPen® is for single person use only.

Levemir® should not be used if it does not appear clear and colourless.
Levemir® which has been frozen must not be used.
Patients should be advised to discard the needle after each injection.

4.3 Contraindications

- Hypersensitivity to insulin detemir or to any of the excipients of Levemir® (see section 6.1).
- Intravenous administration.
- Hypoglycaemia.

4.4 Special warnings and precautions for use

Before travelling between different time zones, the patient should seek the doctor's advice since this may mean that the patient has to take Levemir® and meals at different times.

Hyperglycaemia
Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes (insulin-dependent diabetes mellitus) may lead to hyperglycaemia and diabetic ketoacidosis. Usually the first symptoms of hyperglycaemia develop gradually over a period of hours or days. They include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal.

Hypoglycaemia
The most frequently reported side effect is hypoglycaemia. It may occur if the Levemir® dose is too high in relation to the insulin requirement. Severe hypoglycaemia may lead to unconsciousness and or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur

suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation.

Omission of a meal or unplanned strenuous exercise may lead to hypoglycaemia. In children, care should be taken to match insulin doses (especially in basal-bolus regimens) with food intake and physical activities in order to minimise the risk of hypoglycaemia.

Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. In case of hypoglycaemia or if hypoglycaemia is suspected, Levemir® must not be injected. After stabilisation of the patient's blood glucose, adjustment of the dose should be considered (see sections 4.8 and 4.9).

Patients whose blood glucose is greatly improved e.g., intensified insulin treatment, may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes mellitus.

Concomitant illness, especially infections and feverish conditions, usually increases the patient's insulin requirements.
Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in insulin dose.

When patients are transferred between different types of insulin medicines, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin.

Anaphylactic reaction
The occurrence of generalised hypersensitivity reactions is potentially life-threatening. The symptoms of generalised hypersensitivity may include generalised skin rash, itching, sweating, gastrointestinal upset, angioedema, difficulties in breathing, palpitation and reduction in blood pressure.

Transfer from other insulin medicines
Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type, origin (animal, human, human insulin analogue) and/or method of manufacture (recombinant DNA versus animal source insulin) may result in the need for a change in dosage. Patients taking Levemir® from another type of insulin may require a change in dosage from that used with their usual insulin. If an adjustment is needed, it may occur with the first dose or during the first few weeks or months.

Levemir® should not be administered intravenously as it may result in severe hypoglycaemia (see section 4.3).

Absorption after intramuscular administration is faster and greater than absorption after subcutaneous administration.

Injection site reactions
As with any insulin therapy, injection site reactions may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area may help to reduce or prevent these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of Levemir®.

Skin and subcutaneous tissue disorders
Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site from an affected to an unaffected area, and dose adjustment of antidiabetic medicines may be considered.

Hypoalbuminaemia
There are limited data in patients with severe hypoalbuminaemia. Careful monitoring is recommended in these patients.

Combination of pioglitazone and insulin medicines
Cases of congestive heart failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of congestive heart failure. This should be kept in mind if treatment with the combination of pioglitazone and Levemir® is considered. If the combination is used, patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema.

Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs.

General
At the beginning of the Levemir® treatment, refraction anomalies and oedema of the eye may occur.

Rapid improvement in blood glucose control may be associated with acute painful neuropathy.

Intensification of insulin therapy with abrupt improvement in glycaemic control may worsen diabetic retinopathy.

Avoidance of accidental mix-ups/medication errors
Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Levemir® and other insulin products.

4.5 Interaction with other medicines and other forms of interaction

A number of medicines are known to interact with the glucose metabolism.
The following medicines may reduce the patient's Levemir® requirements:
- Oral hypoglycaemic medicines, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOIs) including linezolid, beta blockers, angiotensin converting enzyme (ACE)- inhibitors, anabolic steroids, sulphonamides, angiotensin receptor blockers (ARBs), and renin antagonists, such as aliskiren and salicylates.

The following medicines may increase the patient's Levemir® requirements:
- Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, beta-sympathomimetics, growth hormone and danazol.

Beta blocking medicines may mask the symptoms of hypoglycaemia and delay recovery from hypoglycaemia.

Octreotide/lanreotide and somatostatic analogues such as pasireotide may both increase and decrease Levemir® requirement.

Alcohol may intensify, prolong or reduce the hypoglycaemic effect of Levemir®.

Substances added to the Levemir® may cause degradation of Levemir® e.g., if the medicine contains thiols or sulphites.

Levemir® should not be added to infusion fluids.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of Levemir® in pregnant women with diabetes has been investigated in a clinical trial and in a prospective non-interventional post-authorisation safety study (see section 5.1).
Post-marketing data in pregnant women using Levemir®, with more than 4 500 pregnancy outcomes do not indicate any increased risk of malformative or feto/neonatal toxicity. Treatment with Levemir® can be considered during pregnancy, if clinically needed.

In general, intensified blood glucose control and monitoring of pregnant women with diabetes are recommended throughout pregnancy and when contemplating pregnancy. Insulin requirements usually fall in the first trimester and increase subsequently during the second and third trimester. After delivery, insulin requirements normally return rapidly to pre-pregnancy values.

Lactation

It is unknown whether insulin detemir is excreted in human milk. No metabolic effects of ingested insulin detemir on the breastfed newborn/infant are anticipated since insulin detemir, as a peptide, is digested into amino acids in the human gastrointestinal tract.
Breastfeeding women may require adjustments in insulin dose and diet.

Fertility

Animal studies do not indicate harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g., driving a car or operating machinery). Patients should be advised to take precautions in order to avoid hypoglycaemia while driving. This is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Adverse reactions observed in patients using Levemir® are mainly due to the pharmacologic effect of insulin. The overall percentage of treated patients expected to experience adverse reactions is estimated to be 12 %.
The most frequently observed side effect during treatment is hypoglycaemia.

From clinical investigations, it is known that major hypoglycaemia, defined as requirement for third party intervention, occurs in approximately 6 % of the patients treated with Levemir®.

Injection site reactions are seen more frequently during treatment with Levemir® than with human insulin products. These reactions include pain, redness, hives, inflammation, bruising, swelling and itching at the injection site. Most of the injection site reactions are minor and of a transitory nature, i.e., they normally disappear during continued treatment in a few days to a few weeks.

At the beginning of the insulin treatment, refraction anomalies and oedema may occur; these reactions are usually of transitory nature. Fast improvement in blood glucose control may be associated with acute painful neuropathy, which is usually reversible. Intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy, while long-term improved glycaemic control decreases the

risk of progression of diabetic retinopathy.
The side effects listed below are classified according to the system organ class (SOC) MedDRA. Frequency categories are defined according to the following convention:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

System organ class	**Frequency and side effect**
Immune system disorders	*Uncommon* Allergic reactions, potentially allergic reactions, urticaria, rash, eruptions*
	Very rare Generalised hypersensitivity (Anaphylactic reactions)*
Metabolism and nutrition disorders	*Very common* Change in blood glucose: Hypoglycaemia*/hyperglycaemia
Nervous system disorders	*Rare* Peripheral neuropathy (painful neuropathy)
Eye disorders	*Uncommon* Refraction disorders Transient refraction anomalies
	Uncommon Diabetic retinopathy Transient flare up of diabetic retinopathy
Skin and subcutaneous	*Uncommon*
tissue disorders	Lipodystrophy*: Lipodystrophy may occur at the injection site especially if injection sites are not frequently changed
	Not known Cutaneous amyloidosis *#
General disorders and administration site conditions	*Common* Injection site reactions, including redness, swelling and itching
	Uncommon Oedema

**see description of selected adverse events below.*
#adverse events from post-marketing experience.

Description of selected adverse reactions
Allergic reactions, potentially allergic reactions, urticaria, rash, eruptions
Allergic reactions, potentially allergic reactions, urticaria, rash and eruptions are uncommon when Levemir® is used in basal-bolus regimen. However, when used in combination with oral antidiabetic medicines, three clinical studies have shown a frequency of common (2,2 % of allergic reactions and potentially allergic reactions have been observed).

Skin and subcutaneous tissue disorders
Lipodystrophy (including lipohypertrophy, lipoatrophy) and cutaneous amyloidosis may occur at

the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Paediatric population
Based on post-marketing sources and clinical trials, the frequency, type and severity of adverse reactions observed in the paediatric population do not indicate any differences to the broader experience in the general diabetes population.

Other special populations
Based on post-marketing sources and clinical trials, the frequency, type and severity of adverse reactions observed in elderly patients and in patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of Levemir®. is important. It allows continued monitoring of the benefit/risk balance of Levemir®. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
A specific overdose for Levemir® cannot be defined; however, hypoglycaemia may develop over sequential stages if too high doses relative to the patient's requirements are administered.
- Mild hypoglycaemic episodes can be treated by oral administration of glucose or sugary products. It is therefore recommended that the diabetic patient always carry sugar containing products.
- Severe hypoglycaemic episodes, where the patient has become unconscious, can be treated by glucagon (0,5 to1 mg) given intramuscularly or subcutaneously by a trained person, or by glucose given intravenously by a medical professional.

Glucose must also be given intravenously if the patient does not respond to glucagon within 10 to 15 minutes.

Upon regaining consciousness administration of oral carbohydrate is recommended for the patient in order to prevent a relapse.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Category and class: A 21.1 Insulin preparations
Pharmacotherapeutic group: Drugs used in diabetes. Insulins and analogues for injection, long-acting
ATC code: A10AE05
Insulin detemir is a soluble, long-acting basal insulin analogue with a flat and predictable dose dependent action profile.

The prolonged action of insulin detemir is mediated by the strong self-association of insulin detemir molecules at the injection site and albumin binding via the fatty acid side-chain.

The blood glucose lowering effect of insulin detemir is due to the facilitated uptake of glucose following binding of insulin to receptors on muscle and fat cells and to the simultaneous inhibition of glucose output from the liver.
The duration of action is up to 24 hours depending on dose. The hypoglycaemic effect may last up to 14 hours.

Dose proportionality in pharmacodynamic response (*maximum effect, duration of action, total effect*) is observed after subcutaneous administration.

Pregnancy
In a prospective non-interventional post-authorisation safety study, pregnant women with type 1 or type 2 diabetes exposed to Levemir® (n=727, 680 liveborn infants) or other basal insulins (n=730, 668 liveborn infants) were monitored for pregnancy outcomes.
No statistically significant difference was observed between Levemir® and other basal insulins for the components of the malformation endpoint (induced abortion due to major congenital malformations, major congenital malformations or minor congenital malformations). The results from the study indicated that Levemir® is not associated with an excess risk of adverse pregnancy outcomes, when compared to other basal insulins, in women with pre-existing diabetes.

Levemir® has been studied in an open-label randomised controlled clinical trial, in which pregnant women with type 1 diabetes (n=310) were treated with a basal-bolus treatment regimen with Levemir® (n=152) or NPH insulin (n=158) as basal insulin, both in combination with NovoRapid®. Levemir® was non-inferior to NPH insulin as measured by HbA_{1c} at gestational week (GW) 36, and the reduction in mean HbA_{1c} through pregnancy was similar.

Paediatric population
The efficacy and safety of Levemir® has been studied for up to 12 months, in three randomised controlled clinical trials in adolescents and children (n=1 045 in total); the trials included in total 167 children aged 1 – 5 years. The trials demonstrated that glycaemic control (HbA_{1c}) with Levemir® is comparable to NPH insulin and insulin degludec when given as basal-bolus therapy, using a non-inferiority margin of 0,4 %. In the trial comparing Levemir® vs. insulin degludec, the rate of hyperglycaemic episodes with ketosis was significantly higher for Levemir®, 1,09 and 0,68 episodes per patient-year of exposure, respectively. Less weight gain (SD score, weight corrected for gender and age) was observed with Levemir® than with NPH insulin.

The trial including children above 2 years was extended for an additional 12 months (total of 24 months treatment data) to assess antibody formation after long-term treatment with Levemir®. After an increase in insulin antibodies during the first year, the insulin antibodies decreased during the second year to a level slightly higher than pre-trial level. Results indicate that antibody development had no negative effect on glycaemic control and Levemir® dose.

Efficacy and safety data for adolescent patients with type 2 diabetes mellitus have been extrapolated from data for children, adolescent and adult patients with type 1 diabetes mellitus and adult patients with type 2 diabetes mellitus. Results support the use of Levemir® in adolescent patients with type 2 diabetes mellitus.

5.2 Pharmacokinetic properties
Dose proportionality in serum concentrations (*maximum concentration, extent of absorption*) is observed after subcutaneous administration.
The terminal half-life after subcutaneous administration is determined by the rate of absorption from the subcutaneous tissue. The terminal half-life in patients with Type 1 diabetes mellitus is between 5 and 7 hours depending on dose. Maximum serum concentration is reached between 6 and 8 hours after administration.

An apparent volume of distribution for insulin detemir (approximately 0,1 L/kg) indicates that a high fraction of insulin detemir is circulating in the blood**.**

The degradation of insulin detemir is similar to that of human insulin, all metabolites formed are inactive**.**

The results of the *in vitro* and *in vivo* protein binding studies demonstrate that there is no clinically relevant interaction between insulin detemir and fatty acids or other protein bound medicines.

Special populations

Elderly, renal and hepatic impairment
There was no clinically relevant difference in pharmacokinetics of insulin detemir between elderly and young subjects, or between subjects with renal or hepatic impairment and healthy subjects.

Gender
There are no clinically relevant differences between genders in pharmacokinetic properties of insulin detemir.

Paediatric population
The pharmacokinetic properties of Levemir® were investigated in young children (1 – 5 years), children (6 – 12 years) and adolescents (13 – 17 years) and compared to adults with type 1 diabetes. There were no clinically relevant differences in pharmacokinetic properties between young children, children, adolescents and adults.

5.3 Preclinical safety data
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. Receptor affinity data and in vitro mitogenicity tests revealed no evidence of an increased mitogenic potential compared to human insulin.

6. Pharmaceutical particulars

6.1 List of excipients
Disodium phosphate dihydrate;
Glycerol (E422);
Hydrochloric acid (for pH-adjustment) (E507);
Metacresol (preservative);
Phenol (preservative);
Sodium chloride,
Sodium hydroxide (for pH-adjustment) (E524);
Water for injection.; and
Zinc acetate (E650).

6.2 Incompatibilities
Substances added to Levemir® may cause degradation of insulin detemir, e.g., if the medicine contains thiols or sulphites.
Levemir® should not be added to infusion fluids.
Levemir® must not be mixed with other medicines.
Levemir® should not be mixed with other insulins.
Levemir® is not to be used in insulin infusion pumps.

6.3 Shelf life
Before opening: 30 months.

During use or when carried as a spare: The product can be stored for a maximum of 6 weeks.

6.4 Special precautions for storage
Before opening: Store between 2 ˚C and 8 ˚C (in a refrigerator), not near a freezing compartment.
Protect from light.
Keep away from cooling element. Do not freeze.

Levemir® Penfill® cartridges and FlexPen® in-use or carried as a spare should be kept at ambient temperature (below 30 ˚C) for up to 6 weeks but should not be exposed to excessive heat or sunlight.
In order to protect from light Levemir® Penfill® cartridges should be kept in the outer carton and Levemir® FlexPen® should be kept with the cap on.
Do not store cartridges and FlexPens in-use in the refrigerator.
Never use insulin after expiry date.

6.5 Nature and contents of container
Levemir® Penfill®:
Cartridges (5 x 3 mL) are made of glass, containing a bromobutyl rubber plunger and closed with a bromobutyl/polyisoprene rubber closure and sealed with a cap made of aluminium. The cartridges are packed into a carton box.

Levemir® Flexpen® (5 x 3 mL):
Pre-filled multi-dose disposable insulin delivery device in which a Penfill® cartridge of 3 mL made of glass, containing a bromobutyl rubber closure plunger and closed with a bromobutyl/polyisoprene rubber closure is inserted. The FlexPens are packed into a carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Levemir® should not be used if it does not appear clear and colourless.
Levemir® which has been frozen must not be used.
The patient should be advised to discard the needle after each injection.

Any unused product or waste material should be disposed of in accordance with local requirements.

Needles, cartridges and pre-filled pens must not be shared.

The cartridge must not be refilled.

7. Holder of certificate of registration
Novo Nordisk (Pty) Ltd
150 Rivonia Road
10 Marion Street Office Park
Building C1
Sandton
Johannesburg 2196

8. Registration number
38/21.1/0084

9. Date of first authorisation/renewal of the authorisation
Date of registration: 23 September 2005

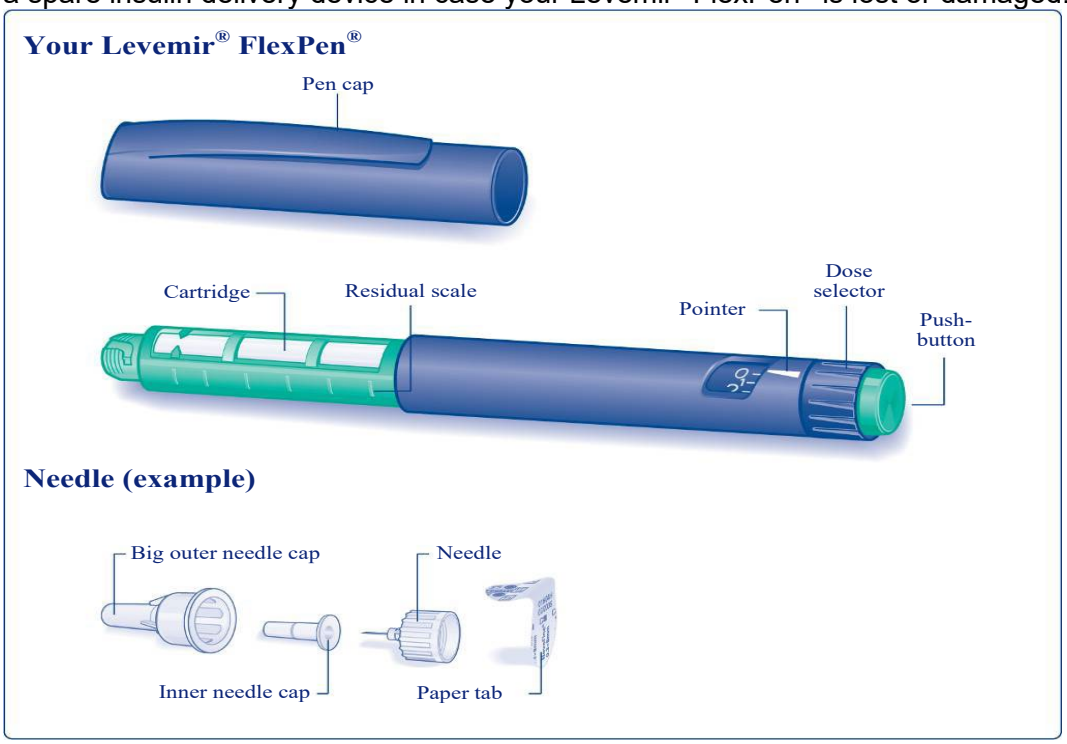
10. Date of revision of the text
Date of revision: 14 July 2023

Levemir®, FlexPen®, Penfill®, NovoTwist® and Novofine® are trademarks owned by Novo Nordisk A/S, Denmark
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Novo Nordisk A/S

Instructions for use
Levemir® solution for injection in pre-filled pen, FlexPen®

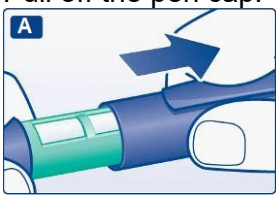
Please read the following instructions carefully before using your Levemir® FlexPen®.

Your Levemir® FlexPen® is a unique dial-a-dose insulin pen. You can select doses from 1 to 60 units in increments of 1 unit. The Levemir® FlexPen® is designed to be used with NovoFine® or NovoTwist® disposable needles up to a length of 8 mm. As a precautionary measure, always carry a spare insulin delivery device in case your Levemir® FlexPen® is lost or damaged.



Maintenance
- Your Levemir® FlexPen® is designed to work accurately and safely. It must be handled with care.
- If it is dropped, damaged or crushed, there is a risk of insulin leakage.
- You can clean the exterior of your Levemir® FlexPen® by wiping it with a medicinal swab. Do not soak, wash or lubricate it as it may damage the pen.
- Do not refill your Levemir® FlexPen®.

Preparing your Levemir® FlexPen®
Check the label to make sure that your FlexPen® contains the correct type of insulin.
A
Pull off the pen cap.

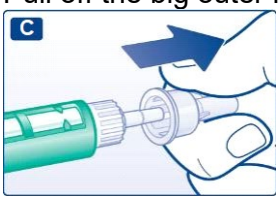


B
Remove the paper tab from a new disposable needle.

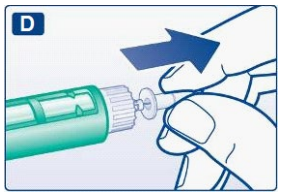
Screw the needle straight and tightly onto your FlexPen®.



C
Pull off the big outer needle cap and keep it for later.



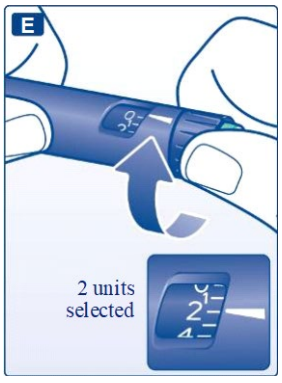
D
Pull off the inner needle cap and dispose of it.



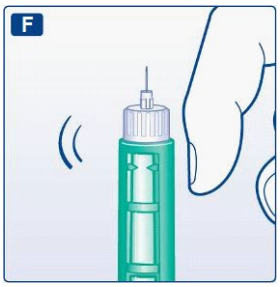
- Always use a new needle for each injection to prevent contamination.
- Be careful not to bend or damage the needle before use.
- To reduce the risk of unexpected needle sticks, never put the inner needle cap back on when you have removed it from the needle.

Checking the insulin flow
Prior to each injection, small amounts of air may collect in the cartridge during normal use. To avoid injection of air and ensure proper dosing:

E
Turn the dose selector to select 2 units.



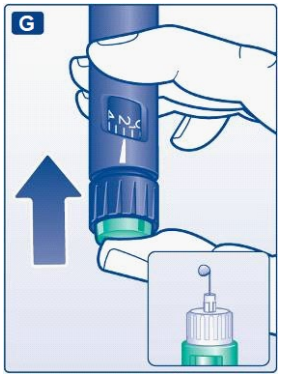
F
Hold your FlexPen® with the needle pointing upwards and tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge.



G
Keeping the needle upwards, press the push-button all the way in. The dose selector returns to 0.

A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

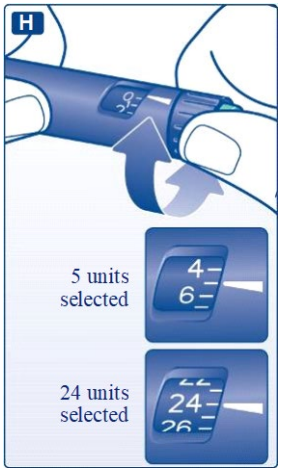
If a drop of insulin still does not appear, the pen is defective, and you must use a new one.



Selecting your dose
Check that the dose selector is set at 0.

H
Turn the dose selector to select the number of units you need to inject.

The dose can be corrected either up or down by turning the dose selector in either direction until the correct dose lines up with the pointer. When turning the dose selector, be careful not to push the push-button as insulin will come out.
You cannot select a dose larger than the number of units left in the cartridge.



- Do not use the residual scale to measure your dose of insulin.

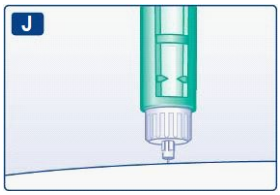
Making the injection
Insert the needle into your skin. Use the injection technique shown by your doctor or nurse.

I
Inject the dose by pressing the push-button all the way in until 0 lines up with the pointer. Be careful only to push the push-button when injecting.

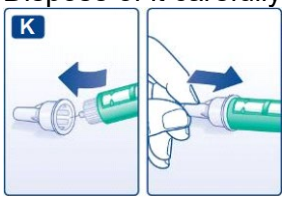
Turning the dose selector will not inject insulin.



J
Keep the push-button fully depressed and let the needle remain under the skin for at least 6 seconds. This will make sure you get the full dose.



K
Lead the needle into the big outer needle cap without touching it. When the needle is covered, carefully push the big outer needle cap completely on and then unscrew the needle. Dispose of it carefully and put the pen cap back on.



- Always remove the needle after each injection and store your Levemir® FlexPen® without the needle attached. Otherwise, the liquid may leak out which can cause inaccurate dosing.
- Caregivers should be most careful when handling used needles to avoid needle sticks.
- Dispose of the used Levemir® FlexPen® carefully without the needle attached.
- Needles and Levemir® FlexPen® must not be shared.