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

Norditropin® 10 mg

NordiFlex®
Solution for injection in pre-filled pen

Active ingredient
somatropin 10 mg/1.5 ml
Inactive ingredients and allergens in the preparation: see section 6 - Further information.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine**.** If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

This leaflet contains instructions for using your Norditropin NordiFlex pen.

1. What is this medicine intended for?

❖ **In children:**
- to treat children with short stature due to failed or inadequate secretion of growth hormone by the pituitary
- to treat children with short stature due to Turner syndrome
- to treat children with short stature due to renal insufficiency
- to treat children with short stature associated with Noonan syndrome
- growth disturbance in short children born small for gestational age (SGA) who failed to show catch-up growth by 4 years of age.

❖ **In adults:**
To treat adults with hypothalamic-pituitary disease due to an organic problem or pituitary tumours, treated medicinally, surgically or by radiotherapy or patients with childhood onset of growth hormone deficiency.

Therapeutic group: somatropin and somatropin agonists

Norditropin contains a biosynthetic human growth hormone called somatropin which is identical to the growth hormone produced naturally in the body. Children need growth hormone to help them grow; However, adults also need it for their normal health.

2. Before using the medicine

Do not use this medicine if:

- you are **sensitive** (allergic) to somatropin, to phenol, or to any of the other ingredients in this medicine (see section 6)
- you have had a **kidney transplant**
- you have an **active tumour (cancer)**. The tumour must be inactive and you must have finished your anti-cancer treatment before you start your treatment with Norditropin NordiFlex

- you have an **acute critical illness** e.g. open heart surgery, abdominal surgery, multiple accidental trauma, or acute respiratory failure
- you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency

Special warnings about using this medicine

Before using Norditropin, tell your doctor if:
- you have **diabetes**
- you had **cancer** or another kind of **tumour**
- you have recurrent **headaches, eyesight problems, nausea or vomiting**
- you have abnormal **thyroid** function
- there is an increase in sideways curvature of the spine (scoliosis) which may progress in any child during rapid growth. During treatment with Norditropin, your doctor will check you (or your child) for signs of scoliosis.
- you walk with a limp or if you start to limp during your growth hormone treatment
- you are **over 60 years of age,** or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- you suffer from a **kidney disease,** as your kidney function should be monitored by your doctor
- you receive **a replacement therapy with glucocorticoids.** Consult your doctor regularly, because you may need adjustment of your glucocorticoid dose.
- Norditropin may cause an inflammation of the pancreas, which causes severe pain in the abdomen and back. Contact your doctor if you or your child develops stomach ache after taking Norditropin.

Drug Interactions
Tell the doctor or pharmacist if you are taking or if you have recently taken other medicines, including nonprescription medicines and dietary supplements. In particular, inform your doctor if you are taking, or have recently taken, any of the following medicines. Your doctor may need to adjust the dose of Norditropin or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin and glucocorticoids at the same time.
- **Cyclosporin** (immunosuppressive) – your dose may need to be adjusted.
- **Insulin** – your dose may need to be adjusted.
- **Thyroid** hormone – your dose may need to be adjusted.
- **Gonadotrophin** (gonad stimulating hormone) – your dose may need to be adjusted.
- **Anticonvulsants** – your dose may need to be adjusted.
- **Estrogen** taken orally or other sex hormones.

Pregnancy and breast-feeding
Somatropin containing products are not recommended for women of childbearing potential not using contraception.
- **Pregnancy** - Stop the treatment and tell your doctor if you become pregnant while you are using Norditropin.
- **Breast-feeding** - Do not use Norditropin if you are breast-feeding because somatropin might pass into your milk.

Driving and using machines
Norditropin does not affect the use of any machines or the ability to drive safely.

Important information about some of this medicine's ingredients
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, therefor it is considered 'sodium-free'.

3. How to use the medicine?

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

The recommended dose is usually:
The dose for children depends on their body weight and body surface area. Later in life, the dose depends on your height, weight, gender and growth hormone sensitivity and will be adjusted until you are on the right dose.

- **Children with low production or lack of growth hormone:**
  The usual dose is 0.025 to 0.035 mg per kg body weight per day or 0.7 to 1.0 mg per m^2 body surface area per day.
- **Children with Turner syndrome:**
  The usual dose is 0.045 to 0.067 mg per kg body weight per day or 1.3 to 2.0 mg per m^2 body surface area per day.
- **Children with Noonan syndrome:**
  The usual dose is up to 0.066 mg per kg body weight per day.
- **Children with kidney disease:**
  The usual dose is 0.050 mg per kg body weight per day or 1.4 mg per m^2 body surface area per day.
- **Children born small for gestational age (SGA):**
  The usual dose is 0.035 mg per kg body weight per day or 1.0 mg per m^2 body surface area per day until final height is reached (In clinical trials of short children born small for gestational age, doses of 0.033 and 0.067 mg per kg body weight per day have typically been used).
- **Adults with low production or lack of growth hormone:**
  If your growth hormone deficiency continues after completion of growth, treatment should be continued. The usual starting dose is 0.2 to 0.5 mg per day. Dose will be adjusted until you are on the right dose. If your growth hormone deficiency starts during adult life, the usual starting dose is 0.1 to 0.3 mg per day. Your doctor will increase this dose each month until you are getting the dose you need. The usual maximum dose is 1.0 mg per day.

Do not exceed the recommended dose.

When to use Norditropin
Inject your daily dose into the skin every evening before bedtime.

How to use Norditropin NordiFlex
Norditropin growth hormone solution comes in a multi-dose disposable 1.5 ml pre-filled pen called NordiFlex. Full instructions on how to use the Norditropin NordiFlex pen are given at the end of the leaflet. Key points during use are as follows:
- Check the solution before use by turning the pen upside down once or twice. Do not use the pen if the solution is cloudy or discoloured.
- Norditropin NordiFlex is designed to be used with NovoFine® or NovoTwist® disposable needles up to a length of 8 mm.
- Always use a new needle for each injection.
- Vary the area you inject to avoid harming your skin.
- To make sure you get the proper dose and do not inject air, check the growth hormone flow before the first injection from a new Norditropin NordiFlex pen. Do not use the pen if a drop of growth hormone solution does not appear at the needle tip.
- Do not share your Norditropin NordiFlex pen with anyone else.

Treatment duration
- Children with growth failure because of Turner syndrome, kidney disease, children who were born small for gestation age (SGA), or children with Noonan syndrome: Your doctor will recommend you continue treatment until you stop growing.
- Children or adolescents who lack growth hormone: Your doctor will recommend you continue treatment into adulthood.
- Do not stop using Norditropin NordiFlex without discussing it with your doctor first.

If you have accidently taken a higher dosage
Long-term overdosing can cause abnormal growth and coarsening of facial features. If you have taken an overdose, or if a child has accidentally injected himself with some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to use the medicine
If you forget to take the medicine at the scheduled time, take the next dose at the normal time and consult your doctor. **Do not take a double dose** to make up for a forgotten 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 using the medicine
Do not stop using Norditropin NordiFlex without consulting your doctor first.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them. Consult your doctor or pharmacist if you have any further questions about using this medicine.

4. <u>Side effects</u>

As with any medicine, using Norditropin may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Effects seen in children and adults (unknown frequency):
- **Rash; wheezing; swollen eyelids, face or lips; complete collapse.** Any of these may be signs of allergic reaction.
- **Headache, eyesight problems, nausea**, **and vomiting.** These may be signs of raised pressure in the brain.
- **Serum thyroxin** level may decrease.
- **Hyperglycaemia** (elevated levels of blood sugar).

If you get any of these effects, **see a doctor as soon as possible.** Stop using Norditropin NordiFlex until your doctor says you can continue treatment.

Formation of antibodies directed against somatropin has been rarely observed during Norditropin therapy.
Increased levels of liver enzymes have been reported.
Cases of leukaemia and relapse of brain tumours have also been reported in patients treated with somatropin (the active ingredient in Norditropin NordiFlex), although there is no evidence that somatropin was responsible.
If you think you are suffering from any of these diseases, talk to your doctor.

Additional side effects in children:

Uncommon (may affect up to 1 in 100 children):
- **Headache**
- **Redness**, itching and pain in the area of injection
- **Breast enlargement.**

Rare (may affect up to 1 in 1,000 children):
- **Rash**
- **Muscle** and joint pain
- **Swollen hands** and feet due to fluid retention.

In rare cases, children using Norditropin have experienced hip and knee pain or have started limping. These symptoms may be caused by a disease affecting the top of the thigh bone (*Legg-Calvé disease*) or because the end of the bone has slipped from the cartilage (*slipped capital femoral epiphysis*) and may not necessarily be due to Norditropin.

In children with **Turner syndrome**, a few cases of **increased growth of hands and feet** compared to height have been observed in clinical trials.
A clinical trial in children with Turner syndrome has shown that high doses of Norditropin can possibly increase the risk of getting ear infections.

Additional side effects in adults:

Very common (may affect more than 1 in 10 adults):
- **Swollen hands** and feet due to fluid retention.

Common (may affect up to 1 in 10 adults):
- **Headache**
- Feeling of **skin crawling** (formication) and numbness or pain mainly in fingers
- **Joint pain** and stiffness; muscle pain.

Uncommon (may affect up to 1 in 100 adults):
- **Type 2 diabetes**
- **Carpal tunnel *syndrome*;** tingling and pain in fingers and hands
- **Itching** (can be intense) and pain in the area of injection
- **Muscle stiffness**
- **Breast enlargement.**

Consult your doctor if you experience any side effect, if any side effect gets worse or if you experience a side effect not listed in this leaflet, as your dose may need to be reduced.

Reporting of 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 refers to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use this medicine after the expiry date (Exp. Date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions

Store **unused** Norditropin NordiFlex pens in a refrigerator (2°C – 8°C) in the outer carton, in order to protect them from light. Do not freeze or expose to heat. Do not store close to the cooling elements.

While using Norditropin NordiFlex 10 mg/1.5 ml pen, you can:
- Keep it for up to 4 weeks in a refrigerator (2°C – 8°C), **or**
- Keep it for up to 3 weeks at room temperature (below 25°C).

- Do not use Norditropin NordiFlex pens if they have been frozen or exposed to excessive temperatures.
- Do not use Norditropin NordiFlex pens if the growth hormone solution is cloudy or discoloured.
- Always store Norditropin NordiFlex without a needle attached.
- Always keep the pen cap fully closed on the Norditropin NordiFlex pen when you are not using it.
- Always use a new needle for each injection.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Further information

In addition to the active ingredient, the medicine also contains:
mannitol; poloxamer 188; phenol; histidine; water for injection; hydrochloric acid and sodium hydroxide.

What the medicine looks like and contents of the pack:
Norditropin is a clear and colourless solution for injection in a multi-dose, disposable, 1.5 ml pre-filled pen.
1 ml of solution contains 6.7 mg somatropin.
1 mg of somatropin is equivalent to 3 IU of somatropin.

Norditropin NordiFlex is marketed in two strengths:
10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 6.7 mg/ml and 10 mg/ml, respectively).
Not all strengths may be marketed.

License holder's name and address:
Novo Nordisk Ltd.,
1 Atir Yeda street
Kfar Saba, 4464301

Manufacturer's name and address:
Novo Nordisk A/S,
Novo Allé, DK-2880 Bagsværd, Denmark

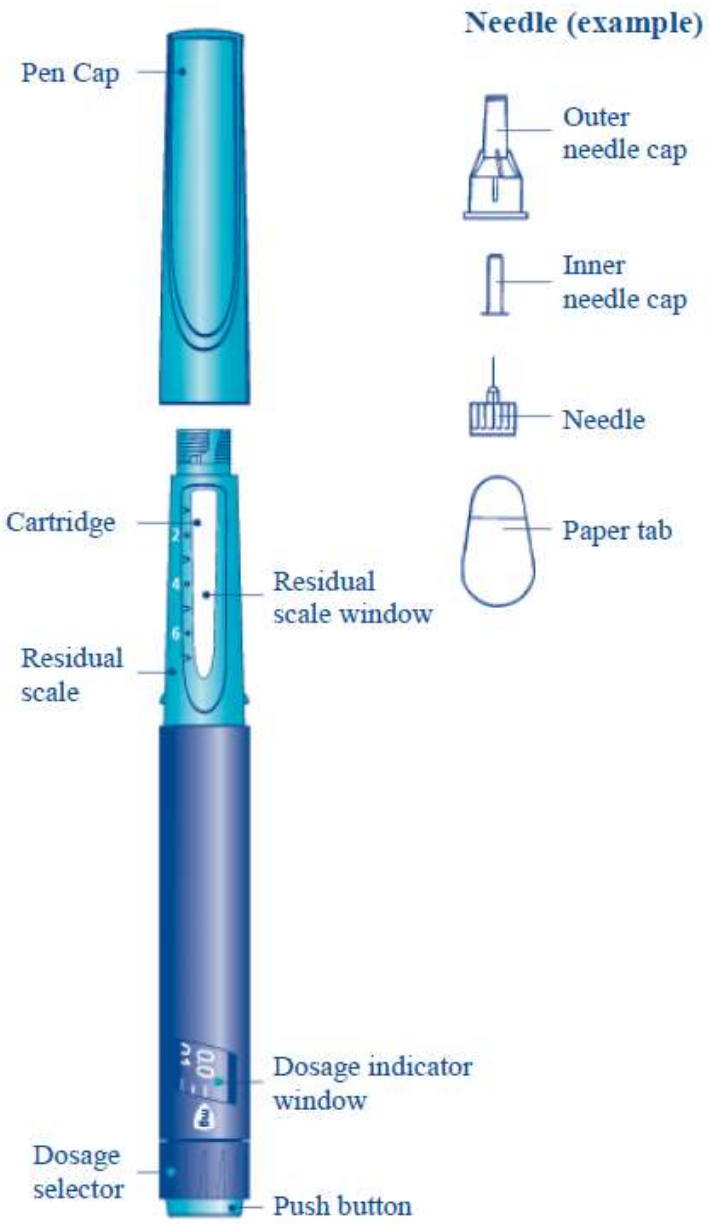
This leaflet was revised in July 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of Ministry of Health:
118-74-29921

Instructions for using Norditropin NordiFlex pen 10 mg/1.5 ml

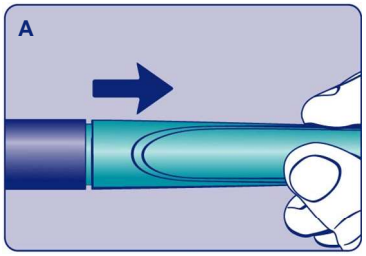
Read these instructions carefully before using Norditropin NordiFlex.

- Norditropin NordiFlex 10 mg/1.5 ml is a multi-dose, pre-filled injection pen with human growth hormone solution.
- You can use the dosage selector to select any dose from 0.05 to 3.00 mg, in increments of 0.05 mg. Your doctor will decide the correct dose for you.
- Norditropin NordiFlex is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.
- Start by checking the name, strength, and colour of the label of your Norditropin NordiFlex pen to make sure that it contains the growth hormone strength you need.
- Only use the pen if the solution inside the cartridge is clear and colourless.
- Always use a new needle for each injection.
- Always check the flow before the first injection from a new pen. See step 3 - ‘Check the flow’.
- Never share your pen or your needles with anyone else. It might lead to cross-infection.
- Always keep your pen and needles out of reach and sight of children.
- Caregivers must be very careful when handling used needles in order to reduce the risk of needle sticks and cross-infection.


Needle (example)
Pen Cap
Outer needle cap
Inner needle cap
Needle
Paper tab
Cartridge
Residual scale window
Residual scale
Dosage indicator window
Dosage selector
Push button

1. Check the pen

- **Check the name, strength and colour of the label of your Norditropin NordiFlex pen to make sure that it contains the growth hormone strength you need.**
- Pull off the pen cap **(A)**.
- Check that the solution inside the cartridge is clear and colourless by tipping the pen upside down once or twice.
- Do not use the pen if the solution inside the cartridge is unclear or cloudy.

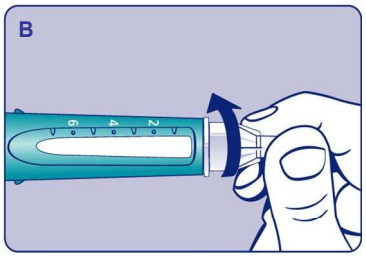


2. Attach the needle

- **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of solution, blocked needles and inaccurate dosing. Never bend or damage the needle.
- Remove the protective paper tab from the needle.
- Screw the needle straight onto the pen **(B)**. Make sure the needle is on tight.

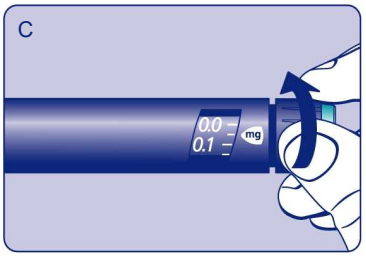
The needle has two caps. You need to remove them both:

- Pull off the outer needle cap and keep it to correctly remove the needle from the pen after the injection.
- Remove the inner needle cap by pulling on the central tip and throw it away.

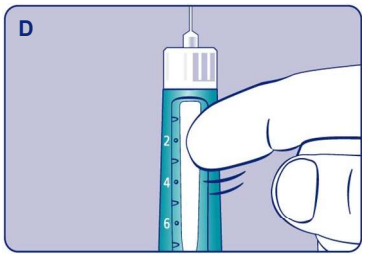


3. Check the flow:

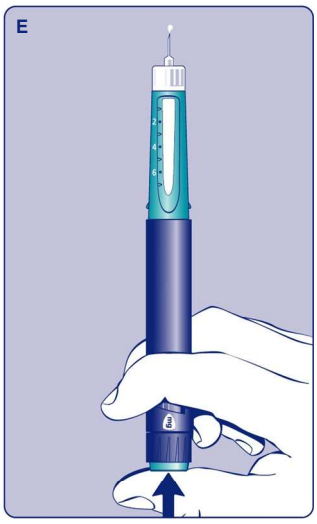
- **Before your first injection with each new pen, you need to check the flow** to make sure you get the proper dose and do not inject any air:
  Select 0.05 mg **(C)**. This is one ‘click’ after 0.0 on the dosage selector at the end of the pen.



- Hold the pen with the needle pointing upwards and tap the top of the pen a few times to let any air bubbles rise to the top **(D)**.

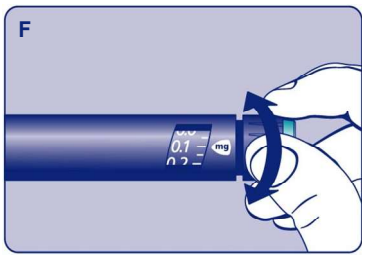


- Holding the pen with the needle upwards, press the push-button at the bottom of the pen all the way in **(E)**. A drop of solution will appear at the needle tip.
- If no drop appears, repeat steps (C) to (E) up to 6 times until a drop appears. If there is still no drop, change the needle and repeat steps (C) to (E) once more.
- **Do not use the pen if a drop does not appear.** Use a new pen.
- Always check the flow before the first injection from a new pen.
  Check the flow again if your pen has been dropped or knocked against a hard surface, or if you suspect something is wrong with it.



4. Select the dose

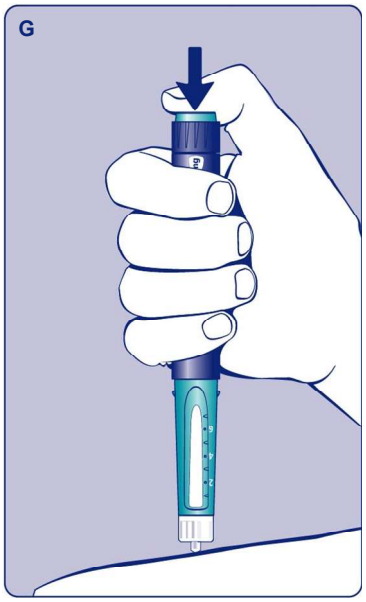
- Check that the dosage selector is set at 0.0.
  Select the number of mg your doctor has prescribed for you **(F)**.
- The dose can be increased or decreased by turning the dosage selector backwards or forwards. When turning the dosage selector backwards, be careful not to press the push-button because the solution will come out. You cannot set a dose larger than the number of mg left in the pen.



5. Inject the dose

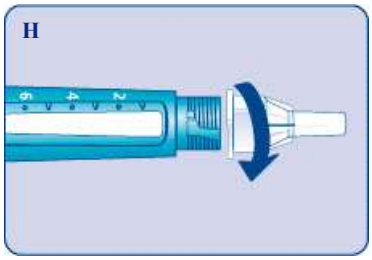
- Use the injection method shown to you by your doctor or nurse.
- Vary the area you inject so you do not harm your skin.
- Insert the needle into your skin. Deliver the dose by pressing the push-button all the way in. Be careful to press the push-button only when injecting **(G)**.

- **Keep the push-button fully depressed and let the needle remain under the skin for at least 6 seconds.** This ensures that you get the full dose.



6. Remove the needle

- Carefully put the outer needle cap back on the needle without touching the needle. Unscrew the needle and throw it away carefully as instructed by your doctor or nurse **(H)**. **Never put the inner needle cap back on** once you have removed it from the needle. You may accidentally stick yourself with the needle.
- Put the pen cap back on after every use.
- **Always remove and dispose of the needle after each injection and store the pen without the needle attached.** This reduces the risk of infection, contamination, leakage of solution, blocked needles and inaccurate dosing.
- When the pen is empty, throw it away without the needle attached, as advised by your doctor or nurse and local authorities.
- **Caregivers must be very careful when handling used needles to reduce the risk of needle sticks and cross-infection.**



7. Maintenance

- Your Norditropin NordiFlex pen must be handled with care.
- Do not drop your pen or knock it against hard surfaces. If you drop it or suspect that something is wrong with it, always screw on a new needle and check the flow before you inject.
- Do not try to refill your pen – it is pre-filled.
- Do not try to repair your pen or pull it apart.
- Protect your pen from dust, dirt, frost and direct sunlight.
- Do not try to wash, soak, or lubricate your pen. If necessary clean it with a mild detergent on a moistened cloth.
- Do not freeze your pen and do not store it close to the cooling elements, for example in the fridge.

- For information about storing your pen - see section 5 of the patient leaflet ‘How to store this medicine’.