SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 5 mg/1.5 ml, solution for injection in pre-filled pen
Norditropin NordiFlex 10 mg/1.5 ml, solution for injection in pre-filled pen
Norditropin NordiFlex 15 mg/1.5 ml, solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Norditropin NordiFlex: 5 mg/1.5 ml
One ml of solution contains 3.3 mg somatropin

Norditropin NordiFlex: 10 mg/1.5 ml
One ml of solution contains 6.7 mg somatropin

Norditropin NordiFlex: 15 mg/1.5 ml
One ml of solution contains 10 mg somatropin

Somatropin (recombinant DNA origin produced in E-coli)

1 mg of somatropin corresponds to 3 IU (International Unit) of somatropin

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled pen

Clear, colourless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Children:
Growth failure due to growth hormone deficiency (GHD)

Growth failure in girls due to gonadal dysgenesis (Turner syndrome)

Growth retardation in prepubertal children due to chronic renal disease

Growth disturbance (current height SDS < -2.5 and parental adjusted height SDS < -1) in short children born small for gestational age (SGA), with a birth weight and/or length below -2 SD, who failed to show catch-up growth (HV SDS < 0 during the last year) by 4 years of age or later.

Growth failure due to Noonan syndrome.

Adults:
Childhood onset growth hormone deficiency:
Patients with childhood onset GHD should be re-evaluated for growth hormone secretory capacity after growth completion. Testing is not required for those with more than three pituitary hormone deficits, with severe GHD due to a defined genetic cause, due to structural hypothalamic pituitary abnormalities, due to central nervous system tumours or due to high-dose cranial irradiation, or with GHD secondary to a pituitary/hypothalamic disease or insult, if measurements of serum insulin-like growth factor 1 (IGF-1) is < -2 SDS after at least four weeks off growth hormone treatment.

In all other patients an IGF-1 measurement and one growth hormone stimulation test is required.

Adult onset growth hormone deficiency:
Pronounced GHD in known hypothalamic-pituitary disease, cranial irradiation and traumatic brain injury. GHD should be associated with one other deficient axis, other than prolactin. GHD should be demonstrated by one provocative test after institution of adequate replacement therapy for any other deficient axis.

In adults, the insulin tolerance test is the provocative test of choice. When the insulin tolerance test is contraindicated, alternative provocative tests must be used. The combined arginine-growth hormone releasing hormone is recommended. An arginine or glucagon test may also be considered; however, these tests have less established diagnostic value than the insulin tolerance test.

4.2 Posology and method of administration

Norditropin should only be prescribed by doctors with special knowledge of the therapeutic indication of use.

Posology

The dosage is individual and must always be adjusted in accordance with the individual's clinical and biochemical response to therapy.

Generally recommended dosages:

Paediatric population:
Growth hormone insufficiency
0.025-0.035 mg/kg/day or 0.7-1.0 mg/m^2/day
When GHD persists after growth completion, growth hormone treatment should be continued to achieve full somatic adult development including lean body mass and bone mineral accrual (for guidance on dosing, see Replacement therapy in adults).

Turner syndrome
0.045-0.067 mg/kg/day or 1.3-2.0 mg/m^2/day

Chronic renal disease
0.050 mg/kg/day or 1.4 mg/m^2/day (see section 4.4)

Small for Gestational Age
0.035 mg/kg/day or 1.0 mg/m^2/day

A dose of 0.035 mg/kg/day is usually recommended until final height is reached (see section 5.1).
Treatment should be discontinued after the first year of treatment, if the height velocity SDS is below +1.
Treatment should be discontinued if height velocity is < 2 cm/year and, if confirmation is required, bone age is > 14 years (girls) or > 16 years (boys), corresponding to closure of the epiphyseal growth plates.

Noonan syndrome:
0.066 mg/kg/day is the recommended dose, however in some cases 0.033 mg/kg/day may be sufficient (see section 5.1).
Treatment should be discontinued at the time of epiphyseal closure (see section 4.4).

Adult population:
Replacement therapy in adults
The dosage must be adjusted to the need of the individual patient.

In patients with childhood onset GHD, the recommended dose to restart is 0.2-0.5 mg/day with subsequent dose adjustment on the basis of IGF-1 concentration determination.
In patients with adult onset GHD, it is recommended to start treatment with a low dose: 0.1-0.3 mg/day. It is recommended to increase the dosage gradually at monthly intervals based on the clinical response and the patient's experience of adverse events. Serum IGF-1 can be used as guidance for the dose titration. Women may require higher doses than men, with men showing an increasing IGF-1 sensitivity over time. This means that there is a risk that women, especially those on oral oestrogen replacement are undertreated while men are overtreated.
Dose requirements decline with age. Maintenance dosages vary considerably from person to person, but seldom exceed 1.0 mg/day.

Method of administration

Generally, daily subcutaneous administration in the evening is recommended. The injection site should be varied to prevent lipoatrophy.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Somatropin must not be used when there is any evidence of activity of a tumour. Intracranial tumours must be inactive and antitumour therapy must be completed prior to starting growth hormone (GH) therapy. Treatment should be discontinued if there is evidence of tumour growth.

Somatropin should not be used for longitudinal growth promotion in children with closed epiphyses.

Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure, or similar conditions should not be treated with somatropin (see section 4.4).

In children with chronic renal disease, treatment with Norditropin NordiFlex should be discontinued at renal transplantation.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Children treated with somatropin should be regularly assessed by a specialist in child growth. Somatropin treatment should always be instigated by a physician with special knowledge of growth hormone insufficiency and its treatment. This is true also for the management of Turner syndrome, chronic renal disease, SGA and Noonan syndrome. Data of final adult height following the use of Norditropin are limited for children with Noonan Syndrome and are not available for children with chronic renal disease.

The maximum recommended daily dose should not be exceeded (see section 4.2).

The stimulation of longitudinal growth in children can only be expected until epiphyseal closure.

Children
Treatment of growth hormone deficiency in patients with Prader-Willi syndrome
There have been reports of sudden death after initiating somatropin therapy in patients with Prader-Willi syndrome, who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnoea, or unidentified respiratory infection.

Small for Gestational Age

In short children born SGA other medical reasons or treatments that could explain growth disturbance should be ruled out before starting treatment.

Experience in initiating treatment in SGA patients near onset of puberty is limited. It is therefore not recommended to initiate treatment near onset of puberty.
Experience with patients with Silver-Russell syndrome is limited.

Turner syndrome
Monitoring of growth of hands and feet in Turner syndrome patients treated with somatropin is recommended, and a dose reduction to the lower part of the dose range should be considered if increased growth is observed.

Girls with Turner syndrome generally have an increased risk of otitis media, which is why otological evaluation is recommended on at least an annual basis.

Chronic renal disease
The dosage in children with chronic renal disease is individual and must be adjusted according to the individual response to therapy (see section 4.2). The growth disturbance should be clearly established before somatropin treatment by following growth on optimal treatment for renal disease over one year. Conservative management of uraemia with customary medicinal product and if needed dialysis should be maintained during somatropin therapy.

Patients with chronic renal disease normally experience a decline in renal function as part of the natural course of their illness. However, as a precautionary measure during somatropin treatment, renal function should be monitored for an excessive decline or increase in the glomerular filtration rate (which could imply hyperfiltration).

Scoliosis
Scoliosis is known to be more frequent in some of the patient groups treated with somatropin for example Turner syndrome and Noonan syndrome. In addition, rapid growth in any child can cause progression of scoliosis. Somatropin has not been shown to increase the incidence or severity of scoliosis. Signs of scoliosis should be monitored during treatment.

Blood glucose and insulin
In Turner syndrome and SGA children it is recommended to measure fasting insulin and blood glucose before start of treatment and annually thereafter. In patients with increased risk of diabetes mellitus (e.g. familial history of diabetes, obesity, severe insulin resistance, acanthosis nigricans), oral glucose tolerance testing (OGTT) should be performed. If overt diabetes occurs, somatropin should not be administered.

Somatropin has been found to influence carbohydrate metabolism, therefore, patients should be observed for evidence of glucose intolerance.

IGF-1
In Turner syndrome and SGA children it is recommended to measure the IGF-1 level before start of treatment and twice a year thereafter. If on repeated measurements IGF-1 levels exceed +2 SD compared to references for age and pubertal status, the dose should be reduced to achieve an IGF-1 level within the normal range.
Some of the height gain obtained with treating short children born SGA with somatropin may be lost if treatment is stopped before final height is reached.

Adults
Growth hormone deficiency in adults
Growth hormone deficiency in adults is a lifelong disease and needs to be treated accordingly, however, experience in patients older than 60 years and in patients with more than five years of treatment in adult growth hormone deficiency is still limited.

Adults and Children

Pancreatitis

Although rare, pancreatitis should be considered in somatropin-treated patients who develop abdominal pain, especially in children.

General

Neoplasms

There is no evidence for increased risk of new primary cancers in children or in adults treated with somatropin.

In patients in complete remission from tumours or malignant disease, somatropin therapy has not been associated with an increased relapse rate.

An overall slight increase in second neoplasms has been observed in childhood cancer survivors treated with growth hormone, with the most frequent being intracranial tumours. The dominant risk factor for second neoplasms seems to be prior exposure to radiation.

Patients who have achieved complete remission of malignant disease should be followed closely for relapse after commencement of somatropin therapy.

Leukaemia

Leukaemia has been reported in a small number of growth hormone deficient patients, some of whom have been treated with somatropin. However, there is no evidence that leukaemia incidence is increased in somatropin recipients without predisposition factors.

Benign intracranial hypertension

In the event of severe or recurrent headache, visual problems, nausea, and/or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed, a diagnosis of benign intracranial hypertension should be considered and if appropriate the somatropin treatment should be discontinued.

At present there is insufficient evidence to guide clinical decision making in patients with resolved intracranial hypertension. If somatropin treatment is restarted, careful monitoring for symptoms of intracranial hypertension is necessary.

Patients with growth hormone deficiency secondary to an intracranial lesion should be examined frequently for progression or recurrence of the underlying disease process.

Thyroid function

Somatropin increases the extrathyroidal conversion of T4 to T3 and may, as such, unmask incipient hypothyroidism. Monitoring of thyroid function should therefore be conducted in all patients. In patients with hypopituitarism, standard replacement therapy must be closely monitored when somatropin therapy is administered.

In patients with a pituitary disease in progression, hypothyroidism may develop.
Patients with Turner syndrome have an increased risk of developing primary hypothyroidism associated with anti-thyroid antibodies. As hypothyroidism interferes with the response to somatropin therapy patients should have their thyroid function tested regularly and should receive replacement therapy with thyroid hormone when indicated.

Insulin sensitivity

Because somatropin may reduce insulin sensitivity, patients should be monitored for evidence of glucose intolerance (see section 4.5). For patients with diabetes mellitus, the insulin dose may require adjustment after somatropin containing product therapy is instituted. Patients with diabetes or glucose intolerance should be monitored closely during somatropin therapy.

Antibodies

As with all somatropin containing products, a small percentage of patients may develop antibodies to somatropin. The binding capacity of these antibodies is low, and there is no effect on growth rate. Testing for antibodies to somatropin should be carried out in any patient who fails to respond to therapy.

Acute adrenal insufficiency
Introduction of somatropin treatment may result in inhibition of 11βHSD-1 and reduced serum cortisol concentrations. In patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked and glucocorticoid replacement may be required. In addition, patients treated with glucocorticoid replacement therapy for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses, following initiation of somatropin treatment (see section 4.5).

Use with oral oestrogen therapy
If a woman taking somatropin begins oral oestrogen therapy, the dose of somatropin may need to be increased to maintain the serum IGF-1 levels within the normal age-appropriate range. Conversely, if a woman on somatropin discontinues oral oestrogen therapy, the dose of somatropin may need to be reduced to avoid excess of growth hormone and/or side effects (see section 4.5).

Slipped capital femoral epiphysis
In patients with endocrine disorders, including growth hormone deficiency, slipped epiphyses of the hip may occur more frequently than in the general population. A patient treated with somatropin who develops a limp or complains of hip or knee pain should be evaluated by a physician.

Clinical trial experience
Two placebo-controlled clinical trials of patients in intensive care units have demonstrated an increased mortality among patients suffering from acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure, who were treated with somatropin in high doses (5.3-8 mg/day). The safety of continuing somatropin treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with somatropin in patients having acute critical illnesses should be weighed against the potential risk.

One open-label, randomised clinical trial (dose range 0.045-0.090 mg/kg/day) with patients with Turner syndrome indicated a tendency for a dose-dependent risk of otitis externa and otitis media. The increase in ear infections did not result in more ear operations/tube insertions compared to the lower dose group in the trial.

Excipients
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with glucocorticoids inhibits the growth-promoting effect of Norditropin. Patients with ACTH deficiency should have their glucocorticoid replacement therapy carefully adjusted to avoid any inhibitory effect on growth.
Growth hormone decreases the conversion of cortisone to cortisol and may unmask previously undiscovered central hypoadrenalism or render low glucocorticoid replacement doses ineffective (see section 4.4).

In women on oral oestrogen replacement, a higher dose of growth hormone may be required to achieve the treatment goal (see section 4.4).

Data from an interaction study performed in growth hormone deficient adults suggest that somatropin administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes. The clearance of compounds metabolised by cytochrome P450 3A4 (e.g. sex

steroids, corticosteroids, anticonvulsants and cyclosporine) may be especially increased resulting in lower plasma levels of these compounds. The clinical significance of this is unknown.

The effect of somatropin on final height can also be influenced by additional therapy with other hormones, e.g. gonadotropin, anabolic steroids, oestrogen and thyroid hormone.

In insulin treated patients adjustment of insulin dose may be needed after initiation of somatropin treatment (see section 4.4).

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies are insufficient with regard to effects on pregnancy, embryo-foetal development, parturition or postnatal development. No clinical data on exposed pregnancies are available. Therefore, somatropin containing products are not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

There have been no clinical studies conducted with somatropin containing products in breast-feeding women. It is not known whether somatropin is excreted in human milk. Therefore caution should be exercised when somatropin containing products are administered to breast-feeding women.

Fertility

Fertility studies with Norditropin have not been performed.

4.7 Effects on ability to drive and use machines

Norditropin NordiFlex has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Growth hormone deficient patients are characterised by extracellular volume deficit. When treatment with somatropin is initiated, this deficit is corrected. Fluid retention with peripheral oedema may occur especially in adults. Carpal tunnel syndrome is uncommon, but may be seen in adults. The symptoms are usually transient, dose dependent and may require transient dose reduction.
Mild arthralgia, muscle pain and paresthesia may also occur but are usually self-limiting.

Adverse reactions in children are uncommon or rare.

Clinical trial experience:

System organ classes	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)
Metabolism and nutrition disorders			In adults Diabetes mellitus type 2	
Nervous system		In adults headache and	In adults carpal tunnel syndrome.	

disorders		paraesthesia	In children headache	
Skin and subcutaneous tissue disorders			In adults pruritus	In children rash
Musculoskeletal, connective tissue disorders		In adults arthralgia, joint stiffness and myalgia	In adults muscle stiffness	In children arthralgia and myalgia
Reproductive system and breast disorders			In adults and children Gynecomastia	
General disorders and administration site conditions	In adults peripheral oedema (see text above)		In adults and children injection site pain. In children injection site reaction	In children peripheral oedema

In children with Turner syndrome increased growth of hands and feet has been reported during somatropin therapy.

A tendency for increased incidence of otitis media in Turner syndrome patients treated with high doses of Norditropin has been observed in one open-label randomised clinical trial. However, the increase in ear infections did not result in more ear operations/tube insertions compared to the lower dose group in the trial.

Post-marketing experience:

In addition to the above mentioned adverse drug reactions, those presented below have been spontaneously reported and are by an overall judgement considered possibly related to Norditropin treatment. Frequencies of these adverse events cannot be estimated from the available data:

- Neoplasms benign and malignant (including cysts and polyps): Leukaemia has been reported in a small number of growth hormone deficiency patients (see section 4.4)
- Immune system disorders: Hypersensitivity (see section 4.3). Formation of antibodies directed against somatropin. The titres and binding capacities of these antibodies have been very low and have not interfered with the growth response to Norditropin administration
- Endocrine disorders: Hypothyroidism. Decrease in serum thyroxin levels (see section 4.4)
- Metabolism and nutrition disorders: Hyperglycaemia (see section 4.4)
- Nervous system disorders: Benign intracranial hypertension (see section 4.4)
- Musculoskeletal and connective tissue disorders: Legg-Calvé-Perthes disease. Legg-Calvé-Perthes disease may occur more frequently in patients with short stature
- Investigations: Increase in blood alkaline phosphatase level.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Acute overdosage can lead to low blood glucose levels initially, followed by high blood glucose levels. These decreased glucose levels have been detected biochemically, but without clinical signs of

hypoglycaemia. Long-term overdosage could result in signs and symptoms consistent with the known effects of human growth hormone excess.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Somatropin and somatropin agonists. ATC: H01AC01.

Mechanism of action

Norditropin NordiFlex contains somatropin, which is human growth hormone produced by recombinant DNA-technology. It is an anabolic peptide of 191 amino acids stabilised by two disulphide bridges with a molecular weight of approximately 22,000 Daltons.

The major effects of somatropin are stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes.

Pharmacodynamic effects

When growth hormone deficiency is treated a normalisation of body composition takes place resulting in an increase in lean body mass and a decrease in fat mass.
Somatropin exerts most of its actions through insulin-like growth factor 1 (IGF-1), which is produced in tissues throughout the body but predominantly by the liver.
More than 90% of IGF-1 is bound to binding proteins (IGFBPs) of which IGFBP-3 is the most important.

A lipolytic and protein sparing effect of the hormone becomes of particular importance during stress.

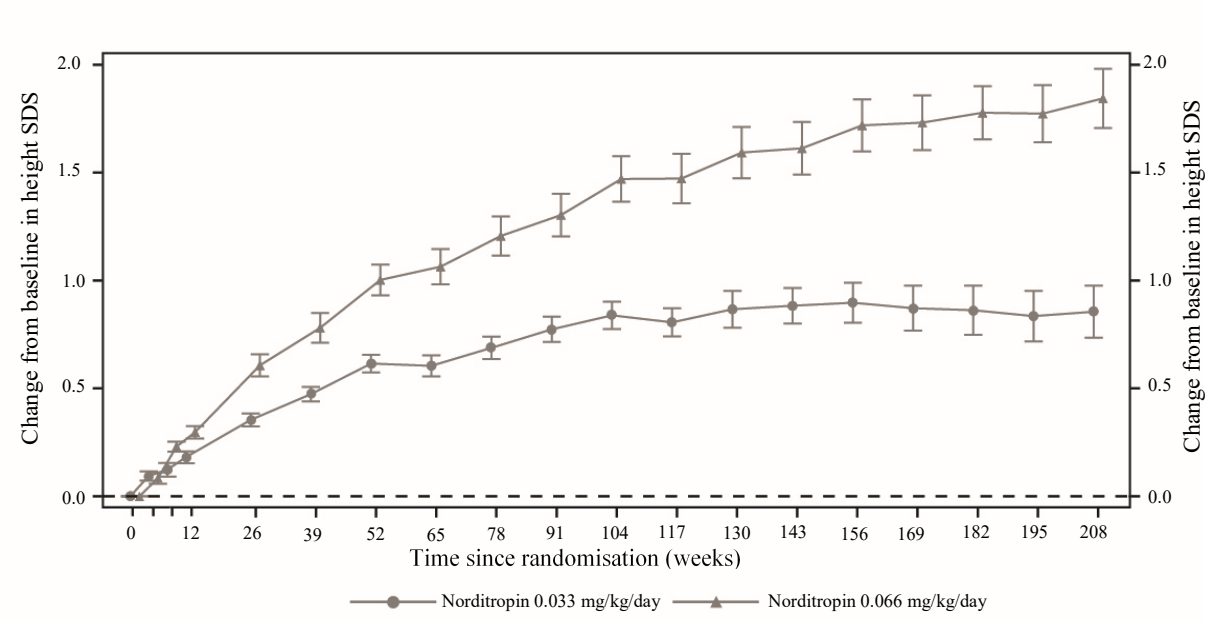
Somatropin also increases bone turnover indicated by an increase in plasma levels of biochemical bone markers. In adults bone mass is slightly decreased during the initial months of treatment due to more pronounced bone resorption, however, bone mass increases with prolonged treatment.

Clinical efficacy and safety

In clinical trials in short children born SGA doses of 0.033 and 0.067 mg/kg/day have been used for treatment until final height. In 56 patients who were continuously treated and have reached (near) final height, the mean change from height at start of treatment was +1.90 SDS (0.033 mg/kg/day) and +2.19 SDS (0.067 mg/kg/day). Literature data from untreated SGA children without early spontaneous catch-up suggest a late growth of 0.5 SDS. Long-term safety data are still limited.

A growth promoting effect was observed following 104 weeks (primary endpoint) and 208 weeks treatment with once-daily dosing of Norditropin 0.033 mg/kg/day and 0.066 mg/kg/day in 51 children aged 3 to <11 years with short stature due to Noonan syndrome.

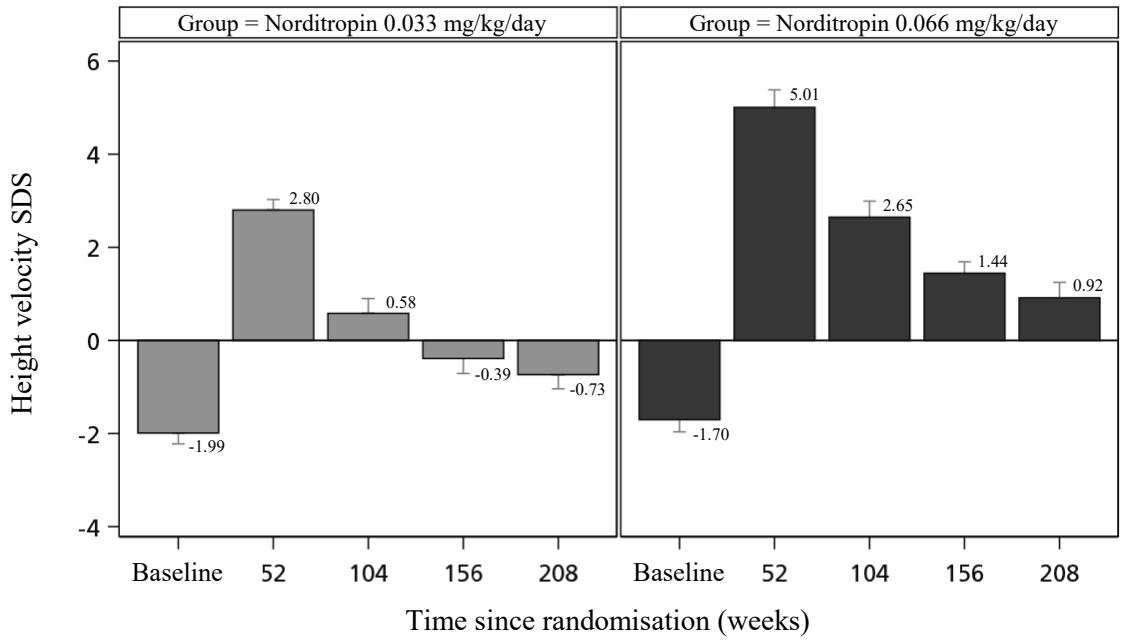
A statistically significant increase from baseline in mean height SDS at 104 weeks (primary endpoint) was observed with 0.033 mg/kg/day (0.84 SDS) and 0.066 mg/kg/day (1.47 SDS). A mean difference of 0.63 SDS [95 % CI: 0.38; 0.88] was observed between the groups at 104 weeks; the difference was greater after 208 weeks with an mean difference of 0.99 SDS [95 % CI: 0.62; 1.36] (figure 1).



Full analysis set, LOCF imputed data.
Error bars are 1*SEM.

Figure 1 Height SDS (national) change from baseline to week 208

The mean height velocity and height velocity SDS increased markedly from baseline during the first year of treatment with a greater increase with 0.066 mg/kg/day than with 0.033 mg/kg/day. The mean height velocity SDS was maintained above 0 in both groups after a two-year treatment and also after four years of treatment in the 0.066 mg/kg/day group. The height velocity SDS was greater with 0.066 mg/kg/day than with 0.033 mg/kg/day throughout the trial period (figure 2).



Full analysis set, LOCF imputed data.
Baseline: Height velocity from 1 year prior to screening to week 0.
Error bars are 1*SEM.

Figure 2 Height velocity SDS (national) from baseline to week 208

Final height data were collected in 24 paediatric patients (18 included in a two-year prospective, open label, randomised, parallel group study and six who had followed the protocol without randomisation).

After the initial two-years prospective study, Norditropin continued until final height. At the end of the treatment the majority of the subjects (16/24) achieved a final height within the normal national reference range (> 2 SDS).

5.2 Pharmacokinetic properties

I.v. infusion of Norditropin (33 ng/kg/min for 3 hours) to nine growth hormone deficient patients, gave the following results: serum half-life of 21.1±1.7 min., metabolic clearance rate of 2.33±0.58 ml/kg/min. and a distribution space of 67.6±14.6 ml/kg.

S.c. injection of Norditropin SimpleXx (Norditropin SimpleXx is the cartridge containing the solution for injection in Norditropin NordiFlex) 2.5 mg/m^2 in 31 healthy subjects (with endogenous somatropin suppressed by continuous infusion of somatostatin) gave the following results:
Maximal concentration of human growth hormone (42-46 ng/ml) after approximately 4 hours.
Thereafter human growth hormone declined with a half-life of approximately 2.6 hours.
In addition the different strengths of Norditropin SimpleXx were demonstrated to be bioequivalent to each other and to Norditropin for reconstitution after subcutaneous injection to healthy subjects.

5.3 Preclinical safety data

The general pharmacological effects on the CNS, cardiovascular and respiratory systems following administration of Norditropin SimpleXx with and without forced degradation were investigated in mice and rats; renal function was also evaluated. The degraded product showed no difference in effect when compared with Norditropin SimpleXx and Norditropin. All three preparations showed the expected dose dependent decrease in urine volume and retention of sodium and chloride ions.

In rats, similar pharmacokinetics has been demonstrated between Norditropin SimpleXx and Norditropin. Degraded Norditropin SimpleXx has also been demonstrated to be bioequivalent with Norditropin SimpleXx.

Single and repeated dose toxicity and local tolerance studies of Norditropin SimpleXx or the degraded product did not reveal any toxic effect or damage to the muscle tissue.

The toxicity of poloxamer 188 has been tested in mice, rats, rabbits, and dogs and no findings of toxicological relevance were revealed.
Poloxamer 188 was rapidly absorbed from the injection site with no significant retention of the dose at the site of injection. Poloxamer 188 was excreted primarily via the urine.

Norditropin SimpleXx is the cartridge containing the solution for injection in Norditropin NordiFlex.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Histidine
Poloxamer 188
Phenol
Water for injection
Hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.
After first opening: Store for a maximum of 4 weeks in a refrigerator (2°C – 8°C).
Alternatively, the medicinal product may be stored for a maximum of 3 weeks below 25°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C) in the outer carton, in order to protect it from light. Do not freeze. Do not store close to any cooling elements. For storage conditions after first opening of the medicinal product, see section 6.3. Do not freeze.

When in use, always replace the pen cap on the Norditropin NordiFlex pre-filled pen after each injection. Always use a new needle for each injection.
The needle must not be screwed onto the pre-filled pen when it is not in use.

6.5 Nature and contents of container

Norditropin NordiFlex 5 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a plastic pen-injector. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured orange. Pack sizes of 1 pre-filled pen and multipacks with 5 and 10 x 1 pre-filled pens. Not all pack sizes may be marketed.

Norditropin NordiFlex 10 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a plastic pen-injector. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured blue. Pack sizes of 1 pre-filled pen and multipacks with 5 and 10 x 1 pre-filled pens. Not all pack sizes may be marketed.

Norditropin NordiFlex 15 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a plastic pen-injector. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured green. Pack sizes of 1 pre-filled pen and multipacks with 5 and 10 x 1 pre-filled pens. Not all pack sizes may be marketed.

The pre-filled pen is packed in a carton.

6.6 Special precautions for disposal and other handling

Norditropin NordiFlex is a pre-filled pen designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.

Norditropin NordiFlex 5 mg/1.5 ml delivers a maximum of 1.5 mg somatropin per dose, in increments of 0.025 mg somatropin.
Norditropin NordiFlex 10 mg/1.5 ml delivers a maximum of 3.0 mg somatropin per dose, in increments of 0.050 mg somatropin.
Norditropin NordiFlex 15 mg/1.5 ml delivers a maximum of 4.5 mg somatropin per dose, in increments of 0.075 mg somatropin.

To ensure proper dosing and avoid injection of air, check the growth hormone flow before the first injection. Do not use Norditropin NordiFlex if a drop of growth hormone does not appear at the needle tip. A dose is selected by turning the dose selector, until the desired dose appears at the window of the

housing. If the wrong dose is selected, the dose can be corrected by turning the dosage selector the opposite way. The push button is pressed to inject the dose.

Norditropin NordiFlex should not be shaken vigorously at any time.

Do not use Norditropin NordiFlex if the growth hormone solution for injection is cloudy or discoloured. Check this by turning the pen upside down once or twice.

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

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08-December-2003
Date of latest renewal: 14-January-2009

10. DATE OF REVISION OF THE TEXT

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 5 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 3.3 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol,water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C – 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 5 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 5 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 3.3 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
10 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C – 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 5 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 10 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 6.7 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol,water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C – 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

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11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 10 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 10 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 6.7 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
10 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C – 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
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11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 10 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 15 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 10 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C – 8°C)
Keep the container in the outer carton in order to protect it from light
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11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 15 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

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18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin NordiFlex 15 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 10 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
10 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin NordiFlex 15 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin NordiFlex 5 mg/1.5 ml
Solution for injection

Somatropin 5 mg/1.5 ml
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin NordiFlex 10 mg/1.5 ml
Solution for injection

Somatropin 10 mg/1.5 ml
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin NordiFlex 15 mg/1.5 ml
Solution for injection

Somatropin 15 mg/1.5 ml
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

PACKAGE LEAFLET

Package leaflet: Information for the user

Norditropin NordiFlex 5 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin NordiFlex is and what it is used for

Norditropin NordiFlex 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, but adults also need it for their general health.

Norditropin NordiFlex is used to treat growth failure in children:
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin NordiFlex is used as a growth hormone replacement in adults:
In adults Norditropin NordiFlex is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin NordiFlex

Do not use Norditropin NordiFlex
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin NordiFlex
• If you have an **acute critical illness** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin NordiFlex
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin NordiFlex, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin NordiFlex 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 NordiFlex.

Other medicines and Norditropin NordiFlex
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 NordiFlex or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiFlex and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially 'sodium-free'.

3. How to use Norditropin NordiFlex

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose
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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin NordiFlex
Norditropin NordiFlex growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen.
Full instructions on how to use the Norditropin NordiFlex pen are given overleaf. The instructional key points 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 so you do not harm your skin
- To make sure you get the proper dose and do not inject air, check the growth hormone flow (called 'priming' the pen) 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.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 use more Norditropin NordiFlex than you should

Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin NordiFlex
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin NordiFlex
Do not stop using Norditropin NordiFlex without discussing it with your doctor first.

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.

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

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 rarely been 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 for this.
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** (gynaecomastia).

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 NordiFlex 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 be due to Norditropin NordiFlex.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin NordiFlex

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 package after EXP/. The expiry date refers to the last day of that month.

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 any cooling elements.

While using Norditropin NordiFlex 5 mg/1.5 ml you can **either**:
- 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 continue to 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 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 Norditropin NordiFlex contains
- The active substance is somatropin

- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin NordiFlex looks like and contents of the pack
Norditropin NordiFlex is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 3.3 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin NordiFlex is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively).

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Czech Republic, Denmark, Greece, Finland, Hungary, Croatia, Ireland, Iceland, Italy, Lithuania, Luxembourg, Norway, Poland, Portugal, Romania, Spain, Sweden, Slovak Republic, Slovenia, United Kingdom: Norditropin NordiFlex 5 mg/1.5 ml

France: Norditropine NordiFlex 5 mg/1.5 ml

This leaflet was last revised in

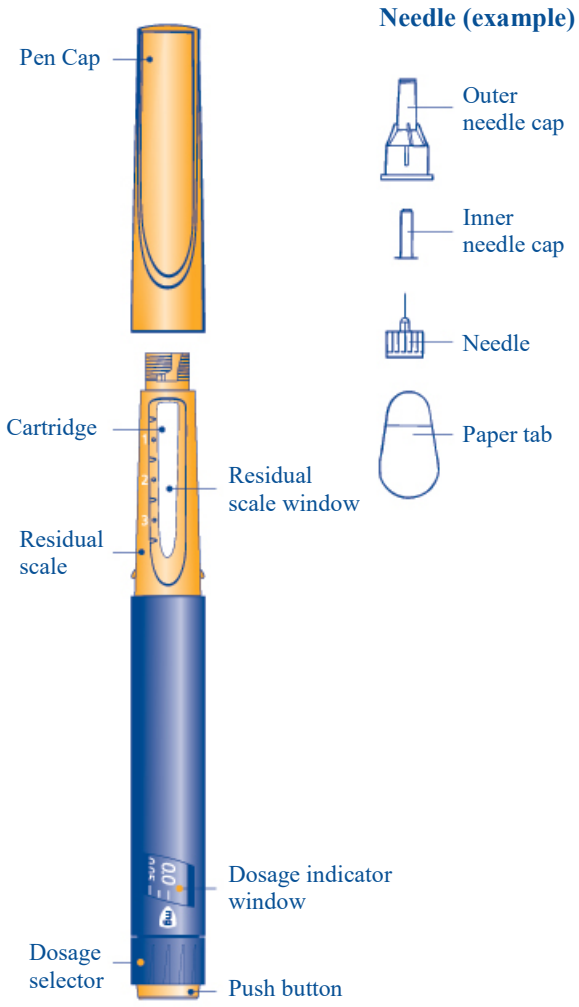
Other sources of information
Detailed information on this medicine is available on the website of: (name of MS/Agency)

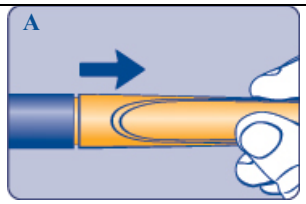
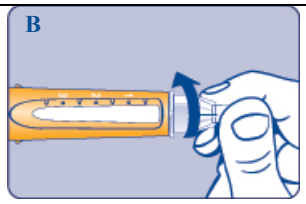
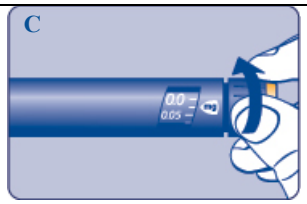
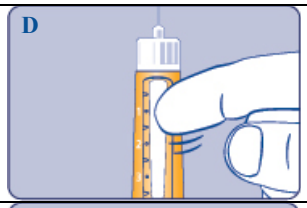
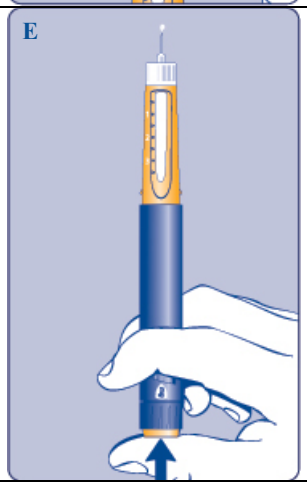
Norditropin NordiFlex
5 mg/1.5 ml

Instructions on how to use the Norditropin NordiFlex pen

Read these instructions carefully before using Norditropin NordiFlex.

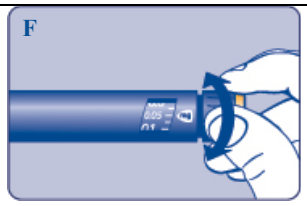
- Norditropin NordiFlex 5 mg/1.5 ml is a multidose injection pen pre-filled with human growth hormone solution.
- You can use the dosage selector to select any dose from 0.025 to 1.50 mg, in increments of 0.025 mg. Your doctor will decide the correct dose for you.
- Norditropin NordiFlex is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.
- Start by checking the name, strength and coloured label of your Norditropin NordiFlex pen to make sure that it contains the growth hormone strength you need.
- Only use the pen if the growth hormone solution inside the cartridge is clear and colourless.
- Always use a new needle for each injection.
- Always check the flow before the first injection with each 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 sight and reach of children.
- Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.



1. Check the pen • **Check the name, strength and coloured 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 needle 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 correct dose and do not inject any air: Select 0.025 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 up 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 up, 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 step **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 with each 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.	

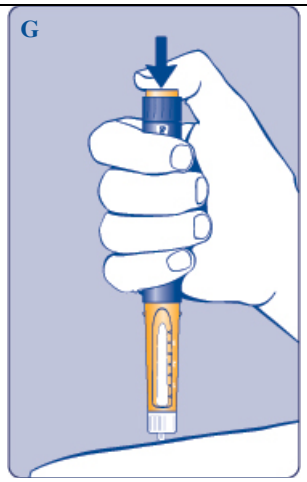
4. Select the dose

- 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 in either direction. When turning the dosage selector backwards, be careful not to press the push button as solution will come out. You cannot set a dose larger than the number of mg left in the pen.



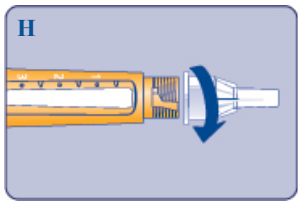
5. Inject the dose

- 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 only to press the push button when injecting **[G].**
- **Keep the push button fully depressed and let the needle remain under the skin for at least 6 seconds.** This will ensure that the full dose has been delivered.



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 contamination, infection, leakage of solution, blocked needles, and inaccurate dosing.
- When the pen is empty, throw it away without a needle on 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 or store it close to any cooling element, e.g. in a refrigerator.
- See section 5 “How to store Norditropin NordiFlex” on the reverse page for information about how to store your pen.

Package leaflet: Information for the user

Norditropin NordiFlex 10 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin NordiFlex is and what it is used for

Norditropin NordiFlex 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, but adults also need it for their general health.

Norditropin NordiFlex is used to treat growth failure in children:
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin NordiFlex is used as a growth hormone replacement in adults:
In adults Norditropin NordiFlex is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin NordiFlex

Do not use Norditropin NordiFlex
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin NordiFlex
• If you have an **acute critical illness** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin NordiFlex
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin NordiFlex, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin NordiFlex 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 NordiFlex.

Other medicines and Norditropin NordiFlex
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 NordiFlex or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiFlex and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

3. How to use Norditropin NordiFlex

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose
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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin NordiFlex
Norditropin NordiFlex growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen.
Full instructions on how to use the Norditropin NordiFlex pen are given overleaf. The instructional key points 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 so you do not harm your skin
- To make sure you get the proper dose and do not inject air, check the growth hormone flow (called 'priming' the pen) 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.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 use more Norditropin NordiFlex than you should

Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin NordiFlex
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin NordiFlex
Do not stop using Norditropin NordiFlex without discussing it with your doctor first.

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.

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

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 rarely been 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 for this.
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** (gynaecomastia).

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 NordiFlex 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 be due to Norditropin NordiFlex.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin NordiFlex

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 package after EXP/. The expiry date refers to the last day of that month.

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 any cooling elements.

While using Norditropin NordiFlex 10 mg/1.5 ml you can **either**:
- 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 continue to 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 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 Norditropin NordiFlex contains
- The active substance is somatropin

- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin NordiFlex looks like and contents of the pack
Norditropin NordiFlex is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 6.7 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin NordiFlex is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively).

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Czech Republic, Denmark, Greece, Finland, Hungary, Croatia, Ireland, Iceland, Italy, Lithuania, Luxembourg, Norway, Poland, Portugal, Romania, Spain, Sweden, Slovak Republic, Slovenia, United Kingdom: Norditropin NordiFlex 10 mg/1.5 ml

France: Norditropine NordiFlex 10 mg/1.5 ml

This leaflet was last revised in

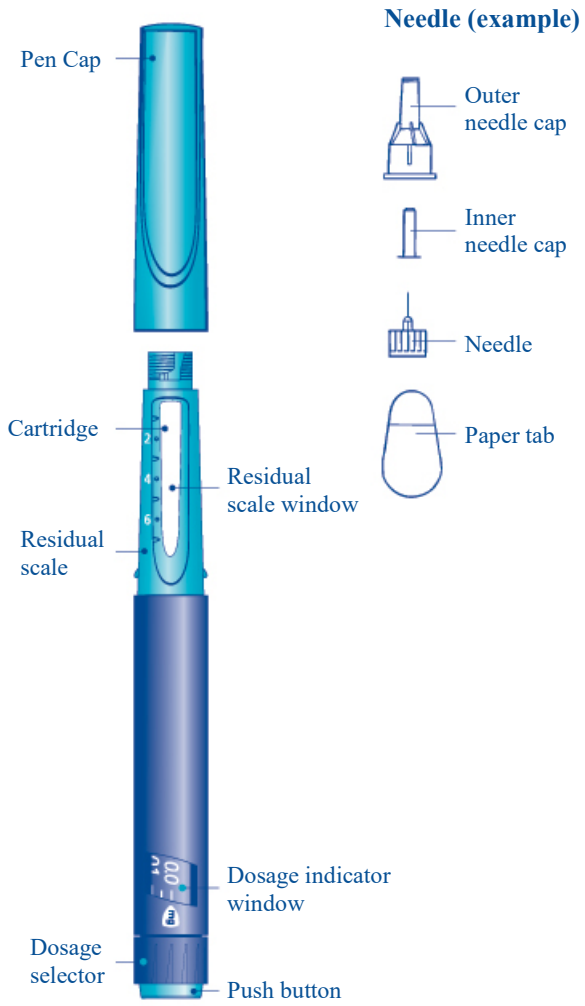
Other sources of information
Detailed information on this medicine is available on the website of: {name of MS/Agency}

Norditropin NordiFlex
10 mg/1.5 ml

Instructions on how to use the Norditropin NordiFlex pen

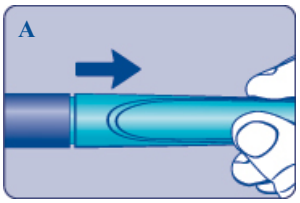
Read these instructions carefully before using Norditropin NordiFlex.

- Norditropin NordiFlex 10 mg/1.5 ml is a multidose injection pen pre-filled 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 coloured label of your Norditropin NordiFlex pen to make sure that it contains the growth hormone strength you need.
- Only use the pen if the growth hormone solution inside the cartridge is clear and colourless.
- Always use a new needle for each injection.
- Always check the flow before the first injection with each 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 sight and reach of children.
- Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.



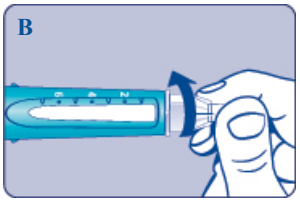
1. Check the pen

- **Check the name, strength and coloured 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.



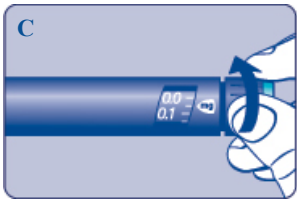
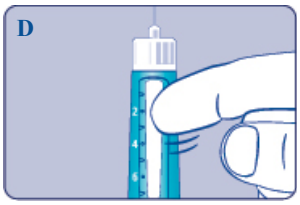
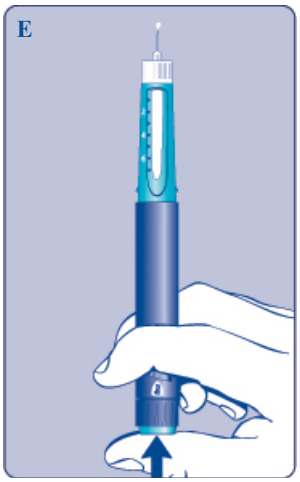
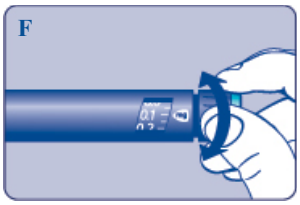
2. Attach the needle

- **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 needle caps. You need to remove them both:

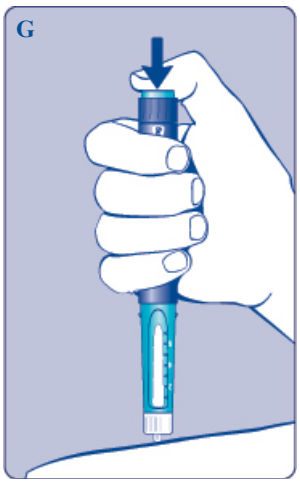
- Pull off the outer needle cap and keep it to correctly remove the needle from the pen after the injection.
- Remove the inner needle cap by pulling on the central tip

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 correct 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 up 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 up, 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 step **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 with each 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 in either direction. When turning the dosage selector backwards, be careful not to press the push button as 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 only to press the push button when injecting **[G].**
- **Keep the push button fully depressed and let the needle remain under the skin for at least 6 seconds.** This will ensure that the full dose has been delivered.

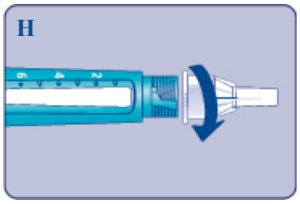
G



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 contamination, infection, leakage of solution, blocked needles and inaccurate dosing.
- When the pen is empty, throw it away without a needle on 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.**

H



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 or store it close to any cooling element, e.g. in a refrigerator.
- See section 5 “How to store Norditropin NordiFlex” on the reverse page for information about how to store your pen.

Package leaflet: Information for the user

Norditropin NordiFlex 15 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin NordiFlex is and what it is used for

Norditropin NordiFlex 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, but adults also need it for their general health.

Norditropin NordiFlex is used to treat growth failure in children:
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin NordiFlex is used as a growth hormone replacement in adults:
In adults Norditropin NordiFlex is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin NordiFlex

Do not use Norditropin NordiFlex
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin NordiFlex
• If you have an **acute critical illness** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin NordiFlex
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin NordiFlex, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin NordiFlex 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 NordiFlex.

Other medicines and Norditropin NordiFlex
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 NordiFlex or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiFlex and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

3. How to use Norditropin NordiFlex

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose
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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin NordiFlex
Norditropin NordiFlex growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen.
Full instructions on how to use the Norditropin NordiFlex pen are given overleaf. The instructional key points 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 so you do not harm your skin
- To make sure you get the proper dose and do not inject air, check the growth hormone flow (called 'priming' the pen) 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.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 use more Norditropin NordiFlex than you should

Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin NordiFlex
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin NordiFlex
Do not stop using Norditropin NordiFlex without discussing it with your doctor first.

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.

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

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 rarely been 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 for this.
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** (gynaecomastia).

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 NordiFlex 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 be due to Norditropin NordiFlex.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin NordiFlex

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 package after EXP/. The expiry date refers to the last day of that month.

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 any cooling elements.

While using Norditropin NordiFlex 15 mg/1.5 ml you can **either:**
- 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 continue to 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 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 Norditropin NordiFlex contains
- The active substance is somatropin

- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin NordiFlex looks like and contents of the pack
Norditropin NordiFlex is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 10 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin NordiFlex is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively).

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Czech Republic, Denmark, Greece, Finland, Hungary, Croatia, Ireland, Iceland, Italy, Luxembourg, Norway, Portugal, Romania, Spain, Sweden, Slovak Republic, Slovenia, United Kingdom: Norditropin NordiFlex 15 mg/1.5 ml

France: Norditropine NordiFlex 15 mg/1.5 ml

This leaflet was last revised in

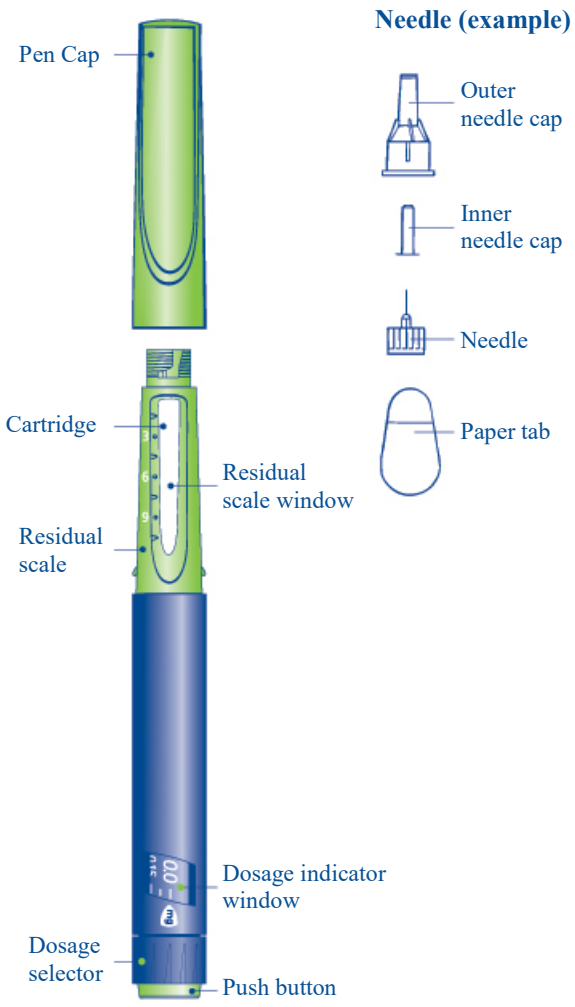
Other sources of information
Detailed information on this medicine is available on the website of: {name of MS/Agency}

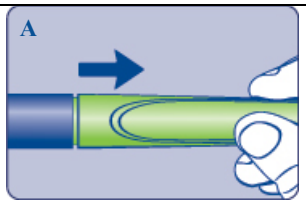
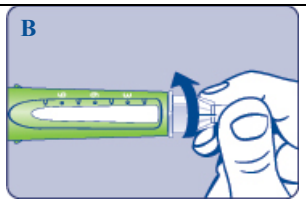
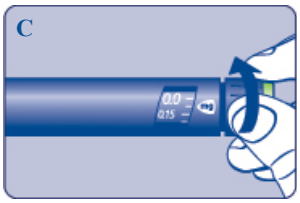
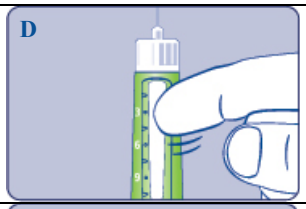
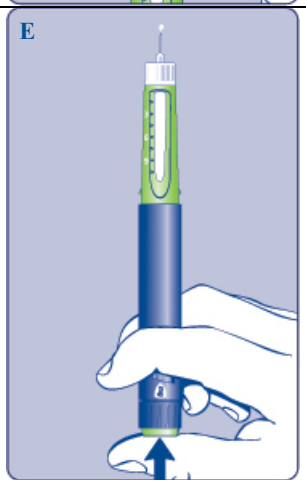
Norditropin NordiFlex
15 mg/1.5 ml

Instructions on how to use the Norditropin NordiFlex pen

Read these instructions carefully before using Norditropin NordiFlex.

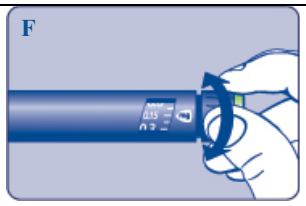
- Norditropin NordiFlex 15 mg/1.5 ml is a multidose injection pen pre-filled with human growth hormone solution.
- You can use the dosage selector to select any dose from 0.075 to 4.50 mg, in increments of 0.075 mg. Your doctor will decide the correct dose for you.
- Norditropin NordiFlex is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.
- Start by checking the name, strength and coloured label of your Norditropin NordiFlex pen to make sure that it contains the growth hormone strength you need.
- Only use the pen if the growth hormone solution inside the cartridge is clear and colourless.
- Always use a new needle for each injection.
- Always check the flow before the first injection with each 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 sight and reach of children.
- Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.



1. Check the pen • **Check the name, strength and coloured 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 needle 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 correct dose and do not inject any air: Select 0.075 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 up 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 up, 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 step **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 with each 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.	

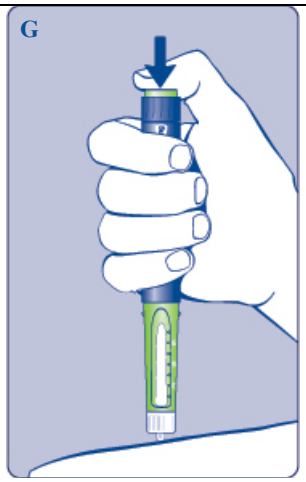
4. Select the dose

- 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 in either direction. When turning the dosage selector backwards, be careful not to press the push button as solution will come out. You cannot set a dose larger than the number of mg left in the pen.



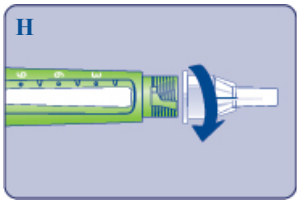
5. Inject the dose

- 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 only to press the push button when injecting **[G].**
- **Keep the push button fully depressed and let the needle remain under the skin for at least 6 seconds.** This will ensure that the full dose has been delivered.



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 contamination, infection, leakage of solution, blocked needles and inaccurate dosing.
- When the pen is empty, throw it away without a needle on 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 or store it close to any cooling element, e.g. in a refrigerator.
- See section 5 “How to store Norditropin NordiFlex” on the reverse page for information about how to store your pen.

SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 5 mg/1.5 ml, solution for injection in pre-filled pen
Norditropin FlexPro 10 mg/1.5 ml, solution for injection in pre-filled pen
Norditropin FlexPro 15 mg/1.5 ml, solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Norditropin FlexPro: 5 mg/1.5 ml
One ml of solution contains 3.3 mg somatropin

Norditropin FlexPro: 10 mg/1.5 ml
One ml of solution contains 6.7 mg somatropin

Norditropin FlexPro: 15 mg/1.5 ml
One ml of solution contains 10 mg somatropin

Somatropin (recombinant DNA origin produced in E-coli)

1 mg of somatropin corresponds to 3 IU (International Unit) of somatropin

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled pen

Clear, colourless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Children:
Growth failure due to growth hormone deficiency (GHD)

Growth failure in girls due to gonadal dysgenesis (Turner syndrome)

Growth retardation in prepubertal children due to chronic renal disease

Growth disturbance (current height SDS < -2.5 and parental adjusted height SDS < -1) in short children born small for gestational age (SGA), with a birth weight and/or length below -2 SD, who failed to show catch-up growth (HV SDS < 0 during the last year) by 4 years of age or later.

Growth failure due to Noonan syndrome.

Adults:
Childhood onset growth hormone deficiency:
Patients with childhood onset GHD should be re-evaluated for growth hormone secretory capacity after growth completion. Testing is not required for those with more than three pituitary hormone deficits, with severe GHD due to a defined genetic cause, due to structural hypothalamic pituitary abnormalities, due to central nervous system tumours or due to high-dose cranial irradiation, or with GHD secondary to a pituitary/hypothalamic disease or insult, if measurements of serum insulin-like growth factor 1 (IGF-1) is < -2 SDS after at least four weeks off growth hormone treatment.

In all other patients an IGF-1 measurement and one growth hormone stimulation test is required.

Adult onset growth hormone deficiency:
Pronounced GHD in known hypothalamic-pituitary disease, cranial irradiation and traumatic brain injury. GHD should be associated with one other deficient axis, other than prolactin. GHD should be demonstrated by one provocative test after institution of adequate replacement therapy for any other deficient axis.

In adults, the insulin tolerance test is the provocative test of choice. When the insulin tolerance test is contraindicated, alternative provocative tests must be used. The combined arginine-growth hormone releasing hormone is recommended. An arginine or glucagon test may also be considered; however, these tests have less established diagnostic value than the insulin tolerance test.

4.2 Posology and method of administration

Norditropin should only be prescribed by doctors with special knowledge of the therapeutic indication of use.

Posology

The dosage is individual and must always be adjusted in accordance with the individual's clinical and biochemical response to therapy.

Generally recommended dosages:

Paediatric population:
Growth hormone insufficiency
0.025-0.035 mg/kg/day or 0.7-1.0 mg/m^2/day
When GHD persists after growth completion, growth hormone treatment should be continued to achieve full somatic adult development including lean body mass and bone mineral accrual (for guidance on dosing, see Replacement therapy in adults).

Turner syndrome
0.045-0.067 mg/kg/day or 1.3-2.0 mg/m^2/day

Chronic renal disease
0.050 mg/kg/day or 1.4 mg/m^2/day (see section 4.4)

Small for Gestational Age
0.035 mg/kg/day or 1.0 mg/m^2/day

A dose of 0.035 mg/kg/day is usually recommended until final height is reached (see section 5.1).
Treatment should be discontinued after the first year of treatment, if the height velocity SDS is below +1.
Treatment should be discontinued if height velocity is < 2 cm/year and, if confirmation is required, bone age is > 14 years (girls) or > 16 years (boys), corresponding to closure of the epiphyseal growth plates.

Noonan syndrome:
0.066 mg/kg/day is the recommended dose, however in some cases 0.033 mg/kg/day may be sufficient (see section 5.1).
Treatment should be discontinued at the time of epiphyseal closure (see section 4.4).

Adult population:
Replacement therapy in adults
The dosage must be adjusted to the need of the individual patient.

In patients with childhood onset GHD, the recommended dose to restart is 0.2-0.5 mg/day with subsequent dose adjustment on the basis of IGF-1 concentration determination.
In patients with adult onset GHD, it is recommended to start treatment with a low dose: 0.1-0.3 mg/day. It is recommended to increase the dosage gradually at monthly intervals based on the clinical response and the patient's experience of adverse events. Serum IGF-1 can be used as guidance for the dose titration. Women may require higher doses than men, with men showing an increasing IGF-1 sensitivity over time. This means that there is a risk that women, especially those on oral oestrogen replacement are undertreated while men are overtreated.
Dose requirements decline with age. Maintenance dosages vary considerably from person to person, but seldom exceed 1.0 mg/day.

Method of administration

Generally, daily subcutaneous administration in the evening is recommended. The injection site should be varied to prevent lipoatrophy.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Somatropin must not be used when there is any evidence of activity of a tumour. Intracranial tumours must be inactive and antitumour therapy must be completed prior to starting growth hormone (GH) therapy. Treatment should be discontinued if there is evidence of tumour growth.

Somatropin should not be used for longitudinal growth promotion in children with closed epiphyses.

Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure, or similar conditions should not be treated with somatropin (see section 4.4).

In children with chronic renal disease, treatment with Norditropin FlexPro should be discontinued at renal transplantation.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Children treated with somatropin should be regularly assessed by a specialist in child growth. Somatropin treatment should always be instigated by a physician with special knowledge of growth hormone insufficiency and its treatment. This is true also for the management of Turner syndrome, chronic renal disease, SGA and Noonan syndrome. Data of final adult height following the use of Norditropin are limited for children with Noonan Syndrome and are not available for children with chronic renal disease.

The maximum recommended daily dose should not be exceeded (see section 4.2).

The stimulation of longitudinal growth in children can only be expected until epiphyseal closure.

Children
Treatment of growth hormone deficiency in patients with Prader-Willi syndrome
There have been reports of sudden death after initiating somatropin therapy in patients with Prader-Willi syndrome, who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnoea, or unidentified respiratory infection.

Small for Gestational Age

In short children born SGA other medical reasons or treatments that could explain growth disturbance should be ruled out before starting treatment.

Experience in initiating treatment in SGA patients near onset of puberty is limited. It is therefore not recommended to initiate treatment near onset of puberty.
Experience with patients with Silver-Russell syndrome is limited.

Turner syndrome
Monitoring of growth of hands and feet in Turner syndrome patients treated with somatropin is recommended, and a dose reduction to the lower part of the dose range should be considered if increased growth is observed.

Girls with Turner syndrome generally have an increased risk of otitis media, which is why otological evaluation is recommended on at least an annual basis.

Chronic renal disease
The dosage in children with chronic renal disease is individual and must be adjusted according to the individual response to therapy (see section 4.2). The growth disturbance should be clearly established before somatropin treatment by following growth on optimal treatment for renal disease over one year. Conservative management of uraemia with customary medicinal product and if needed dialysis should be maintained during somatropin therapy.

Patients with chronic renal disease normally experience a decline in renal function as part of the natural course of their illness. However, as a precautionary measure during somatropin treatment, renal function should be monitored for an excessive decline or increase in the glomerular filtration rate (which could imply hyperfiltration).

Scoliosis
Scoliosis is known to be more frequent in some of the patient groups treated with somatropin for example Turner syndrome and Noonan syndrome. In addition, rapid growth in any child can cause progression of scoliosis. Somatropin has not been shown to increase the incidence or severity of scoliosis. Signs of scoliosis should be monitored during treatment.

Blood glucose and insulin
In Turner syndrome and SGA children it is recommended to measure fasting insulin and blood glucose before start of treatment and annually thereafter. In patients with increased risk of diabetes mellitus (e.g. familial history of diabetes, obesity, severe insulin resistance, acanthosis nigricans), oral glucose tolerance testing (OGTT) should be performed. If overt diabetes occurs, somatropin should not be administered.

Somatropin has been found to influence carbohydrate metabolism, therefore, patients should be observed for evidence of glucose intolerance.

IGF-1
In Turner syndrome and SGA children it is recommended to measure the IGF-1 level before start of treatment and twice a year thereafter. If on repeated measurements IGF-1 levels exceed +2 SD compared to references for age and pubertal status, the dose should be reduced to achieve an IGF-1 level within the normal range.
Some of the height gain obtained with treating short children born SGA with somatropin may be lost if treatment is stopped before final height is reached.

Adults
Growth hormone deficiency in adults
Growth hormone deficiency in adults is a lifelong disease and needs to be treated accordingly, however, experience in patients older than 60 years and in patients with more than five years of treatment in adult growth hormone deficiency is still limited.

Adults and Children

Pancreatitis

Although rare, pancreatitis should be considered in somatropin-treated patients who develop abdominal pain, especially in children.

General

Neoplasms

There is no evidence for increased risk of new primary cancers in children or in adults treated with somatropin.

In patients in complete remission from tumours or malignant disease, somatropin therapy has not been associated with an increased relapse rate.

An overall slight increase in second neoplasms has been observed in childhood cancer survivors treated with growth hormone, with the most frequent being intracranial tumours. The dominant risk factor for second neoplasms seems to be prior exposure to radiation.

Patients who have achieved complete remission of malignant disease should be followed closely for relapse after commencement of somatropin therapy.

Leukaemia

Leukaemia has been reported in a small number of growth hormone deficient patients, some of whom have been treated with somatropin. However, there is no evidence that leukaemia incidence is increased in somatropin recipients without predisposition factors.

Benign intracranial hypertension

In the event of severe or recurrent headache, visual problems, nausea, and/or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed, a diagnosis of benign intracranial hypertension should be considered and if appropriate the somatropin treatment should be discontinued.

At present there is insufficient evidence to guide clinical decision making in patients with resolved intracranial hypertension. If somatropin treatment is restarted, careful monitoring for symptoms of intracranial hypertension is necessary.

Patients with growth hormone deficiency secondary to an intracranial lesion should be examined frequently for progression or recurrence of the underlying disease process.

Thyroid function

Somatropin increases the extrathyroidal conversion of T4 to T3 and may, as such, unmask incipient hypothyroidism. Monitoring of thyroid function should therefore be conducted in all patients. In patients with hypopituitarism, standard replacement therapy must be closely monitored when somatropin therapy is administered.

In patients with a pituitary disease in progression, hypothyroidism may develop.
Patients with Turner syndrome have an increased risk of developing primary hypothyroidism associated with anti-thyroid antibodies. As hypothyroidism interferes with the response to somatropin therapy patients should have their thyroid function tested regularly and should receive replacement therapy with thyroid hormone when indicated.

Insulin sensitivity

Because somatropin may reduce insulin sensitivity, patients should be monitored for evidence of glucose intolerance (see section 4.5). For patients with diabetes mellitus, the insulin dose may require adjustment after somatropin containing product therapy is instituted. Patients with diabetes or glucose intolerance should be monitored closely during somatropin therapy.

Antibodies

As with all somatropin containing products, a small percentage of patients may develop antibodies to somatropin. The binding capacity of these antibodies is low, and there is no effect on growth rate. Testing for antibodies to somatropin should be carried out in any patient who fails to respond to therapy.

Acute adrenal insufficiency
Introduction of somatropin treatment may result in inhibition of 11βHSD-1 and reduced serum cortisol concentrations. In patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked and glucocorticoid replacement may be required. In addition, patients treated with glucocorticoid replacement therapy for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses, following initiation of somatropin treatment (see section 4.5).

Use with oral oestrogen therapy
If a woman taking somatropin begins oral oestrogen therapy, the dose of somatropin may need to be increased to maintain the serum IGF-1 levels within the normal age-appropriate range. Conversely, if a woman on somatropin discontinues oral oestrogen therapy, the dose of somatropin may need to be reduced to avoid excess of growth hormone and/or side effects (see section 4.5).

Slipped capital femoral epiphysis
In patients with endocrine disorders, including growth hormone deficiency, slipped epiphyses of the hip may occur more frequently than in the general population. A patient treated with somatropin who develops a limp or complains of hip or knee pain should be evaluated by a physician.

Clinical trial experience
Two placebo-controlled clinical trials of patients in intensive care units have demonstrated an increased mortality among patients suffering from acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure, who were treated with somatropin in high doses (5.3-8 mg/day). The safety of continuing somatropin treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with somatropin in patients having acute critical illnesses should be weighed against the potential risk.

One open-label, randomised clinical trial (dose range 0.045-0.090 mg/kg/day) with patients with Turner syndrome indicated a tendency for a dose-dependent risk of otitis externa and otitis media. The increase in ear infections did not result in more ear operations/tube insertions compared to the lower dose group in the trial.

Excipients
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with glucocorticoids inhibits the growth-promoting effect of Norditropin. Patients with ACTH deficiency should have their glucocorticoid replacement therapy carefully adjusted to avoid any inhibitory effect on growth.
Growth hormone decreases the conversion of cortisone to cortisol and may unmask previously undiscovered central hypoadrenalism or render low glucocorticoid replacement doses ineffective (see section 4.4).

In women on oral oestrogen replacement, a higher dose of growth hormone may be required to achieve the treatment goal (see section 4.4).

Data from an interaction study performed in growth hormone deficient adults suggest that somatropin administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes. The clearance of compounds metabolised by cytochrome P450 3A4 (e.g. sex

steroids, corticosteroids, anticonvulsants and cyclosporine) may be especially increased resulting in lower plasma levels of these compounds. The clinical significance of this is unknown.

The effect of somatropin on final height can also be influenced by additional therapy with other hormones, e.g. gonadotropin, anabolic steroids, oestrogen and thyroid hormone.

In insulin treated patients adjustment of insulin dose may be needed after initiation of somatropin treatment (see section 4.4).

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies are insufficient with regard to effects on pregnancy, embryo-foetal development, parturition or postnatal development. No clinical data on exposed pregnancies are available. Therefore, somatropin containing products are not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

There have been no clinical studies conducted with somatropin containing products in breast-feeding women. It is not known whether somatropin is excreted in human milk. Therefore caution should be exercised when somatropin containing products are administered to breast-feeding women.

Fertility

Fertility studies with Norditropin have not been performed.

4.7 Effects on ability to drive and use machines

Norditropin FlexPro has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Growth hormone deficient patients are characterised by extracellular volume deficit. When treatment with somatropin is initiated, this deficit is corrected. Fluid retention with peripheral oedema may occur especially in adults. Carpal tunnel syndrome is uncommon, but may be seen in adults. The symptoms are usually transient, dose dependent and may require transient dose reduction.
Mild arthralgia, muscle pain and paresthesia may also occur but are usually self-limiting.

Adverse reactions in children are uncommon or rare.

Clinical trial experience:

System organ classes	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)
Metabolism and nutrition disorders			In adults Diabetes mellitus type 2	
Nervous system		In adults headache and	In adults carpal tunnel syndrome.	

disorders		paraesthesia	In children headache	
Skin and subcutaneous tissue disorders			In adults pruritus	In children rash
Musculoskeletal, connective tissue disorders		In adults arthralgia, joint stiffness and myalgia	In adults muscle stiffness	In children arthralgia and myalgia
Reproductive system and breast disorders			In adults and children Gynecomastia	
General disorders and administration site conditions	In adults peripheral oedema (see text above)		In adults and children injection site pain. In children injection site reaction	In children peripheral oedema

In children with Turner syndrome increased growth of hands and feet has been reported during somatropin therapy.

A tendency for increased incidence of otitis media in Turner syndrome patients treated with high doses of Norditropin has been observed in one open-label randomised clinical trial. However, the increase in ear infections did not result in more ear operations/tube insertions compared to the lower dose group in the trial.

Post-marketing experience:

In addition to the above mentioned adverse drug reactions, those presented below have been spontaneously reported and are by an overall judgement considered possibly related to Norditropin treatment. Frequencies of these adverse events cannot be estimated from the available data:

- Neoplasms benign and malignant (including cysts and polyps): Leukaemia has been reported in a small number of growth hormone deficiency patients (see section 4.4)
- Immune system disorders: Hypersensitivity (see section 4.3). Formation of antibodies directed against somatropin. The titres and binding capacities of these antibodies have been very low and have not interfered with the growth response to Norditropin administration
- Endocrine disorders: Hypothyroidism. Decrease in serum thyroxin levels (see section 4.4)
- Metabolism and nutrition disorders: Hyperglycaemia (see section 4.4)
- Nervous system disorders: Benign intracranial hypertension (see section 4.4)
- Musculoskeletal and connective tissue disorders: Legg-Calvé-Perthes disease. Legg-Calvé-Perthes disease may occur more frequently in patients with short stature
- Investigations: Increase in blood alkaline phosphatase level.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Acute overdosage can lead to low blood glucose levels initially, followed by high blood glucose levels. These decreased glucose levels have been detected biochemically, but without clinical signs of

hypoglycaemia. Long-term overdosage could result in signs and symptoms consistent with the known effects of human growth hormone excess.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Somatropin and somatropin agonists. ATC: H01AC01.

Mechanism of action

Norditropin FlexPro contains somatropin, which is human growth hormone produced by recombinant DNA-technology. It is an anabolic peptide of 191 amino acids stabilised by two disulphide bridges with a molecular weight of approximately 22,000 Daltons.

The major effects of somatropin are stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes.

Pharmacodynamic effects

When growth hormone deficiency is treated a normalisation of body composition takes place resulting in an increase in lean body mass and a decrease in fat mass.
Somatropin exerts most of its actions through insulin-like growth factor 1 (IGF-1), which is produced in tissues throughout the body but predominantly by the liver.
More than 90% of IGF-1 is bound to binding proteins (IGFBPs) of which IGFBP-3 is the most important.

A lipolytic and protein sparing effect of the hormone becomes of particular importance during stress.

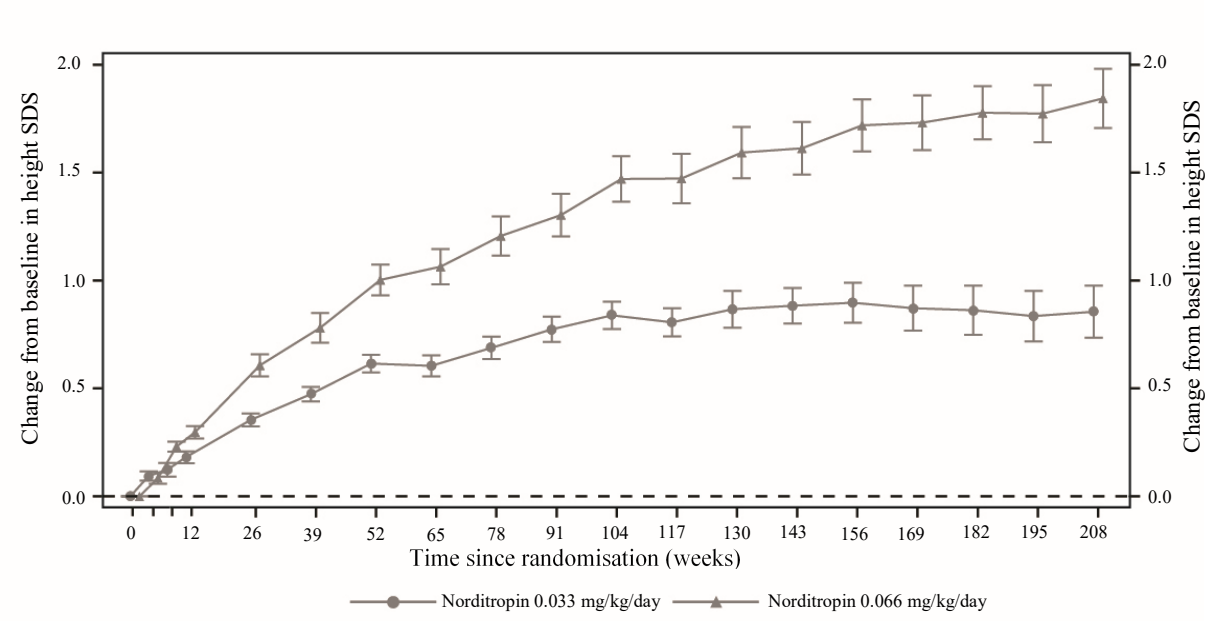
Somatropin also increases bone turnover indicated by an increase in plasma levels of biochemical bone markers. In adults bone mass is slightly decreased during the initial months of treatment due to more pronounced bone resorption, however, bone mass increases with prolonged treatment.

Clinical efficacy and safety

In clinical trials in short children born SGA doses of 0.033 and 0.067 mg/kg/day have been used for treatment until final height. In 56 patients who were continuously treated and have reached (near) final height, the mean change from height at start of treatment was +1.90 SDS (0.033 mg/kg/day) and +2.19 SDS (0.067 mg/kg/day). Literature data from untreated SGA children without early spontaneous catch-up suggest a late growth of 0.5 SDS. Long-term safety data are still limited.

A growth promoting effect was observed following 104 weeks (primary endpoint) and 208 weeks treatment with once-daily dosing of Norditropin 0.033 mg/kg/day and 0.066 mg/kg/day in 51 children aged 3 to <11 years with short stature due to Noonan syndrome.

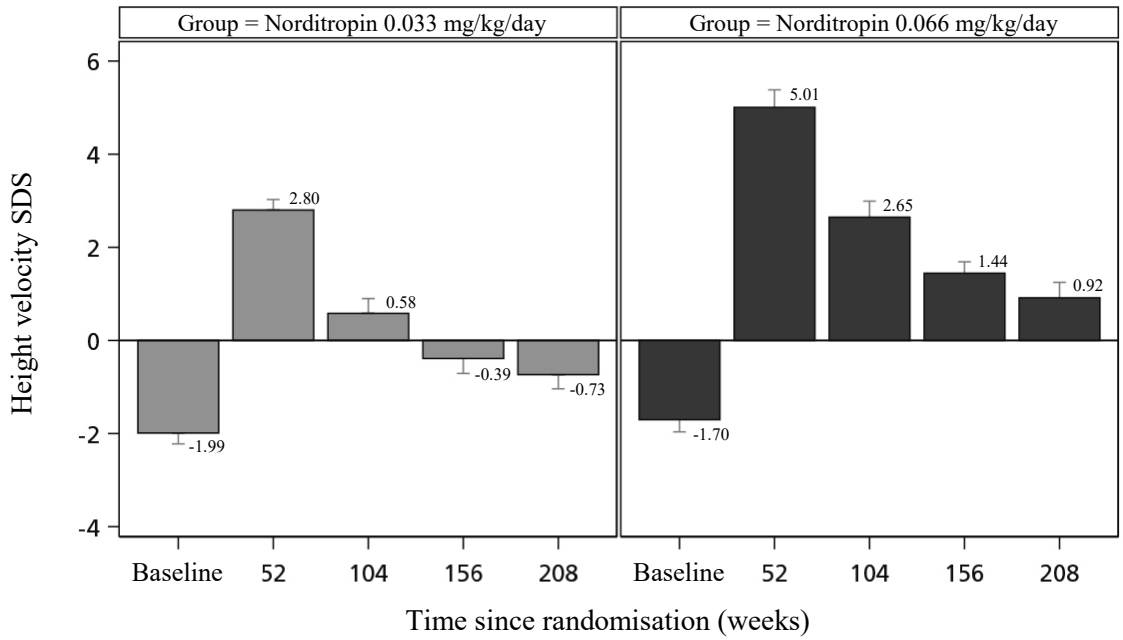
A statistically significant increase from baseline in mean height SDS at 104 weeks (primary endpoint) was observed with 0.033 mg/kg/day (0.84 SDS) and 0.066 mg/kg/day (1.47 SDS). A mean difference of 0.63 SDS [95 % CI: 0.38; 0.88] was observed between the groups at 104 weeks; the difference was greater after 208 weeks with an mean difference of 0.99 SDS [95 % CI: 0.62; 1.36] (figure 1).



Full analysis set, LOCF imputed data.
Error bars are 1*SEM.

Figure 1 Height SDS (national) change from baseline to week 208

The mean height velocity and height velocity SDS increased markedly from baseline during the first year of treatment with a greater increase with 0.066 mg/kg/day than with 0.033 mg/kg/day. The mean height velocity SDS was maintained above 0 in both groups after a two-year treatment and also after four years of treatment in the 0.066 mg/kg/day group. The height velocity SDS was greater with 0.066 mg/kg/day than with 0.033 mg/kg/day throughout the trial period (figure 2).



Full analysis set, LOCF imputed data.
Baseline: Height velocity from 1 year prior to screening to week 0.
Error bars are 1*SEM.

Figure 2 Height velocity SDS (national) from baseline to week 208

Final height data were collected in 24 paediatric patients (18 included in a two-year prospective, open label, randomised, parallel group study and six who had followed the protocol without randomisation).

After the initial two-years prospective study, Norditropin continued until final height. At the end of the treatment the majority of the subjects (16/24) achieved a final height within the normal national reference range (> 2 SDS).

5.2 Pharmacokinetic properties

I.v. infusion of Norditropin (33 ng/kg/min for 3 hours) to nine growth hormone deficient patients, gave the following results: serum half-life of 21.1±1.7 min., metabolic clearance rate of 2.33±0.58 ml/kg/min. and a distribution space of 67.6±14.6 ml/kg.

S.c. injection of Norditropin SimpleXx (Norditropin SimpleXx is the cartridge containing the solution for injection in Norditropin FlexPro) 2.5 mg/m^2 in 31 healthy subjects (with endogenous somatropin suppressed by continuous infusion of somatostatin) gave the following results:
Maximal concentration of human growth hormone (42-46 ng/ml) after approximately 4 hours.
Thereafter human growth hormone declined with a half-life of approximately 2.6 hours.
In addition the different strengths of Norditropin SimpleXx were demonstrated to be bioequivalent to each other and to Norditropin for reconstitution after subcutaneous injection to healthy subjects.

5.3 Preclinical safety data

The general pharmacological effects on the CNS, cardiovascular and respiratory systems following administration of Norditropin SimpleXx with and without forced degradation were investigated in mice and rats; renal function was also evaluated. The degraded product showed no difference in effect when compared with Norditropin SimpleXx and Norditropin. All three preparations showed the expected dose dependent decrease in urine volume and retention of sodium and chloride ions.

In rats, similar pharmacokinetics has been demonstrated between Norditropin SimpleXx and Norditropin. Degraded Norditropin SimpleXx has also been demonstrated to be bioequivalent with Norditropin SimpleXx.

Single and repeated dose toxicity and local tolerance studies of Norditropin SimpleXx or the degraded product did not reveal any toxic effect or damage to the muscle tissue.

The toxicity of poloxamer 188 has been tested in mice, rats, rabbits, and dogs and no findings of toxicological relevance were revealed.
Poloxamer 188 was rapidly absorbed from the injection site with no significant retention of the dose at the site of injection. Poloxamer 188 was excreted primarily via the urine.

Norditropin SimpleXx is the cartridge containing the solution for injection in Norditropin FlexPro.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Histidine
Poloxamer 188
Phenol
Water for injection
Hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.
After first opening: Store for a maximum of 4 weeks in a refrigerator (2°C – 8°C).
Alternatively, the medicinal product may be stored for a maximum of 3 weeks below 25°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C) in the outer carton, in order to protect it from light. Do not freeze.
Do not store close to any cooling elements.
For storage conditions after first opening of the medicinal product, see section 6.3.
Do not freeze.

When in use, always replace the pen cap on the Norditropin FlexPro pre-filled pen after each injection.
Always use a new needle for each injection.
The needle must not be screwed onto the pre-filled pen when it is not in use.

6.5 Nature and contents of container

Norditropin FlexPro 5 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a pen-injector made of plastic components and metal springs. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured orange. Pack sizes of 1 pre-filled pen and a multipack with 5 x 1 pre-filled pens. Not all pack sizes may be marketed.

Norditropin FlexPro 10 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a pen-injector made of plastic components and metal springs. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured blue. Pack sizes of 1 pre-filled pen and a multipack with 5 x 1 pre-filled pens. Not all pack sizes may be marketed.

Norditropin FlexPro 15 mg/1.5 ml is a multidose disposable pre-filled pen, which consists of a cartridge (Type I colourless glass) permanently sealed in a pen-injector made of plastic components and metal springs. The cartridge is closed at the bottom with a rubber stopper (Type I rubber closures) shaped as a plunger and at the top with a laminated rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The push button on the pen-injector is coloured green. Pack sizes of 1 pre-filled pen and a multipack with 5 x 1 pre-filled pens. Not all pack sizes may be marketed.

The pre-filled pen is packed in a carton.

6.6 Special precautions for disposal and other handling

Norditropin FlexPro is a pre-filled pen designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.

Norditropin FlexPro 5 mg/1.5 ml delivers a maximum of 2.0 mg somatropin per dose, in increments of 0.025 mg somatropin.
Norditropin FlexPro 10 mg/1.5 ml delivers a maximum of 4.0 mg somatropin per dose, in increments of 0.050 mg somatropin.
Norditropin Flexpro 15 mg/1.5 ml delivers a maximum of 8.0 mg somatropin per dose, in increments of 0.1 mg somatropin.

To ensure proper dosing and avoid injection of air, check the growth hormone flow before the first injection. Do not use Norditropin FlexPro if a drop of growth hormone does not appear at the needle tip. A dose is selected by turning the dose selector, until the desired dose appears at the window of the housing. If the wrong dose is selected, the dose can be corrected by turning the dose selector the opposite way. The push button is pressed to inject the dose.

Norditropin FlexPro should not be shaken vigorously at any time.

Do not use Norditropin FlexPro if the growth hormone solution for injection is cloudy or discoloured. Check this by turning the pen upside down once or twice.

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

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 December 2009
Date of latest renewal: 13-Feb-2015

10. DATE OF REVISION OF THE TEXT

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 5 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 3.3 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included
Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL: https://www.myflexpro.com/en5

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 5 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 5 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 3.3 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 5 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 10 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 6.7 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included
Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL: https://www.myflexpro.com/en10

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 10 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 10 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 6.7 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 10 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 15 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml solution contains: Somatropin 10 mg

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL:https://www.myflexpro.com/en15

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 15 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE PACKAGING OUTER CARTON ON MULTIPACKS AND CARTON IN MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

Norditropin FlexPro 15 mg/1.5 ml
Solution for injection in pre-filled pen

Somatropin

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml solution contains: Somatropin 10 mg.

3. LIST OF EXCIPIENTS

Mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid, and sodium hydroxide

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen,
1.5 ml
5 x 1.5 ml
This is part of a multipack and not for sale of individual pens
This is a multipack and not for sale of individual pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm
Needles are not included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP/

9. SPECIAL STORAGE CONDITIONS

Before use: Store in a refrigerator (2°C - 8°C)
Keep the container in the outer carton in order to protect it from light
Do not store close to any cooling elements. Do not freeze
When in use: Store *either* in a refrigerator (2°C - 8°C) for 4 weeks, *or* below 25°C for 3 weeks
Do not store close to any cooling elements. Do not freeze

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Norditropin FlexPro 15 mg/1.5 ml

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin FlexPro 5 mg/1.5 ml
Solution for injection

Somatropin
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin FlexPro 10 mg/1.5 ml
Solution for injection

Somatropin
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Norditropin FlexPro 15 mg/1.5 ml
Solution for injection

Somatropin
S.c. use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP/

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 ml

6. OTHER

Novo Nordisk A/S

PACKAGE LEAFLET

Package leaflet: Information for the user

Norditropin FlexPro 5 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin FlexPro is and what it is used for

Norditropin FlexPro 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, but adults also need it for their general health.

Norditropin FlexPro is used to treat growth failure in children
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin FlexPro is used as a growth hormone replacement in adults
In adults Norditropin FlexPro is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin FlexPro

Do not use Norditropin FlexPro
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin FlexPro
• If you have an **acute critical illness,** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin FlexPro
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin FlexPro, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin FlexPro 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 FlexPro.

Other medicines and Norditropin FlexPro
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 FlexPro or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin FlexPro and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

3. How to use Norditropin FlexPro

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose

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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin FlexPro
Norditropin FlexPro growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use Norditropin FlexPro are given overleaf. The instructional key points 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 (see page 8, step A)
- Norditropin FlexPro 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 so you do not harm 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 FlexPro pen. Do not use the pen if a drop of growth hormone solution does not appear at the needle tip (see pages 10 to 11, steps E to G)
- Do not share your Norditropin FlexPro pen with anyone else.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 FlexPro without discussing it with your doctor first.

If you use more Norditropin FlexPro than you should
Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin FlexPro
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin FlexPro
Do not stop using Norditropin FlexPro without discussing it with your doctor first.

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.

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

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

Formation of antibodies directed against somatropin has rarely been 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 FlexPro), although there is no evidence that somatropin was responsible for this.
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** (gynaecomastia).

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 FlexPro have experienced hip and knee pains 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 be due to Norditropin FlexPro.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin FlexPro

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 package after EXP/. The expiry date refers to the last day of that month.

Store unused Norditropin FlexPro 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 any cooling elements.

While using Norditropin FlexPro 5 mg/1.5 ml you can **either:**
- 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 continue to use Norditropin FlexPro pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin FlexPro pens where the growth hormone solution is cloudy or discoloured.

Always store Norditropin FlexPro without a needle attached.
Always keep the pen cap fully closed on the Norditropin FlexPro 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 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 Norditropin FlexPro contains
- The active substance is somatropin
- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin FlexPro looks like and contents of the pack

Norditropin FlexPro is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 3.3 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin FlexPro is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively) in pack sizes of 1 or 5 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Denmark, Finland, Germany, Greece, Ireland, Lithuania, Luxembourg, Malta, Netherlands, Portugal, Romania, Slovenia, United Kingdom: Norditropin FlexPro 5 mg/1.5 ml

Sweden: Somatropin Novo Nordisk 5 mg/1.5 ml

France: Norditropine FlexPro 5 mg/1.5 ml

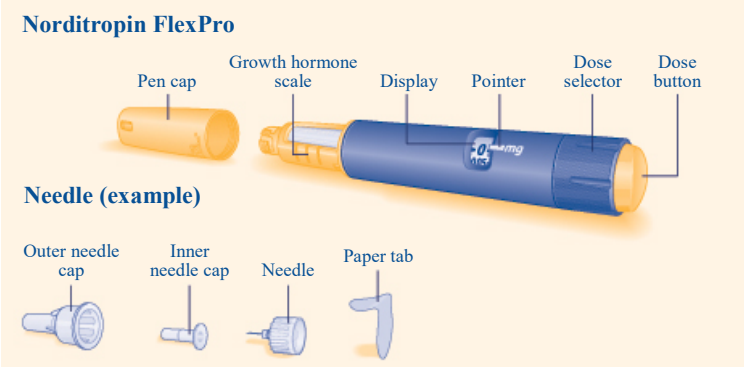
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the website of: (name of MS/Agency)

Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL: https://www.myflexpro.com/en5

Instructions on how to use Norditropin FlexPro
Please read these instructions carefully before using your Norditropin FlexPro pen.
Start by checking the name, strength and coloured label of your Norditropin FlexPro pen to make sure that it contains the growth hormone strength you need.

Read on to learn about:
Preparing your Norditropin FlexPro pen
Checking the growth hormone flow with each new pen
Selecting your dose
Injecting your dose
Caring for your Norditropin FlexPro pen
Important information

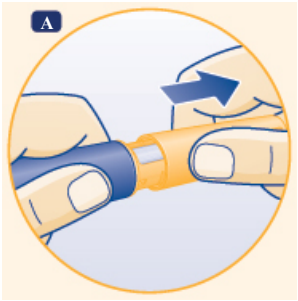


Your Norditropin FlexPro pen is a pre-filled growth hormone pen. Norditropin FlexPro contains 5 mg human growth hormone solution and delivers doses from 0.025 mg to 2.0 mg, in increments of 0.025 mg. Norditropin FlexPro is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.

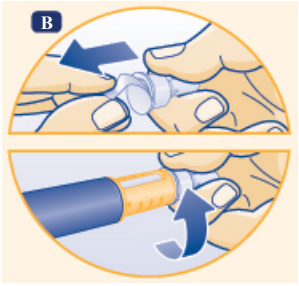
Preparing your Norditropin FlexPro pen
Check the name, strength and coloured label of your Norditropin FlexPro pen to make sure that it contains the growth hormone strength you need.

A Pull off the pen cap.

Check that the growth hormone solution in the pen is clear and colourless by tipping it upside down once or twice. If the solution looks unclear or cloudy, do not use the pen.



B Take a new disposable needle. Tear the paper tab off and screw the needle straight onto the pen. Make sure the needle is on tight.

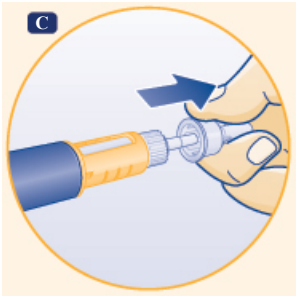


⚠ Always use a new needle for each injection. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.

⚠ Never bend or damage the needle.

C Pull off the outer needle cap and save it.

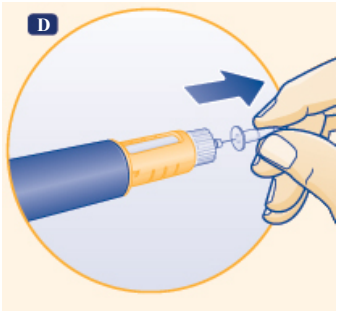
After injection, you will need it to correctly remove the needle from the pen.



D Pull off the inner needle cap and throw it away.

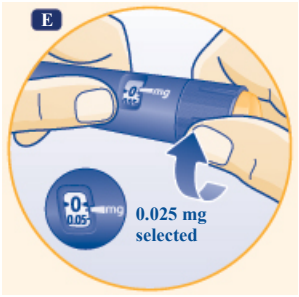
If you try to put it back on, you may accidentally stick yourself with the needle.

A drop of growth hormone may appear at the needle tip. This is normal.



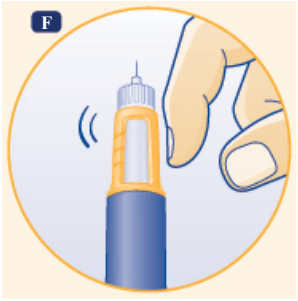
Checking the growth hormone flow with each new pen
Make sure that you receive your full dose by checking the growth hormone flow before you select and inject your first dose with each new pen.

E Turn the dose selector to select the **minimum** dose, 0.025 mg.



F Hold the pen with the needle pointing up.

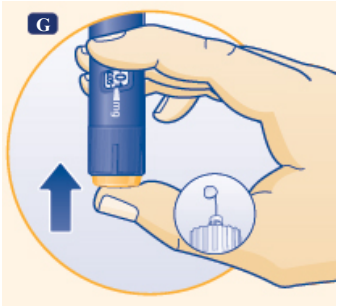
Tap the top of the pen a few times to let any air bubbles rise to the top.



G Press the dose button until the figure 0 in the display lines up with the pointer and a drop of growth hormone appears at the needle tip.

If no drop appears, repeat steps E to G up to 6 times. If no drop appears after these new attempts, change the needle and repeat steps E to G once more.

Do not use the pen if a drop of growth hormone still does not appear.



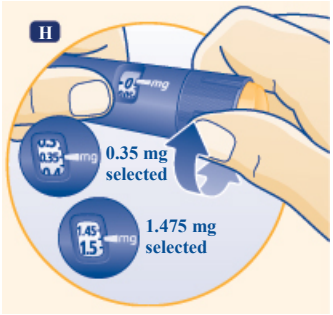
⚠

Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen.

Selecting your dose
Use the dose selector on your Norditropin FlexPro pen to select up to 2.0 mg per dose.

H Select or adjust the dose you need by turning the dose selector forwards or backwards until the right number of mg lines up with the pointer.

When the pen contains less than 2.0 mg, the dose selector stops at the number of mg left.



ⓘ The dose selector clicks differently when turned forwards, backwards or past the number of mg left.

ⓘ **How much growth hormone is left?**
You can use the growth hormone scale to see approximately how much growth hormone is left in the pen.

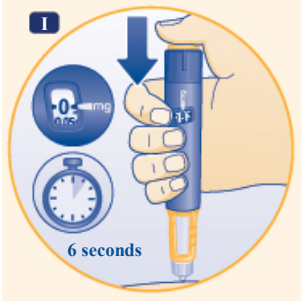
You can use the dose selector to see exactly how much growth hormone is left – if the pen contains less than 2.0 mg:
Turn the dose selector until it stops. The figure that lines up with the pointer shows how many mg are left.

If you need more growth hormone than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen.

⚠ Never use the pen clicks to count the number of mg you select. Only the display and pointer will indicate the exact number of mg.

⚠ Never use the growth hormone scale to measure how much growth hormone to inject. Only the display and pointer will indicate the exact number of mg.

Injecting your dose
Make sure that you receive your full dose by using the right injection technique.

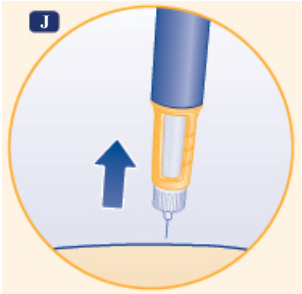


I Insert the needle into your skin as your doctor or nurse has shown you. Press the dose button to inject until the figure 0 in the display lines up with the pointer.

As you do this, you may hear or feel a click.

Leave the needle under the skin for at least **6 seconds** to make sure that you get your full dose.

You can let go of the dose button while you wait.

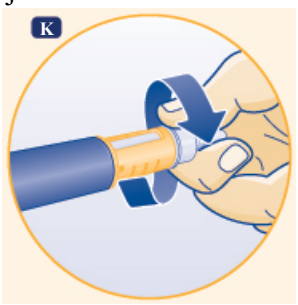


J Remove the needle from the skin.

After that, you may see a drop of growth hormone at the needle tip. This is normal and has no effect on the dose you just received.

⚠ Never use the pen clicks to count the number of mg you inject. Only the display and pointer will indicate the exact number of mg.

⚠ Never touch the display when you inject, as this can block the injection.



K Put the outer needle cap back on carefully without touching the needle. Unscrew the needle and throw it away carefully as instructed by your doctor or nurse.

Put the pen cap back on after every use.

When the pen is empty, throw it away without a needle on as advised by your doctor or nurse and local authorities.

⚠ Never put the inner needle cap back on once you have removed it from the needle. You may accidentally stick yourself with the needle.

⚠ Always store the pen without a needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.

Caring for your Norditropin FlexPro pen
Treat your Norditropin FlexPro pen with care:

- Do not drop your pen or knock it against hard surfaces. If you do drop it or suspect that something is wrong with it, always screw on a new disposable needle and check the growth hormone 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.
- Do not expose your pen to dust, dirt, liquid or direct light.
- 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 or store it close to any cooling element, e.g. in a refrigerator.
- See section 5 ‘How to store Norditropin FlexPro’ for information about how to store your pen.

⚠ **Important information**
- Always keep your pen and needles out of reach of others, especially children.
- **Never share** your pen or your needles with other people. It might lead to cross-infection.
- Caregivers must **be very careful when handling used needles** – to reduce the risk of needle injury and cross-infection.

⚠ **Important information**
Pay special attention to these notes as they are important for safe use of the pen.

ⓘ **Additional information**

Norditropin FlexPro
5 mg/1.5 ml
Somatropin

Package leaflet: Information for the user

Norditropin FlexPro 10 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin FlexPro is and what it is used for

Norditropin FlexPro 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, but adults also need it for their general health.

Norditropin FlexPro is used to treat growth failure in children
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin FlexPro is used as a growth hormone replacement in adults
In adults Norditropin FlexPro is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin FlexPro

Do not use Norditropin FlexPro
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin FlexPro
• If you have an **acute critical illness,** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin FlexPro
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin FlexPro, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin FlexPro 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 FlexPro.

Other medicines and Norditropin FlexPro
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 FlexPro or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin FlexPro and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

3. How to use Norditropin FlexPro

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose

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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin FlexPro
Norditropin FlexPro growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use Norditropin FlexPro are given overleaf. The instructional key points 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 (see page 8, step A)
- Norditropin FlexPro 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 so you do not harm 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 FlexPro pen. Do not use the pen if a drop of growth hormone solution does not appear at the needle tip (see pages 10 to 11, steps E to G)
- Do not share your Norditropin FlexPro pen with anyone else.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 FlexPro without discussing it with your doctor first.

If you use more Norditropin FlexPro than you should
Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin FlexPro
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin FlexPro
Do not stop using Norditropin FlexPro without discussing it with your doctor first.

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.

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

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

Formation of antibodies directed against somatropin has rarely been 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 FlexPro), although there is no evidence that somatropin was responsible for this.
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** (gynaecomastia).

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 FlexPro have experienced hip and knee pains 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 be due to Norditropin FlexPro.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin FlexPro

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 package after EXP/. The expiry date refers to the last day of that month.

Store unused Norditropin FlexPro 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 any cooling elements.

While using Norditropin FlexPro 10 mg/1.5 ml you can **either:**
- 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 continue to use Norditropin FlexPro pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin FlexPro pens where the growth hormone solution is cloudy or discoloured.

Always store Norditropin FlexPro without a needle attached.
Always keep the pen cap fully closed on the Norditropin FlexPro 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 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 Norditropin FlexPro contains
- The active substance is somatropin
- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin FlexPro looks like and contents of the pack

Norditropin FlexPro is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 6.7 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin FlexPro is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively) in pack sizes of 1 or 5 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Denmark, Finland, Germany, Greece, Ireland, Lithuania, Luxembourg, Malta, Netherlands, Portugal, Romania, Slovenia, United Kingdom: Norditropin FlexPro 10 mg/1.5 ml

Sweden: Somatropin Novo Nordisk 10 mg/1.5 ml

France: Norditropine FlexPro 10 mg/1.5 ml

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the website of: {name of MS/Agency}

Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL: https://www.myflexpro.com/en10

Instructions on how to use Norditropin FlexPro
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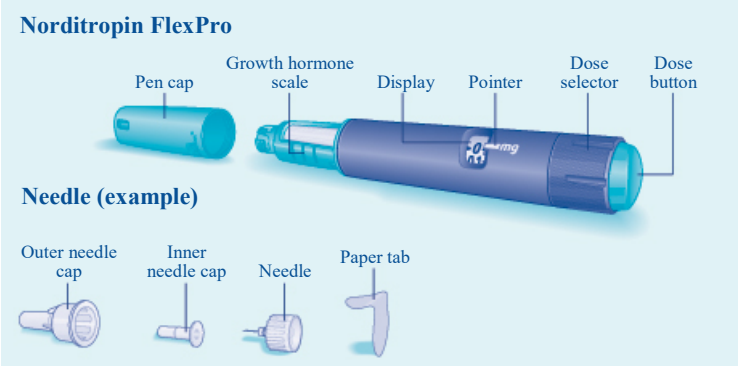
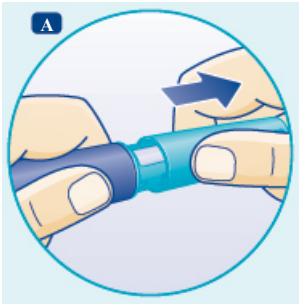


Your Norditropin FlexPro pen is a pre-filled growth hormone pen. Norditropin FlexPro contains 10 mg human growth hormone solution and delivers doses from 0.05 mg to 4.0 mg, in increments of 0.05 mg. Norditropin FlexPro is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.

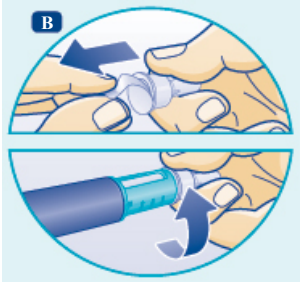
Preparing your Norditropin FlexPro pen
Check the name, strength and coloured label of your Norditropin FlexPro pen to make sure that it contains the growth hormone strength you need.

A Pull off the pen cap.



Check that the growth hormone solution in the pen is clear and colourless by tipping it upside down once or twice. If the solution looks unclear or cloudy, do not use the pen.

B Take a new disposable needle. Tear the paper tab off and screw the needle straight onto the pen. Make sure the needle is on tight.

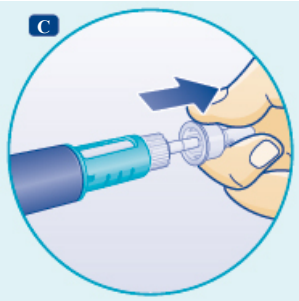


⚠ Always use a new needle for each injection. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.

⚠ Never bend or damage the needle.

C Pull off the outer needle cap and save it.

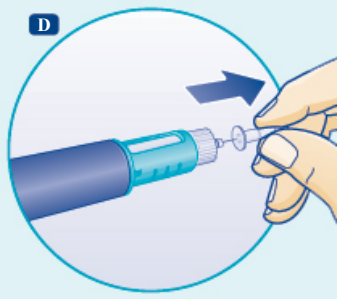
After injection, you will need it to correctly remove the needle from the pen.



D Pull off the inner needle cap and throw it away.

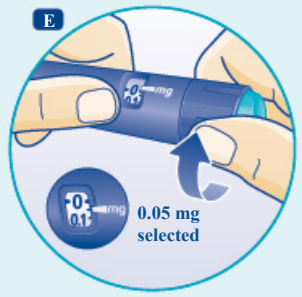
If you try to put it back on, you may accidentally stick yourself with the needle.

A drop of growth hormone may appear at the needle tip. This is normal.



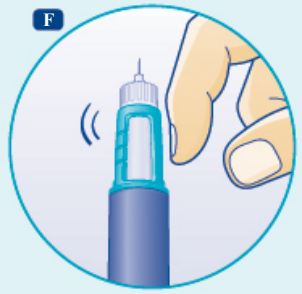
Checking the growth hormone flow with each new pen
Make sure that you receive your full dose by checking the growth hormone flow before you select and inject your first dose with each new pen.

E Turn the dose selector to select the **minimum** dose, 0.05 mg.

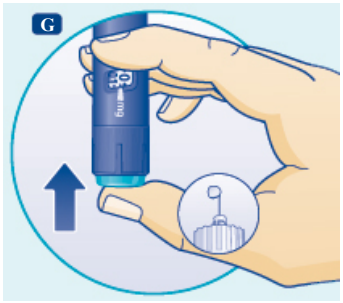


F Hold the pen with the needle pointing up.

Tap the top of the pen a few times to let any air bubbles rise to the top.



G Press the dose button until the figure 0 in the display lines up with the pointer and a drop of growth hormone appears at the needle tip.



If no drop appears, repeat steps E to G up to 6 times. If no drop appears after these new attempts, change the needle and repeat steps E to G once more.

Do not use the pen if a drop of growth hormone still does not appear.

⚠ Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen.

Selecting your dose
Use the dose selector on your Norditropin FlexPro pen to select up to 4.0 mg per dose.

H Select or adjust the dose you need by turning the dose selector forwards or backwards until the right number of mg lines up with the pointer.

When the pen contains less than 4.0 mg, the dose selector stops at the number of mg left.

ⓘ The dose selector clicks differently when turned forwards, backwards or past the number of mg left.

ⓘ **How much growth hormone is left?**
You can use the growth hormone scale to see approximately how much growth hormone is left in the pen.

You can use the dose selector to see exactly how much growth hormone is left – if the pen contains less than 4.0 mg:
Turn the dose selector until it stops. The figure that lines up with the pointer shows how many mg are left.

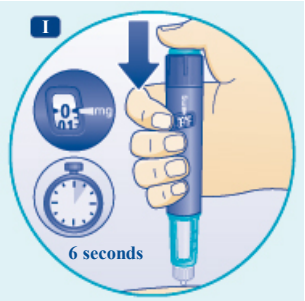
If you need more growth hormone than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen.

⚠ Never use the pen clicks to count the number of mg you select. Only the display and pointer will indicate the exact number of mg.

⚠ Never use the growth hormone scale to measure how much growth hormone to inject. Only the display and pointer will indicate the exact number of mg.

Injecting your dose
Make sure that you receive your full dose by using the right injection technique.

I Insert the needle into your skin as your doctor or nurse has shown you. Press the dose button to inject until the figure 0 in the display lines up with the pointer.

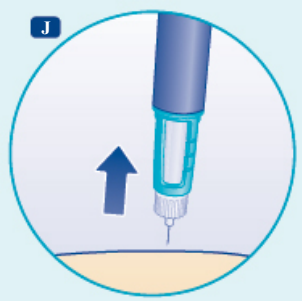


As you do this, you may hear or feel a click.

Leave the needle under the skin for at least **6 seconds** to make sure that you get your full dose.

You can let go of the dose button while you wait.

J Remove the needle from the skin.



After that, you may see a drop of growth hormone at the needle tip. This is normal and has no effect on the dose you just received.

⚠ Never use the pen clicks to count the number of mg you inject. Only the display and pointer will indicate the exact number of mg.

⚠ Never touch the display when you inject, as this can block the injection.

K Put the outer needle cap back on carefully without touching the needle. Unscrew the needle and throw it away carefully as instructed by your doctor or nurse.

Put the pen cap back on after every use.

When the pen is empty, throw it away without a needle on as advised by your doctor or nurse and local authorities.

⚠ Never put the inner needle cap back on once you have removed it from the needle. You may accidentally stick yourself with the needle.

⚠ Always store the pen without a needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.

Caring for your Norditropin FlexPro pen

Treat your Norditropin FlexPro pen with care:

- Do not drop your pen or knock it against hard surfaces. If you do drop it or suspect that something is wrong with it, always screw on a new disposable needle and check the growth hormone 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.
- Do not expose your pen to dust, dirt, liquid or direct light.
- 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 or store it close to any cooling element, e.g. in a refrigerator.

- See section 5 ‘How to store Norditropin FlexPro’ for information about how to store your pen.

⚠ **Important information**

- Always keep your pen and needles out of reach of others, especially children.
- **Never share** your pen or your needles with other people. It might lead to cross-infection.
- Caregivers must **be very careful when handling used needles** – to reduce the risk of needle injury and cross-infection.

⚠ **Important information**
Pay special attention to these notes as they are important for safe use of the pen.

ⓘ **Additional information**

Norditropin FlexPro
10 mg/1.5 ml
Somatropin

Package leaflet: Information for the user

Norditropin FlexPro 15 mg/1.5 ml solution for injection in pre-filled pen
somatropin

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Norditropin FlexPro is and what it is used for

Norditropin FlexPro 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, but adults also need it for their general health.

Norditropin FlexPro is used to treat growth failure in children
• If they have no or very low production of growth hormone (growth hormone deficiency)
• If they have Turner syndrome (a genetic problem which may affect growth)
• If they have reduced kidney function
• If they are short and were born small for gestational age (SGA)
• If they have Noonan syndrome (a genetic problem which may affect growth).

Norditropin FlexPro is used as a growth hormone replacement in adults
In adults Norditropin FlexPro is used to replace growth hormone if their growth hormone production has been decreased since childhood or has been lost in adulthood because of a tumour, treatment of a tumour, or a disease that affects the gland which produces growth hormone. If you have been treated for growth hormone deficiency during childhood, you will be retested after completion of growth. If growth hormone deficiency is confirmed, you should continue treatment.

2. What you need to know before you use Norditropin FlexPro

Do not use Norditropin FlexPro
• If you are **allergic** to somatropin, to phenol, or to any of the other ingredients of this medicine (listed in section 6)
• If you have had a **kidney transplant**
• If you have an **active tumour** (**cancer**). Tumours must be inactive and you must have finished your antitumour treatment before you start your treatment with Norditropin FlexPro
• If you have an **acute critical illness,** e.g. open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure
• If you have stopped growing (closed epiphyses) and you do not have growth hormone deficiency.

Warnings and precautions
Talk to your doctor or pharmacist before using Norditropin FlexPro
- If you have **diabetes**
- If you have ever had a **cancer** or another kind of **tumour**
- If you have recurrent **headaches, eyesight problems, nausea** or if **vomiting** occurs
- If you have abnormal **thyroid** function
- An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Norditropin FlexPro, your doctor will check you (or your child) for signs of scoliosis.
- If you walk with a limp or if you start to limp during your growth hormone treatment, you should inform your doctor.
- If you are **over 60 years of age**, or have received somatropin treatment as an adult for more than 5 years, as experience is limited
- If you suffer from **kidney disease,** as your kidney function should be monitored by your physician
- If you have a **replacement therapy with glucocorticoids,** you should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- Norditropin FlexPro 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 FlexPro.

Other medicines and Norditropin FlexPro
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. 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 FlexPro or of the other medicines:
- **Glucocorticoids** – your adult height may be affected if you use Norditropin FlexPro and glucocorticoids at the same time
- **Cyclosporine** (immunosuppressive) – as your dose may need to be adjusted
- **Insulin** – as your dose may need to be adjusted
- **Thyroid** hormone – as your dose may need to be adjusted
- **Gonadotropin** (gonad stimulating hormone) – as your dose may need to be adjusted
- **Anticonvulsants** – as your dose may need to be adjusted
- **Oestrogen** taken orally or other sex hormones.

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

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

Norditropin contains sodium
Norditropin contains less than 1 mmol sodium (23 mg) per 1.5 ml, that is to say essentially ‘sodium-free’.

3. How to use Norditropin FlexPro

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose

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 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 SGA doses of 0.033 and 0.067 mg per kg body weight per day have typically been used)
- **Children with Noonan syndrome:**
  The usual dose is 0.066 mg per kg body weight per day, however your doctor may decide that 0.033 mg per kg body weight per day is sufficient.
- **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. The 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.

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

How to use Norditropin FlexPro
Norditropin FlexPro growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use Norditropin FlexPro are given overleaf. The instructional key points 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 (see page 8, step A)
- Norditropin FlexPro 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 so you do not harm 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 FlexPro pen. Do not use the pen if a drop of growth hormone solution does not appear at the needle tip (see pages 10 to 11, steps E to G)
- Do not share your Norditropin FlexPro pen with anyone else.

How long you will need treatment for
- Children with growth failure because of Turner syndrome, kidney disease, SGA or 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 FlexPro without discussing it with your doctor first.

If you use more Norditropin FlexPro than you should
Tell your doctor if you inject too much somatropin. Long-term overdosing can cause abnormal growth and coarsening of facial features.

If you forget to use Norditropin FlexPro
Take the next dose as usual, at the normal time. **Do not take a double dose** to make up for a forgotten dose.

If you stop using Norditropin FlexPro
Do not stop using Norditropin FlexPro without discussing it with your doctor first.

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.

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

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

Formation of antibodies directed against somatropin has rarely been 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 FlexPro), although there is no evidence that somatropin was responsible for this.
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** (gynaecomastia).

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 FlexPro have experienced hip and knee pains 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 be due to Norditropin FlexPro.

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.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist, as the dose may need to be reduced.

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** (gynaecomastia).

Reporting of side effects
If you get any side effect, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Norditropin FlexPro

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 package after EXP/. The expiry date refers to the last day of that month.

Store unused Norditropin FlexPro 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 any cooling elements.

While using Norditropin FlexPro 15 mg/1.5 ml you can **either:**
- 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 continue to use Norditropin FlexPro pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin FlexPro pens where the growth hormone solution is cloudy or discoloured.

Always store Norditropin FlexPro without a needle attached.
Always keep the pen cap fully closed on the Norditropin FlexPro 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 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 Norditropin FlexPro contains
- The active substance is somatropin
- The other excipients are mannitol, histidine, poloxamer 188, phenol, water for injection, hydrochloric acid and sodium hydroxide.

What Norditropin FlexPro looks like and contents of the pack

Norditropin FlexPro is a clear and colourless solution for injection in a multidose disposable 1.5 ml pre-filled pen.

1 ml of solution contains 10 mg somatropin.
1 mg of somatropin corresponds to 3 IU of somatropin.

Norditropin FlexPro is available in three strengths:
5 mg/1.5 ml, 10 mg/1.5 ml and 15 mg/1.5 ml (equivalent to 3.3 mg/ml, 6.7 mg/ml and 10 mg/ml, respectively) in pack sizes of 1 or 5 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Cyprus, Denmark, Finland, Germany, Greece, Ireland, Luxembourg, Netherlands, Portugal, Slovenia, United Kingdom: Norditropin FlexPro 15 mg/1.5 ml

Sweden: Somatropin Novo Nordisk 15 mg/1.5 ml

France: Norditropine FlexPro 15 mg/1.5 ml

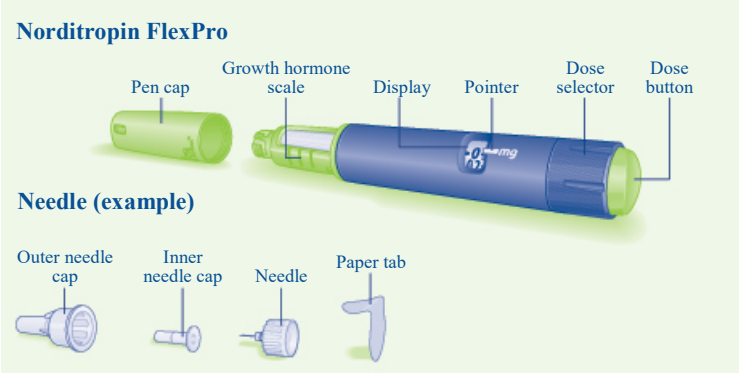
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the website of: (name of MS/Agency)

Detailed and updated information on this product is available by scanning the QR code included in the outer carton with a smartphone. The same information is also available on the following URL:https://www.myflexpro.com/en15

Instructions on how to use Norditropin FlexPro
Please read these instructions carefully before using your Norditropin FlexPro pen.
Start by checking the name, strength and coloured label of your Norditropin FlexPro pen to make sure that it contains the growth hormone strength you need.

Read on to learn about:
Preparing your Norditropin FlexPro pen
Checking the growth hormone flow with each new pen
Selecting your dose
Injecting your dose
Caring for your Norditropin FlexPro pen
Important information

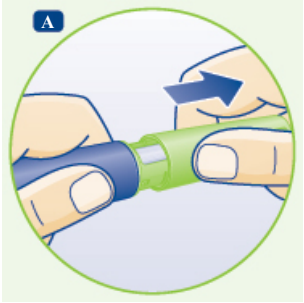


Your Norditropin FlexPro pen is a pre-filled growth hormone pen. Norditropin FlexPro contains 15 mg human growth hormone solution and delivers doses from 0.1 mg to 8.0 mg, in increments of 0.1 mg. Norditropin FlexPro is designed to be used with NovoFine or NovoTwist disposable needles up to a length of 8 mm.

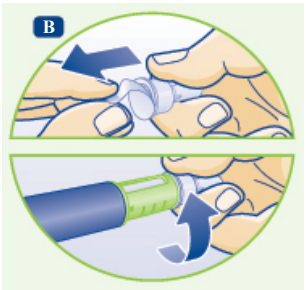
Preparing your Norditropin FlexPro pen
Check the name, strength and coloured label of your Norditropin FlexPro pen to make sure that it contains the growth hormone strength you need.

A Pull off the pen cap.

Check that the growth hormone solution in the pen is clear and colourless by tipping it upside down once or twice. If the solution looks unclear or cloudy, do not use the pen.



B Take a new disposable needle. Tear the paper tab off and screw the needle straight onto the pen. Make sure the needle is on tight.



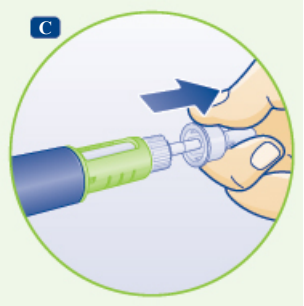
⚠ Always use a new needle for each injection. This reduces the risk of contamination, infection,

leakage of growth hormone, blocked needles and inaccurate dosing.

⚠ Never bend or damage the needle.

C Pull off the outer needle cap and save it.

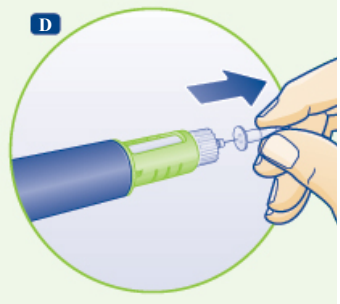
After injection, you will need it to correctly remove the needle from the pen.



D Pull off the inner needle cap and throw it away.

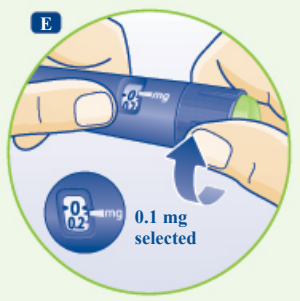
If you try to put it back on, you may accidentally stick yourself with the needle.

A drop of growth hormone may appear at the needle tip. This is normal.



Checking the growth hormone flow with each new pen
Make sure that you receive your full dose by checking the growth hormone flow before you select and inject your first dose with each new pen.

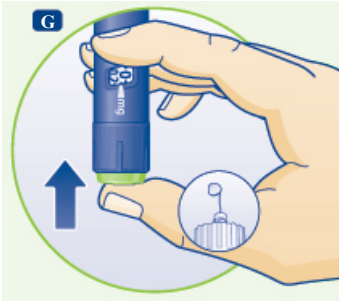
E Turn the dose selector to select the **minimum** dose, 0.1 mg.



F Hold the pen with the needle pointing up.

Tap the top of the pen a few times to let any air bubbles rise to the top.

G Press the dose button until the figure 0 in the display lines up with the pointer and a drop of growth hormone appears at the needle tip.



If no drop appears, repeat steps E to G up to 6 times. If no drop appears after these new attempts, change the needle and repeat steps E to G once more.

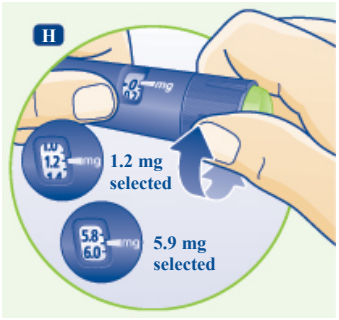
Do not use the pen if a drop of growth hormone still does not appear.

⚠ Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen.

Selecting your dose
Use the dose selector on your Norditropin FlexPro pen to select up to 8.0 mg per dose.

H Select or adjust the dose you need by turning the dose selector forwards or backwards until the right number of mg lines up with the pointer.

When the pen contains less than 8.0 mg, the dose selector stops at the number of mg left.



ⓘ The dose selector clicks differently when turned forwards, backwards or past the number of mg left.

ⓘ **How much growth hormone is left?**
You can use the growth hormone scale to see approximately how much growth hormone is left in the pen.
You can use the dose selector to see exactly how much growth hormone is left – if the pen contains less than 8.0 mg:
Turn the dose selector until it stops. The figure that lines up with the pointer shows how many mg are left.

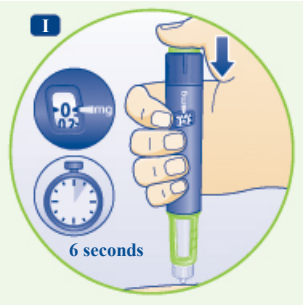
If you need more growth hormone than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen.

⚠ Never use the pen clicks to count the number of mg you select. Only the display and pointer will indicate the exact number of mg.

⚠ Never use the growth hormone scale to measure how much growth hormone to inject. Only the display and pointer will indicate the exact number of mg.

Injecting your dose
Make sure that you receive your full dose by using the right injection technique.

I Insert the needle into your skin as your doctor or nurse has shown you. Press the dose button to inject until the figure 0 in the display lines up with the pointer.

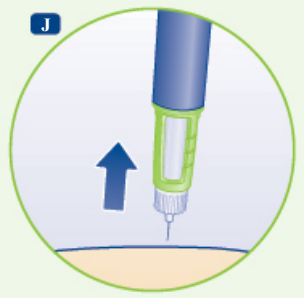


As you do this, you may hear or feel a click.

Leave the needle under the skin for at least **6 seconds** to make sure that you get your full dose.

You can let go of the dose button while you wait.

J Remove the needle from the skin.

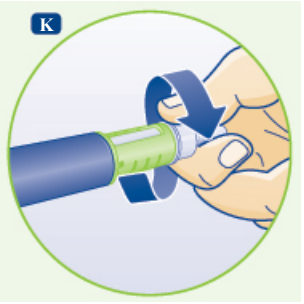


After that, you may see a drop of growth hormone at the needle tip. This is normal and has no effect on the dose you just received.

⚠ Never use the pen clicks to count the number of mg you inject. Only the display and pointer will indicate the exact number of mg.

⚠ Never touch the display when you inject, as this can block the injection.

K Put the outer needle cap back on carefully without touching the needle. Unscrew the needle and throw it away carefully as instructed by your doctor or nurse.



Put the pen cap back on after every use.

When the pen is empty, throw it away without a needle on as advised by your doctor or nurse and local authorities.

⚠ Never put the inner needle cap back on once you have removed it from the needle. You may accidentally stick yourself with the needle.

⚠ Always store the pen without a needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.

Caring for your Norditropin FlexPro pen

Treat your Norditropin FlexPro pen with care:

- Do not drop your pen or knock it against hard surfaces. If you do drop it or suspect that something is wrong with it, always screw on a new disposable needle and check the growth hormone 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.
- Do not expose your pen to dust, dirt, liquid or direct light.
- 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 or store it close to any cooling element, e.g., in a refrigerator.

- See section 5 ‘How to store Norditropin FlexPro’ for information about how to store your pen.

⚠ **Important information**
- Always keep your pen and needles out of reach of others, especially children.
- **Never share** your pen or your needles with other people. It might lead to cross-infection.
- Caregivers must **be very careful when handling used needles** – to reduce the risk of needle injury and cross-infection.

⚠ **Important information**
Pay special attention to these notes as they are important for safe use of the pen.

ⓘ **Additional information**

Norditropin FlexPro
15 mg/1.5 ml
Somatropin