SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

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

Norditropin NordiLet 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 NordiLet 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 may progress in any child during rapid growth. Signs of scoliosis should be monitored during treatment. However, somatropin treatment has not been shown to increase the incidence or severity of scoliosis.

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.

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).

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.

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 NordiLet 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 disorders		In adults headache and paraesthesia	In adults carpal tunnel syndrome. In children headache	
Skin and			In adults pruritus	In children rash

subcutaneous tissue disorders				
Musculoskeletal, connective tissue disorders		In adults arthralgia, joint stiffness and myalgia	In adults muscle stiffness	In children arthralgia and myalgia
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: Slipped capital femoral epiphysis. Slipped capital femoral epiphysis may occur more frequently in patients with endocrine 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 NordiLet 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.

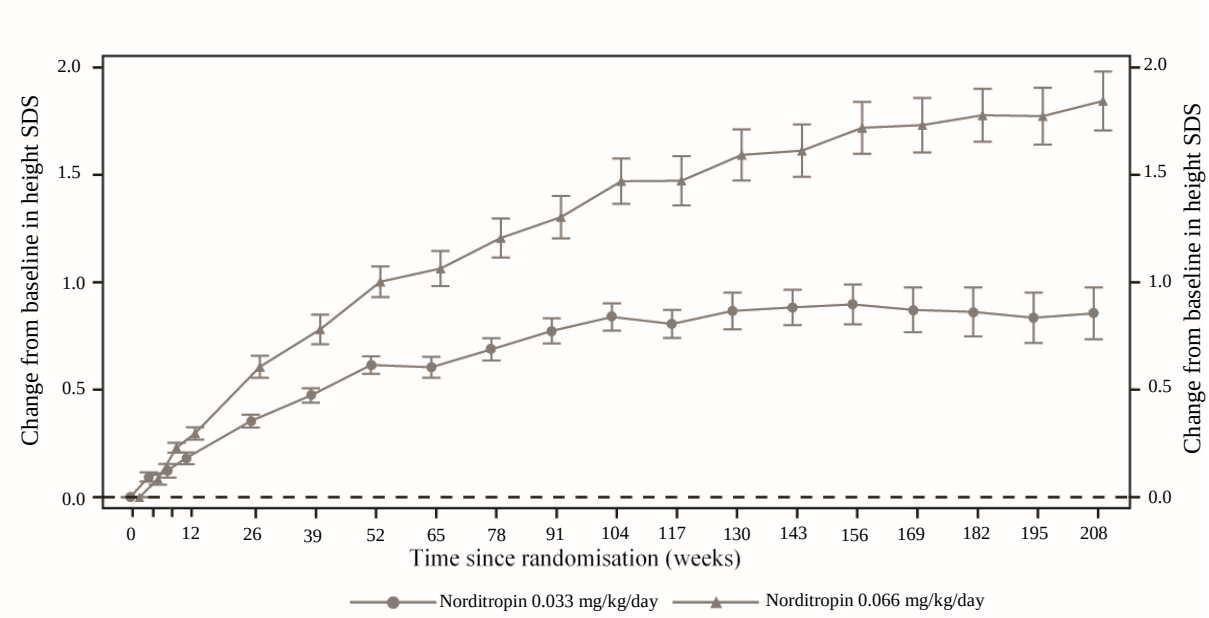
Somatropin also increases bone turnover indicated by an increase in plasma levels of biochemical bone markers. In adults bone mass is slightly decreased during the initial months of treatment due to more pronounced bone resorption, however, bone mass increases with prolonged treatment.

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.

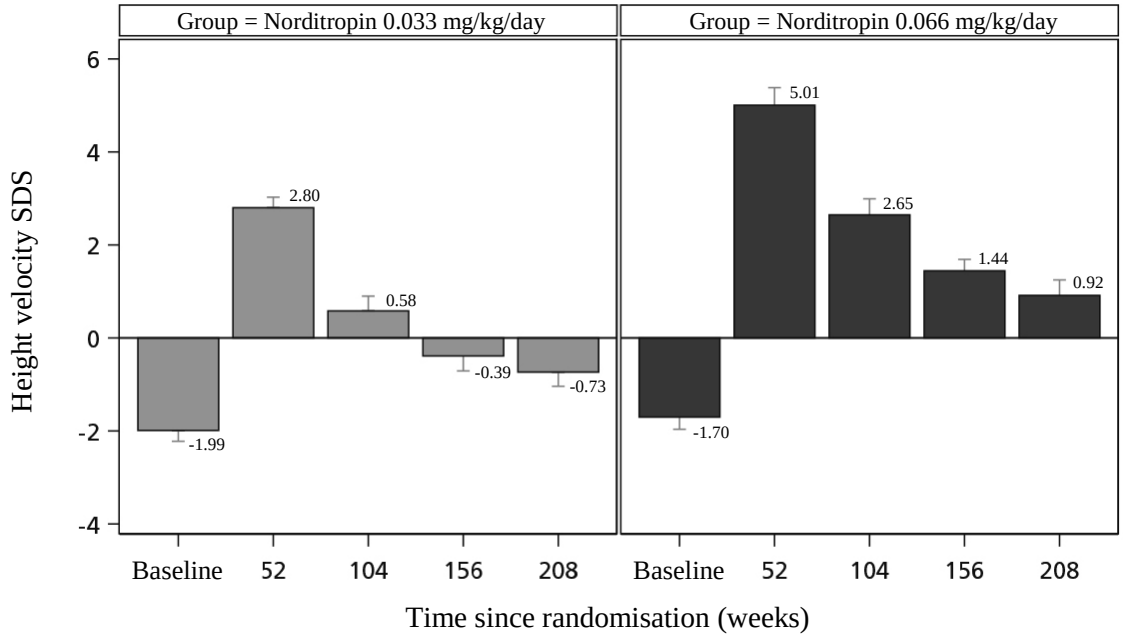
A statistically significant increase from baseline in mean height SDS at 104 weeks (primary endpoint) was observed with 0.033 mg/kg/day (0.84 SDS) and 0.066 mg/kg/day (1.47 SDS). A mean difference of 0.63 SDS [95 % CI: 0.38; 0.88] was observed between the groups at 104 weeks; the difference was greater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

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.
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 NordiLet 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 NordiLet 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.

Norditropin NordiLet 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.

Norditropin NordiLet 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.

The pre-filled pen is packed in a carton.

6.6 Special precautions for disposal and other handling

Norditropin NordiLet is a pre-filled pen designed to be used with NovoFine needles. The dose is delivered in clicks. NordiLet delivers 1-29 clicks in increments of 1 click for each injection. The dose per click is the following for each strength: 0.0667 mg (5 mg/1.5 ml), 0.1333 mg (10 mg/1.5 ml) and 0.2000 mg (15 mg/1.5 ml). In the package leaflet for each strength a range of doses in mg per number of clicks is given in a conversion table.

To ensure proper dosing and avoid injection of air, check the growth hormone flow (prime) before the first injection. Do not use Norditropin NordiLet if a drop of growth hormone does not appear at the needle tip. A dose is dialled in clicks by turning the pen cap. The dialled dose is checked by addition of the figure on the pen cap scale and the figure on the push button scale. The push button is pressed to inject the dose.

Norditropin NordiLet should not be shaken vigorously at any time.

Do not use Norditropin NordiLet 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 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: 20-June-2003
Date of latest renewal: 12-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 NordiLet 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,
5 mg/1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine needles
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
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
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 NordiLet 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 NordiLet 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,
10 mg/1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine needles
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
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
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 NordiLet 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 NordiLet 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,
15 mg/1.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use
Designed to be used with NovoFine needles
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
When in use: Store *either* in a refrigerator (2°C – 8°C) for 4 weeks, *or* below 25°C for 3 weeks
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 NordiLet 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 NordiLet 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 NordiLet 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 NordiLet 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 NordiLet 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 NordiLet is and what it is used for

Norditropin NordiLet 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 NordiLet 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 NordiLet is used as a growth hormone replacement in adults:
In adults Norditropin NordiLet 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 NordiLet

Do not use Norditropin NordiLet
• 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 NordiLet
• 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 NordiLet
- 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
- If you develop a limp or lower back pain as these could be signs of a curved spine (**scoliosis)**
- 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.

Other medicines and Norditropin NordiLet
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 NordiLet or of the other medicines*:*
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiLet 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 NordiLet
- **Breast-feeding –** Do not use Norditropin NordiLet while you are breast-feeding because somatropin might pass into your milk.

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

3. How to use Norditropin NordiLet

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 NordiLet
Inject your daily dose into the skin every evening just before bedtime.

How to use Norditropin NordiLet
Norditropin NordiLet growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use the Norditropin NordiLet 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 NordiLet is designed to be used with NovoFine disposable needles
- 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 NordiLet 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 NordiLet 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 NordiLet without discussing it with your doctor first.

If you use more Norditropin NordiLet 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 NordiLet
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 NordiLet

Do not stop using Norditropin NordiLet 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 NordiLet 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 NordiLet), 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.

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 NordiLet 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 NordiLet.

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.**

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 NordiLet

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 NordiLet 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.

While using Norditropin NordiLet 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 NordiLet pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin NordiLet pens if the growth hormone solution is cloudy or discoloured.

Always store Norditropin NordiLet without a needle attached.
Always keep the pen cap fully closed on the Norditropin NordiLet 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 NordiLet 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 NordiLet looks like and contents of the pack
Norditropin NordiLet 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 NordiLet 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 State of the EEA under the following name:

Denmark: Norditropin NordiLet 5 mg/1.5 ml

This leaflet was last revised in

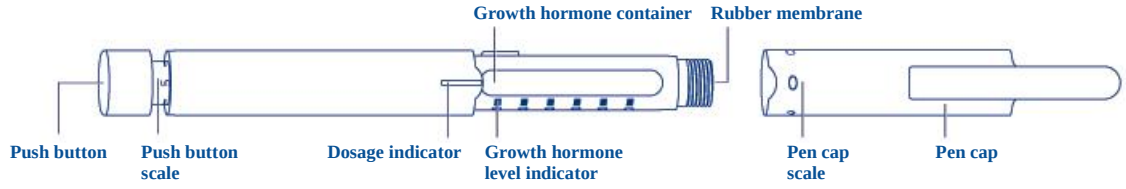
Other sources of information
Detailed information on this medicine is available on the website of: (name of MS/Agency)

Norditropin NordiLet 5 mg/1.5 ml

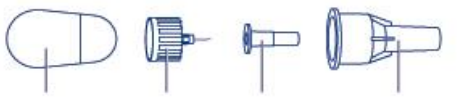
How to use the Norditropin NordiLet pen

Read right through these instructions before using Norditropin NordiLet

- Norditropin NordiLet 5 mg/1.5 ml is a disposable multidose pre-filled pen with human growth hormone solution for injection.
- Norditropin NordiLet is designed to be used with NovoFine disposable needles.
- Only use the pen if the growth hormone inside is clear and colourless.
- Always check the flow (‘prime’ the pen) before the first injection from each new pen – see Step 3.
- Your doctor will tell you what dose of growth hormone you need. You can convert this dose (in mg) to the number of ‘clicks’ of the pen that you need using the conversion table alongside. You can dial any dose from 1 to 29 clicks.
- Always check you are using the correct conversion table for your particular pen. If you have a Norditropin NordiLet 5 mg/1.5 ml pen, you should only use the Norditropin NordiLet pen 5 mg/1.5 ml conversion table.
- You can use the growth hormone level indicator to estimate how many clicks of growth hormone are left in your pen. Do not use the growth hormone level indicator to set your dose.
- Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down.
- Always keep the pen cap fully closed on the pen when you are not using it.
- Always store your pen without the needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Never share your pen or your needles with other people. It might lead to cross-infection.



Needle (example)



Conversion Table
Norditropin NordiLet
5 mg/1.5 ml
Interval in mg

5 mg/1.5 ml

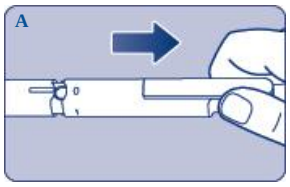
From mg	– To mg	Clicks
0.01	0.09	1
0.10	0.16	2
0.17	0.22	3
0.23	0.29	4
0.30	0.36	5
0.37	0.42	6
0.43	0.49	7
0.50	0.56	8
0.57	0.62	9
0.63	0.69	10
0.70	0.76	11
0.77	0.82	12
0.83	0.89	13
0.90	0.96	14
0.97	1.02	15
1.03	1.09	16
1.10	1.16	17
1.17	1.22	18
1.23	1.29	19
1.30	1.36	20
1.37	1.42	21
1.43	1.49	22
1.50	1.56	23
1.57	1.62	24
1.63	1.69	25
1.70	1.76	26
1.77	1.82	27
1.83	1.89	28
1.90	1.93	29

How to use the conversion table

- Find the dose that has been recommended for you among the dosage intervals in the left-hand column. Now read across for the equivalent number of clicks of the pen in the right-hand column.
- If your doctor says you need a dose of 1.20 mg, you will need 18 clicks of the pen.

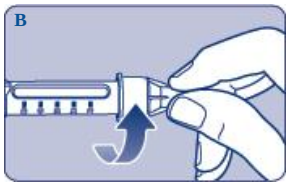
1. Check the pen

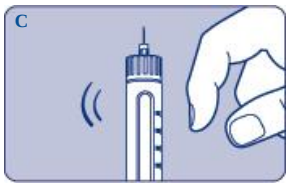
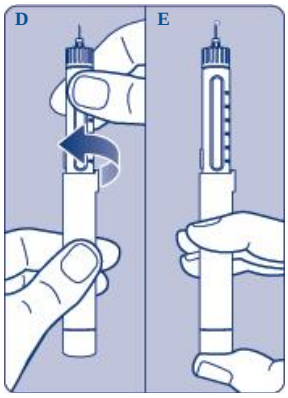
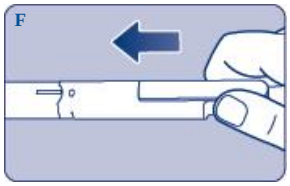
- **Check the name, strength and coloured label of your Norditropin NordiLet pen to make sure that it contains the growth hormone strength you need.**
- Pull off the pen cap [**A**].
- Check the solution inside the pen by turning it upside down once or twice.
- Only use the pen if the growth hormone inside is clear and colourless.

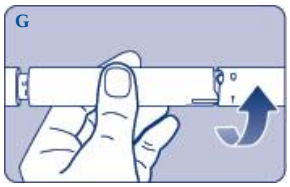
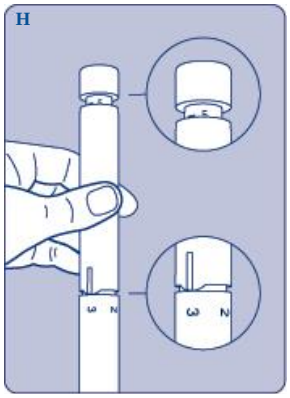


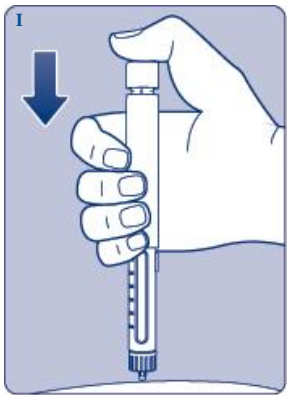
2. Attach the needle

- **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Be careful not to bend or damage the needle before use.
- Take a new needle and **remove the protective paper tab.**
- **Screw the needle** tightly onto the pen [**B**].



The needle has two needle caps. You need to remove them both: • **Pull off the outer needle cap** and keep it to dispose of the used needle later. • **Remove the inner needle cap by pulling on the central tip** and throw it away. • Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.	
3. Check the flow • **Before you use a new pen for the first time, you need to check the flow** (‘prime’ the pen) to make sure you get the correct dose and do not inject any air: • Hold the pen with the needle pointing upwards and tap the cartridge gently with your finger a few times to make sure that any air bubbles collect at the top of the growth hormone container [**C**].	
• Holding the pen with the needle pointing upwards, turn the growth hormone container in the direction of the arrow shown until you dial one click [**D**]. • Holding the pen with the needle still pointing upwards, press the push button at the bottom at the pen all the way in [**E**]. • Repeat steps **C** to **E** until a drop of growth hormone appears at the needle tip. • **Do not use the pen if a drop of growth hormone does not appear** • Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen. This makes sure that the growth hormone flows. If no drop appears, you will not inject any growth hormone. This may indicate a blocked or damaged needle. • Check the flow again if your pen has been dropped or knocked against a hard surface, or if you are not sure that it is working properly. If considered faulty, take it back to your supplier for a new one.	
4. Dial the dose • Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down. • Put the pen cap back on the pen, with ‘0’ next to the dosage indicator [**F**].	

• Hold the pen horizontally and turn the pen cap in the direction shown by the arrow to set the dose your doctor has recommended for you [**G**]. • The scale on the pen cap shows the number of clicks (0, 1, 2, 3, 4 clicks). As the pen cap is turned, the push button moves outwards. • Every time you make a full turn of the pen cap, 5 clicks will be set on the push button scale. So the scale will show 5, 10, 15, 20 or 25 clicks. • Be careful not to put your hand over the push button when you dial the dose. If the push button cannot rise freely, growth hormone will be pushed out of the needle. • You cannot set a dose higher than the number of clicks left. • Always use the pen cap scale and the push button scale to see how many clicks you have dialled before injecting the growth hormone. • If you select and inject the wrong dose, you may get too little or too much growth hormone.	G 
Examples of how to set the dose [H] How to select four clicks: • Turn the cap until ‘4’ is next to the dosage indicator. How to select eight clicks: • Turn the pen cap one full turn so ‘0’ is next to the dosage indicator again. You have now selected five clicks and ‘5’ will show on the push button scale. Continue turning the pen cap scale until ‘3’ is next to the dosage indicator. • Add the ‘3’ from the pen cap scale indicator to the ‘5’ on the push button scale and you have selected eight clicks altogether. **How to check the dose set [H]** • To check the dose set, add the number on the pen cap scale, which lines up with the dosage indicator, to the highest number shown on the push button scale. • If you have set a wrong dose, simply turn the pen cap forwards or backwards until the right number of clicks has been set. The maximum dose you can set is 29 clicks. • If you try to set a dose higher than 29 clicks, growth hormone will leak out of the needle. This may cause inaccurate dosing. • If you do this by mistake, turn the pen cap back as far as you can until the push button is fully down and you can feel resistance. • If ‘0’ is not next to the dosage indicator remove the pen cap and put it back on as shown in picture **F.** • Now start again, remembering that 29 clicks is the	H 

maximum dose. • After the dose is set, remove the pen cap to carry out the injection.	
5. Inject the dose • Use the injection method that has been recommended to you. • 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 [**I**]. • **Keep the needle under the skin for at least 6 seconds** and then withdraw it. Keep the push button fully depressed until the needle is removed from the skin. This ensures that you get the full dose.	
6. Remove the needle • Replace the outer needle cap and unscrew the needle. Throw it away carefully. Replace the pen cap on the pen, with '0' next to the dosage indicator. • **Always remove the needle after each injection and store your pen without the needle attached.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing. • When the pen is empty, throw it away without a needle attached as advised by your doctor or nurse and local authorities. • **Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.** • Always keep your pen and needles out of sight and reach of others, especially children.	
7. Maintenance • Your Norditropin NordiLet pen must be handled with care. If it is dropped, damaged or crushed, there is a risk of leakage of growth hormone. This may cause inaccurate dosing. • Do not shake your pen vigorously. Protect your pen from dust, dirt and direct light and any situation where it might be damaged. • Do not freeze your pen or store it close to any cooling element, e.g. in a refrigerator. • Do not try to wash, soak or lubricate your pen. If necessary, clean it with a mild detergent on a moistened cloth.	

Package leaflet: Information for the user

Norditropin NordiLet 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 NordiLet is and what it is used for

Norditropin NordiLet 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 NordiLet 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 NordiLet is used as a growth hormone replacement in adults:
In adults Norditropin NordiLet 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 NordiLet

Do not use Norditropin NordiLet
• 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 NordiLet
• 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 NordiLet
- 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
- If you develop a limp or lower back pain as these could be signs of a curved spine (**scoliosis**)
- 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.

Other medicines and Norditropin NordiLet
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 NordiLet or of the other medicines*:*
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiLet 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 NordiLet
- **Breast-feeding –** Do not use Norditropin NordiLet while you are breast-feeding because somatropin might pass into your milk.

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

3. How to use Norditropin NordiLet

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 NordiLet
Inject your daily dose into the skin every evening just before bedtime.

How to use Norditropin NordiLet
Norditropin NordiLet growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use the Norditropin NordiLet 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 NordiLet is designed to be used with NovoFine disposable needles
- 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 NordiLet 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 NordiLet 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 NordiLet without discussing it with your doctor first.

If you use more Norditropin NordiLet 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 NordiLet
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 NordiLet

Do not stop using Norditropin NordiLet 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 NordiLet 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 NordiLet), 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.

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 NordiLet 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 NordiLet.

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.**

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 NordiLet

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 NordiLet 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.

While using Norditropin NordiLet 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 NordiLet pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin NordiLet pens if the growth hormone solution is cloudy or discoloured.

Always store Norditropin NordiLet without a needle attached.
Always keep the pen cap fully closed on the Norditropin NordiLet 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 NordiLet 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 NordiLet looks like and contents of the pack
Norditropin NordiLet 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 NordiLet 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 State of the EEA under the following name:

Denmark: Norditropin NordiLet 10 mg/1.5 ml

This leaflet was last revised in

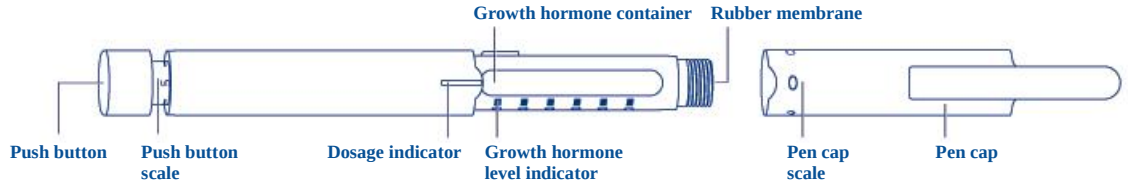
Other sources of information
Detailed information on this medicine is available on the website of: {name of MS/Agency}

Norditropin NordiLet 10 mg/1.5 ml

How to use the Norditropin NordiLet pen

Read right through these instructions before using Norditropin NordiLet

- Norditropin NordiLet 10 mg/1.5 ml is a disposable multidose pre-filled pen with human growth hormone solution for injection.
- Norditropin NordiLet is designed to be used with NovoFine disposable needles.
- Only use the pen if the growth hormone inside is clear and colourless.
- Always check the flow (‘prime’ the pen) before the first injection from each new pen – see Step 3.
- Your doctor will tell you what dose of growth hormone you need. You can convert this dose (in mg) to the number of ‘clicks’ of the pen that you need using the conversion table alongside. You can dial any dose from 1 to 29 clicks.
- Always check you are using the correct conversion table for your particular pen. If you have a Norditropin NordiLet 10 mg/1.5 ml pen, you should only use the Norditropin NordiLet pen 10 mg/1.5 ml conversion table.
- You can use the growth hormone level indicator to estimate how many clicks of growth hormone are left in your pen. Do not use the growth hormone level indicator to set your dose.
- Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down.
- Always keep the pen cap fully closed on the pen when you are not using it.
- Always store your pen without the needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Never share your pen or your needles with other people. It might lead to cross-infection.



Needle (example)

Conversion Table
Norditropin NordiLet
10 mg/1.5 ml
Interval in mg

10 mg/1.5 ml

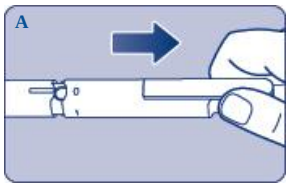
From mg	– To mg	Clicks
0.01	0.19	1
0.20	0.32	2
0.33	0.46	3
0.47	0.59	4
0.60	0.72	5
0.73	0.86	6
0.87	0.99	7
1.00	1.12	8
1.13	1.26	9
1.27	1.39	10
1.40	1.52	11
1.53	1.66	12
1.67	1.79	13
1.80	1.92	14
1.93	2.06	15
2.07	2.19	16
2.20	2.32	17
2.33	2.46	18
2.47	2.59	19
2.60	2.72	20
2.73	2.86	21
2.87	2.99	22
3.00	3.12	23
3.13	3.26	24
3.27	3.39	25
3.40	3.52	26
3.53	3.66	27
3.67	3.79	28
3.80	3.87	29

How to use the conversion table

- Find the dose that has been recommended for you among the dosage intervals in the left-hand column. Now read across for the equivalent number of clicks of the pen in the right-hand column.
- If your doctor says you need a dose of 2.40 mg, you will need 18 clicks of the pen.

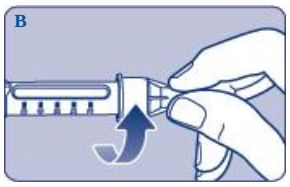
1. Check the pen

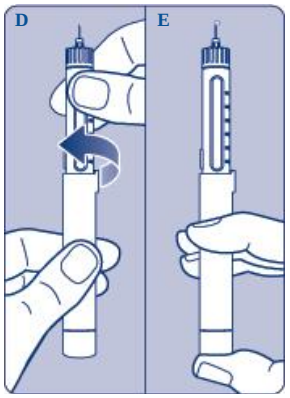
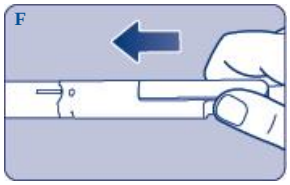
- **Check the name, strength and coloured label of your Norditropin NordiLet pen to make sure that it contains the growth hormone strength you need.**
- Pull off the pen cap [**A**].
- Check the solution inside the pen by turning it upside down once or twice.
- Only use the pen if the growth hormone inside is clear and colourless.

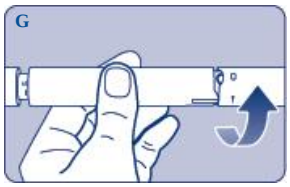
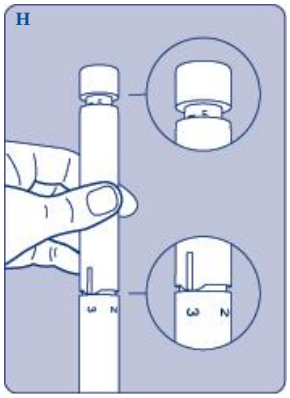


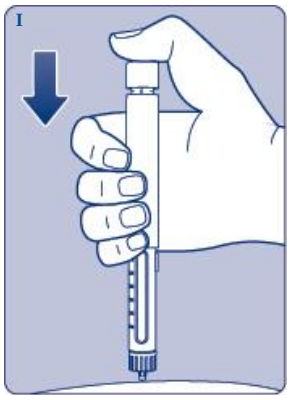
2. Attach the needle

- **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Be careful not to bend or damage the needle before use.
- Take a new needle and **remove the protective paper tab.**
- **Screw the needle** tightly onto the pen [**B**].



The needle has two needle caps. You need to remove them both: • **Pull off the outer needle cap** and keep it to dispose of the used needle later. • **Remove the inner needle cap by pulling on the central tip** and throw it away. • Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.	
3. Check the flow • **Before you use a new pen for the first time, you need to check the flow** (‘prime’ the pen) to make sure you get the correct dose and do not inject any air: • Hold the pen with the needle pointing upwards and tap the cartridge gently with your finger a few times to make sure that any air bubbles collect at the top of the growth hormone container [**C**].	
• Holding the pen with the needle pointing upwards, turn the growth hormone container in the direction of the arrow shown until you dial one click [**D**]. • Holding the pen with the needle still pointing upwards, press the push button at the bottom at the pen all the way in [**E**]. • Repeat steps **C** to **E** until a drop of growth hormone appears at the needle tip. • **Do not use the pen if a drop of growth hormone does not appear.** • Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen. This makes sure that the growth hormone flows. If no drop appears, you will not inject any growth hormone. This may indicate a blocked or damaged needle. • Check the flow again if your pen has been dropped or knocked against a hard surface, or if you are not sure that it is working properly. If considered faulty, take it back to your supplier for a new one.	
4. Dial the dose • Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down. • Put the pen cap back on the pen, with ‘0’ next to the dosage indicator [**F**].	

• Hold the pen horizontally and turn the pen cap in the direction shown by the arrow to set the dose your doctor has recommended for you [**G**]. • The scale on the pen cap shows the number of clicks (0, 1, 2, 3, 4 clicks). As the pen cap is turned, the push button moves outwards. • Every time you make a full turn of the pen cap, 5 clicks will be set on the push button scale. So the scale will show 5, 10, 15, 20 or 25 clicks. • Be careful not to put your hand over the push button when you dial the dose. If the push button cannot rise freely, growth hormone will be pushed out of the needle. • You cannot set a dose higher than the number of clicks left. • Always use the pen cap scale and the push button scale to see how many clicks you have dialled before injecting the growth hormone. • If you select and inject the wrong dose, you may get too little or too much growth hormone.	G 
Examples of how to set the dose [H] How to select four clicks: • Turn the cap until ‘4’ is next to the dosage indicator. How to select eight clicks: • Turn the pen cap one full turn so ‘0’ is next to the dosage indicator again. You have now selected five clicks and ‘5’ will show on the push button scale. Continue turning the pen cap scale until ‘3’ is next to the dosage indicator. • Add the ‘3’ from the pen cap scale indicator to the ‘5’ on the push button scale and you have selected eight clicks altogether. **How to check the dose set [H]** • To check the dose set, add the number on the pen cap scale, which lines up with the dosage indicator, to the highest number shown on the push button scale. • If you have set a wrong dose, simply turn the pen cap forwards or backwards until the right number of clicks has been set. The maximum dose you can set is 29 clicks. • If you try to set a dose higher than 29 clicks, growth hormone will leak out of the needle. This may cause inaccurate dosing. • If you do this by mistake, turn the pen cap back as far as you can until the push button is fully down and you can feel resistance. • If ‘0’ is not next to the dosage indicator remove the pen cap and put it back on as shown in picture **F.** • Now start again, remembering that 29 clicks is the	H 

maximum dose. • After the dose is set, remove the pen cap to carry out the injection.	
5. Inject the dose • Use the injection method that has been recommended to you. • 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 [**I**]. • **Keep the needle under the skin for at least 6 seconds** and then withdraw it. Keep the push button fully depressed until the needle is removed from the skin. This ensures that you get the full dose.	
6. Remove the needle • Replace the outer needle cap and unscrew the needle. Throw it away carefully. Replace the pen cap on the pen, with '0' next to the dosage indicator. • **Always remove the needle after each injection and store your pen without the needle attached.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing. • When the pen is empty, throw it away without a needle attached as advised by your doctor or nurse and local authorities. • **Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.** • Always keep your pen and needles out of sight and reach of others, especially children.	
7. Maintenance • Your Norditropin NordiLet pen must be handled with care. If it is dropped, damaged or crushed, there is a risk of leakage of growth hormone. This may cause inaccurate dosing. • Do not shake your pen vigorously. Protect your pen from dust, dirt and direct light and any situation where it might be damaged. • Do not freeze your pen or store it close to any cooling element, e.g. in a refrigerator. • Do not try to wash, soak or lubricate your pen. If necessary, clean it with a mild detergent on a moistened cloth.	

Package leaflet: Information for the user

Norditropin NordiLet 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 NordiLet is and what it is used for

Norditropin NordiLet 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 NordiLet 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 NordiLet is used as a growth hormone replacement in adults:
In adults Norditropin NordiLet 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 NordiLet

Do not use Norditropin NordiLet
• 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 NordiLet
• 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 NordiLet
- 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
- If you develop a limp or lower back pain as these could be signs of a curved spine (**scoliosis**)
- 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.

Other medicines and Norditropin NordiLet
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 NordiLet or of the other medicines*:*
- **Glucocorticoids** – your adult height may be affected if you use Norditropin NordiLet 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 NordiLet
- **Breast-feeding –** Do not use Norditropin NordiLet while you are breast-feeding because somatropin might pass into your milk.

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

3. How to use Norditropin NordiLet

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 NordiLet
Inject your daily dose into the skin every evening just before bedtime.

How to use Norditropin NordiLet
Norditropin NordiLet growth hormone solution comes in a multidose disposable 1.5 ml pre-filled pen. Full instructions on how to use the Norditropin NordiLet 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 NordiLet is designed to be used with NovoFine disposable needles
- 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 NordiLet 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 NordiLet 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 NordiLet without discussing it with your doctor first.

If you use more Norditropin NordiLet 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 NordiLet
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 NordiLet

Do not stop using Norditropin NordiLet 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 NordiLet 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 NordiLet), 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.

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 NordiLet 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 NordiLet.

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.**

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 NordiLet

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 NordiLet 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.

While using Norditropin NordiLet 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 NordiLet pens if they have been frozen or exposed to excessive temperatures.

Do not use Norditropin NordiLet pens if the growth hormone solution is cloudy or discoloured.

Always store Norditropin NordiLet without a needle attached.
Always keep the pen cap fully closed on the Norditropin NordiLet 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 NordiLet 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 NordiLet looks like and contents of the pack
Norditropin NordiLet 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 NordiLet 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 State of the EEA under the following name:

Denmark: Norditropin NordiLet 15 mg/1.5 ml

This leaflet was last revised in

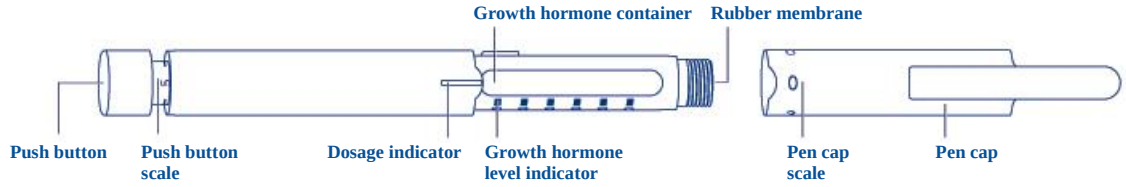
Other sources of information
Detailed information on this medicine is available on the website of: (name of MS/Agency)

Norditropin NordiLet 15 mg/1.5 ml

How to use the Norditropin NordiLet pen

Read right through these instructions before using Norditropin NordiLet

- Norditropin NordiLet 15 mg/1.5 ml is a disposable multidose pre-filled pen with human growth hormone solution for injection.
- Norditropin NordiLet is designed to be used with NovoFine disposable needles.
- Only use the pen if the growth hormone inside is clear and colourless.
- Always check the flow (‘prime’ the pen) before the first injection from each new pen – see Step 3.
- Your doctor will tell you what dose of growth hormone you need. You can convert this dose (in mg) to the number of ‘clicks’ of the pen that you need using the conversion table alongside. You can dial any dose from 1 to 29 clicks.
- Always check you are using the correct conversion table for your particular pen. If you have a Norditropin NordiLet 15 mg/1.5 ml pen, you should only use the Norditropin NordiLet pen 15 mg/1.5 ml conversion table.
- You can use the growth hormone level indicator to estimate how many clicks of growth hormone are left in your pen. Do not use the growth hormone level indicator to set your dose.
- Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down.
- Always keep the pen cap fully closed on the pen when you are not using it.
- Always store your pen without the needle attached. This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Never share your pen or your needles with other people. It might lead to cross-infection.



Needle (example)

Conversion Table
Norditropin NordiLet
15 mg/1.5 ml
Interval in mg

15 mg/1.5 ml

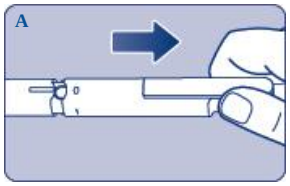
From mg – To mg	Clicks
0.01 - 0.29	1
0.30 - 0.49	2
0.50 - 0.69	3
0.70 - 0.89	4
0.90 - 1.09	5
1.10 - 1.29	6
1.30 - 1.49	7
1.50 - 1.69	8
1.70 - 1.89	9
1.90 - 2.09	10
2.10 - 2.29	11
2.30 - 2.49	12
2.50 - 2.69	13
2.70 - 2.89	14
2.90 - 3.09	15
3.10 - 3.29	16
3.30 - 3.49	17
3.50 - 3.69	18
3.70 - 3.89	19
3.90 - 4.09	20
4.10 - 4.29	21
4.30 - 4.49	22
4.50 - 4.69	23
4.70 - 4.89	24
4.90 - 5.09	25
5.10 - 5.29	26
5.30 - 5.49	27
5.50 - 5.69	28
5.70 - 5.80	29

How to use the conversion table

- Find the dose that has been recommended for you among the dosage intervals in the left-hand column. Now read across for the equivalent number of clicks of the pen in the right-hand column.
- If your doctor says you need a dose of 3.60 mg, you will need 18 clicks of the pen.

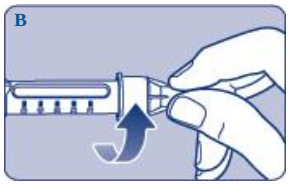
1. Check the pen

- **Check the name, strength and coloured label of your Norditropin NordiLet pen to make sure that it contains the growth hormone strength you need.**
- Pull off the pen cap [**A**].
- Check the solution inside the pen by turning it upside down once or twice.
- Only use the pen if the growth hormone inside is clear and colourless.

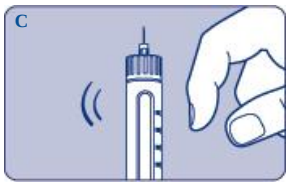
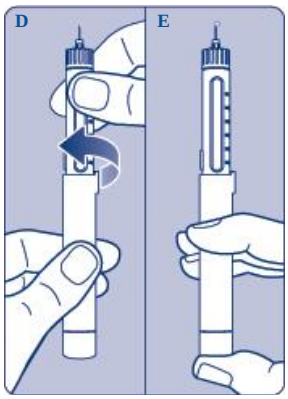
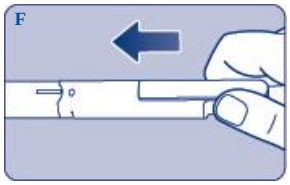


2. Attach the needle

- **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing.
- Be careful not to bend or damage the needle before use.
- Take a new needle and **remove the protective paper tab.**
- **Screw the needle** tightly onto the pen [**B**].

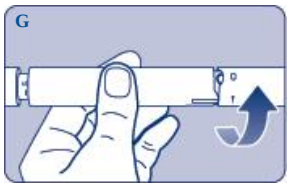


The needle has two needle caps. You need to remove them

both: • **Pull off the outer needle cap** and keep it to dispose of the used needle later. • **Remove the inner needle cap by pulling on the central tip** and throw it away. • Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.	
3. Check the flow • **Before you use a new pen for the first time, you need to check the flow** (‘prime’ the pen) to make sure you get the correct dose and do not inject any air: • Hold the pen with the needle pointing upwards and tap the cartridge gently with your finger a few times to make sure that any air bubbles collect at the top of the growth hormone container [**C**].	
• Holding the pen with the needle pointing upwards, turn the growth hormone container in the direction of the arrow shown until you dial one click [**D**]. • Holding the pen with the needle still pointing upwards, press the push button at the bottom at the pen all the way in [**E**]. • Repeat steps **C** to **E** until a drop of growth hormone appears at the needle tip. • **Do not use the pen if a drop of growth hormone does not appear.** • Always make sure that a drop appears at the needle tip before you inject your first dose with each new pen. This makes sure that the growth hormone flows. If no drop appears, you will not inject any growth hormone. This may indicate a blocked or damaged needle. • Check the flow again if your pen has been dropped or knocked against a hard surface, or if you are not sure that it is working properly. If considered faulty, take it back to your supplier for a new one.	
4. Dial the dose • Always make sure that the push button is fully down, before you use the pen. If not, turn the pen cap until the push button is completely down. • Put the pen cap back on the pen, with ‘0’ next to the dosage indicator [**F**].	

- Hold the pen horizontally and turn the pen cap in the direction shown by the arrow to set the dose your doctor has recommended for you [**G**].
- The scale on the pen cap shows the number of clicks (0, 1, 2, 3, 4 clicks). As the pen cap is turned, the push button moves outwards.
- Every time you make a full turn of the pen cap, 5 clicks will be set on the push button scale. So the scale will show 5, 10, 15, 20 or 25 clicks.
- Be careful not to put your hand over the push button when you dial the dose. If the push button cannot rise freely, growth hormone will be pushed out of the needle.
- You cannot set a dose higher than the number of clicks left.
- Always use the pen cap scale and the push button scale to see how many clicks you have dialled before injecting the growth hormone.
- If you select and inject the wrong dose, you may get too little or too much growth hormone.

G



Examples of how to set the dose [H]

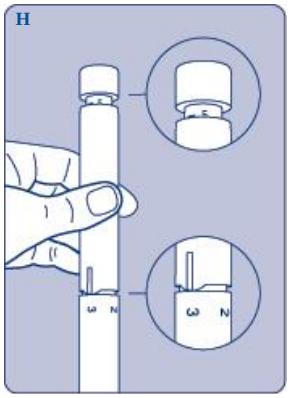
How to select four clicks:

- Turn the cap until ‘4’ is next to the dosage indicator.

How to select eight clicks:

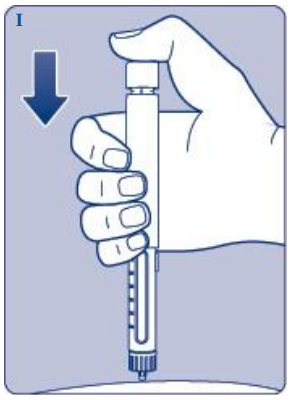
- Turn the pen cap one full turn so ‘0’ is next to the dosage indicator again. You have now selected five clicks and ‘5’ will show on the push button scale. Continue turning the pen cap scale until ‘3’ is next to the dosage indicator.
- Add the ‘3’ from the pen cap scale indicator to the ‘5’ on the push button scale and you have selected eight clicks altogether.

H



How to check the dose set [H]

- To check the dose set, add the number on the pen cap scale, which lines up with the dosage indicator, to the highest number shown on the push button scale.
- If you have set a wrong dose, simply turn the pen cap forwards or backwards until the right number of clicks has been set. The maximum dose you can set is 29 clicks.
- If you try to set a dose higher than 29 clicks, growth hormone will leak out of the needle. This may cause inaccurate dosing.
- If you do this by mistake, turn the pen cap back as far as you can until the push button is fully down and you can feel resistance.
- If ‘0’ is not next to the dosage indicator remove the pen cap and put it back on as shown in picture **F.**
- Now start again, remembering that 29 clicks is the

maximum dose. • After the dose is set, remove the pen cap to carry out the injection.	
5. Inject the dose • Use the injection method that has been recommended to you. • 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 [**I**]. • **Keep the needle under the skin for at least 6 seconds** and then withdraw it. Keep the push button fully depressed until the needle is removed from the skin. This ensures that you get the full dose.	
6. Remove the needle • Replace the outer needle cap and unscrew the needle. Throw it away carefully. Replace the pen cap on the pen, with '0' next to the dosage indicator. • **Always remove the needle after each injection and store your pen without the needle attached.** This reduces the risk of contamination, infection, leakage of growth hormone, blocked needles and inaccurate dosing. • When the pen is empty, throw it away without a needle attached as advised by your doctor or nurse and local authorities. • **Caregivers must be very careful when handling used needles – to reduce the risk of needle sticks and cross-infection.** • Always keep your pen and needles out of sight and reach of others, especially children.	
7. Maintenance • Your Norditropin NordiLet pen must be handled with care. If it is dropped, damaged or crushed, there is a risk of leakage of growth hormone. This may cause inaccurate dosing. • Do not shake your pen vigorously. Protect your pen from dust, dirt and direct light and any situation where it might be damaged. • Do not freeze your pen or store it close to any cooling element, e.g. in a refrigerator. • Do not try to wash, soak or lubricate your pen. If necessary, clean it with a mild detergent on a moistened cloth.	