ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Ngenla 24 mg solution for injection in pre-filled pen
Ngenla 60 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ngenla 24 mg solution for injection in pre-filled pen

One mL of solution contains 20 mg of somatrogon*.
Each pre-filled pen contains 24 mg somatrogon in 1.2 mL solution.
Each pre-filled pen delivers doses from 0.2 mg to 12 mg in a single injection in 0.2 mg increments.

Ngenla 60 mg solution for injection in pre-filled pen

One mL of solution contains 50 mg of somatrogon*.
Each pre-filled pen contains 60 mg somatrogon in 1.2 mL solution.
Each pre-filled pen delivers doses from 0.5 mg to 30 mg in a single injection in 0.5 mg increments.

*Produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

The solution is a clear and colourless to slightly light yellow solution with a pH of 6.6.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ngenla is indicated for the treatment of children and adolescents from 3 years of age with growth disturbance due to insufficient secretion of growth hormone.

4.2 Posology and method of administration

Treatment should be initiated and monitored by physicians who are qualified and experienced in the diagnosis and management of paediatric patients with growth hormone deficiency (GHD).

Posology

The recommended dose is 0.66 mg/kg body weight administered once weekly by subcutaneous injection.

Each pre-filled pen is capable of setting and delivering the dose prescribed by the physician. Dose may be rounded up or down based on the physician's expert knowledge of the individual patient needs. When doses higher than 30 mg are needed (i.e. bodyweight > 45 kg), two injections have to be administered.

Starting dose for patients switching from daily growth hormone medicinal products
For patients switching from daily growth hormone medicinal products, the weekly therapy with somatrogon may be initiated at a dose of 0.66 mg/kg/week on the day following their last daily injection.

Dose titration
Somatrogon dose may be adjusted as necessary, based on growth velocity, adverse reactions, body weight and serum insulin-like growth factor 1 (IGF-1) concentrations.

When monitoring for IGF-1, samples should always be drawn 4 days after the prior dose. Dose adjustments should be targeted to achieve average IGF-1 standard deviation score (SDS) levels in the normal range, i.e. between -2 and +2 (preferably close to 0 SDS).

In patients whose serum IGF-1 concentrations exceed the mean reference value for their age and sex by more than 2 SDS, the dose of somatrogon should be reduced by 15%. More than one dose reduction may be required in some patients.

Treatment evaluation and discontinuation
Evaluation of efficacy and safety should be considered at approximately 6 to 12 month intervals and may be assessed by evaluating auxological parameters, biochemistry (IGF-1, hormones, glucose levels) and pubertal status. Routine monitoring of serum IGF-1 SDS levels throughout the course of treatment is recommended. More frequent evaluations should be considered during puberty.

Treatment should be discontinued when there is evidence of closure of the epiphyseal growth plates (see section 4.3). Treatment should also be discontinued in patients having achieved final height or near final height, i.e. an annualised height velocity < 2 cm/year or a bone age > 14 years in girls or > 16 years in boys.

Missed dose
Patients should maintain their regular dosing day. If a dose is missed, somatrogon should be administered as soon as possible within 3 days after the missed dose, and then the usual once weekly dosing schedule should be resumed. If more than 3 days have passed, the missed dose should be skipped and the next dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

Changing the dosing day
The day of weekly administration can be changed if necessary as long as the time between two doses is at least 3 days. After selecting a new dosing day, the once weekly dosing should be continued.

Special populations

Elderly
The safety and efficacy of somatrogon in patients over the age of 65 years have not been established. No data are available.

Renal impairment
Somatrogon has not been studied in patients with renal impairment. No dose recommendation can be made.

Hepatic impairment
Somatrogon has not been studied in patients with hepatic impairment. No dose recommendation can be made.

Paediatric population
The safety and efficacy of somatrogon in neonates, infants and children less than 3 years of age have not yet been established. No data are available.

Method of administration

Somatrogon is administered by subcutaneous injection.

Somatrogon is to be injected in the abdomen, thighs, buttocks or upper arms. The site of injection should be rotated at each administration to prevent lipoatrophy (see section 4.8). Injections to the upper arms and buttocks should be given by the caregiver.

The patient and caregiver should receive training to ensure understanding of the administration procedure to support self-administration.

If more than one injection is required to deliver a complete dose, each injection should be administered at a different injection site to prevent lipoatrophy.

Somatrogon is to be administered once weekly, on the same day each week, at any time of the day.

Ngenla 24 mg solution for injection in pre-filled pen
The pre-filled pen delivers doses from 0.2 mg to 12 mg of somatrogon in increments of 0.2 mg (0.01 mL).

Ngenla 60 mg solution for injection in pre-filled pen
The pre-filled pen delivers doses from 0.5 mg to 30 mg of somatrogon in increments of 0.5 mg (0.01 mL).

For instructions on the medicinal product before administration, see section 6.6 and at the end of the package leaflet.

4.3 Contraindications

Hypersensitivity to somatrogon (see section 4.4) or to any of the excipients listed in section 6.1.

Somatrogon must not be used when there is any evidence of activity of a tumour based on experience with daily growth hormone medicinal products. 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 (see section 4.4).

Somatrogon must not be used for 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 must not be treated with somatrogon (regarding patients undergoing substitution therapy, see section 4.4).

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.

Hypersensitivity

Serious systemic hypersensitivity reactions (e.g. anaphylaxis, angioedema) have been reported with daily growth hormone medicinal products. If a serious hypersensitivity reaction occurs, use of somatrogon should be immediately discontinued; patients should be treated promptly per standard of care and monitored until signs and symptoms resolve (see section 4.3).

Hypoadrenalism

Based on published data patients receiving daily growth hormone therapy who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of somatrogon treatment (see section 4.5). Patients should be monitored for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism (see section 4.5).

Thyroid function impairment

Growth hormone increases the extrathyroidal conversion of T4 to T3 and may unmask incipient hypothyroidism. Patients with pre-existing hypothyroidism should be treated accordingly prior to the initiation of treatment with somatrogon as indicated based on clinical evaluation. As hypothyroidism interferes with the response to growth hormone therapy, patients should have their thyroid function tested regularly and should receive replacement therapy with thyroid hormone when indicated (see sections 4.5 and 4.8).

Prader-Willi syndrome

Somatrogon has not been studied in patients with Prader-Willi syndrome. Somatrogon is not indicated for the long-term treatment of paediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome unless they also have a diagnosis of GHD. There have been reports of sudden death after initiating therapy with growth hormone in paediatric 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.

Glucose metabolism impairment

Treatment with growth hormone medicinal products may reduce insulin sensitivity and induce hyperglycaemia. Additional monitoring should be considered in patients treated with somatrogon who have glucose intolerance, or additional risk factors for diabetes. In patients treated with somatrogon who have diabetes mellitus, hypoglycaemic medicinal products might require adjustment (see section 4.5).

Neoplasm

In patients with previous malignant disease, special attention should be given to signs and symptoms of relapse. Patients with pre-existing tumours or growth hormone deficiency secondary to an intracranial lesion should be examined routinely for progression or recurrence of the underlying

disease process. In childhood cancer survivors, an increased risk of a second neoplasm has been reported in patients treated with somatropin after their first neoplasm. Intracranial tumours, in particular meningiomas, in patients treated with radiation to the head for their first neoplasm, were the most common of these second neoplasms.

Benign intracranial hypertension

Intracranial hypertension (IH) with papilledema, ataxia, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with growth hormone medicinal products. Funduscopic examination is recommended at the initiation of treatment and as clinically warranted. In patients with clinical or funduscopic evidence of IH, somatrogon should be temporarily discontinued. At present there is insufficient evidence to give specific advice on the continuation of growth hormone treatment in patients with resolved IH. If treatment with somatrogon is restarted, monitoring for signs and symptoms of IH is necessary.

Acute critical illness

In critically ill adult patients suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma or acute respiratory failure mortality was higher in patients treated with 5.3 mg or 8 mg somatropin daily (i.e. 37.1 – 56 mg/week) compared to patients receiving placebo, 42% vs. 19%. Based on this information, these types of patients should not be treated with somatrogon. As there is no information available on the safety of growth hormone substitution therapy in acutely critically ill patients, the benefits of continued somatrogon treatment in this situation should be weighed against the potential risks involved. In all patients developing other or similar acute critical illness, the possible benefit of treatment with somatrogon must be weighed against the potential risk involved.

Pancreatitis

Although rare in patients treated with growth hormone medicinal products, pancreatitis should be considered in somatrogon-treated patients who develop severe abdominal pain during treatment.

Scoliosis

Because somatrogon increases growth rate, signs of development or progression of scoliosis should be monitored during treatment.

Epiphyseal disorders

Epiphyseal disorders, including slipped capital femoral epiphysis may occur more frequently in patients with endocrine disorders or in patients undergoing rapid growth. Post-marketing cases of epiphysiolysis associated with somatrogon use have been reported (see section 4.8). Any paediatric patient with the onset of a limp or complaints of hip or knee pain during treatment should be carefully evaluated.

Oral oestrogen therapy

Oral oestrogen influences the IGF-1 response to growth hormone. If a female patient taking somatrogon begins or discontinues oral oestrogen-containing therapy, IGF-1 value should be monitored to determine if the dose of growth hormone should be adjusted to maintain the serum IGF-1 levels within the normal range (see section 4.2). In female patients on oral oestrogen-containing therapy, a higher dose of somatrogon may be required to achieve the treatment goal (see section 4.5).

Excipients

Sodium content
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium free.'

Metacresol
Myositis is a very rare adverse event that may be related to the preservative metacresol. In the case of myalgia or disproportionate pain at injection site, myositis should be considered and if confirmed, other growth hormone medicinal products without metacresol should be used.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions studies in paediatrics have been performed.

Glucocorticoids

Concomitant treatment with glucocorticoids may inhibit the growth-promoting effects of somatrogon. Patients with adrenocorticotropic hormone (ACTH) deficiency should have their glucocorticoid replacement therapy carefully adjusted to avoid any inhibitory effect on growth. Therefore, patients treated with glucocorticoids should have their growth monitored carefully to assess the potential impact of glucocorticoid treatment 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).

Insulin and hypoglycaemic medicinal products

In patients with diabetes mellitus requiring medicinal product therapy, the dose of insulin and/or oral/injectable hypoglycaemic medicinal products may require adjustment when somatrogon therapy is initiated (see section 4.4).

Thyroid medicinal products

Treatment with daily growth hormone may unmask previously undiagnosed or subclinical central hypothyroidism. Thyroxine replacement therapy may need to be initiated or adjusted (see section 4.4).

Oral oestrogen therapy

In female patients on oral oestrogen-containing therapy, a higher dose of somatrogon may be required to achieve the treatment goal (see section 4.4).

Cytochrome P450 metabolised products

Drug-drug interaction studies have not been performed with somatrogon. Somatrogon has been shown to induce CYP3A4 mRNA expression *in vitro*. The clinical significance of this is unknown. Studies with other human growth hormone (hGH) receptor agonists performed in growth hormone deficient children and adults, and healthy elderly men, suggest that administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes, especially CYP3A. The clearance of compounds metabolised by CYP3A4 (e.g. sex steroids, corticosteroids, anticonvulsants and ciclosporin) may be increased and could result in lower exposure of these compounds.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of somatrogon in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Ngenla is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is unknown whether somatrogon/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from somatrogon therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

The risk of infertility in females or males of reproductive potential has not been studied in humans. In a rat study, the fertility in males and females was not affected (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The commonly reported adverse reactions after treatment with somatrogon are injection site reactions (ISRs) (25.1%), headache (10.7%) and pyrexia (10.2%).

Tabulated list of adverse reactions

Safety data are derived from the phase 2, multi-centre safety and dose-finding study, and the pivotal phase 3, multi-centre non-inferiority study in paediatric patients with GHD (see section 5.1). The data reflect exposure of 265 patients to somatrogon administered once weekly (0.66 mg/kg/week).

Table 1 presents the adverse reactions reported in clinical studies and post-marketing data for somatrogon within the system organ class (SOC). The adverse reactions listed in the table below are presented by SOC and frequency categories, defined using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) or frequency not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 1. Adverse reactions

System organ class	Very common	Common	Uncommon	Rare	Very rare	Frequency not known
Blood and lymphatic system disorders		Anaemia Eosinophilia				
Endocrine disorders		Hypothyroidism	Adrenal insufficiency			
Nervous system disorders	Headache					

System organ class	Very common	Common	Uncommon	Rare	Very rare	Frequency not known
Eye disorders		Conjunctivitis allergic				
Skin and subcutaneous tissue disorders			Rash generalised			Lipoatrophy*,†
Musculoskeletal and connective tissue disorders		Arthralgia Pain in extremity				Epiphysiolysis (including slipped capital femoral epiphysis)*
General disorders and administration site conditions	Injection site reactions[a] Pyrexia					

* Adverse Drug Reaction identified post-marketing.
† See section 4.2.
a Injection site reactions include the following: injection site pain, erythema, pruritus, swelling, induration, bruising, haemorrhage, warmth, hypertrophy, inflammation, deformation, urticaria.

Description of selected adverse reactions

Injection site reaction
In the phase 3 clinical study, reporting of ISRs was actively solicited during the course of the study. In the majority of cases, local ISRs tended to be transient, occurred mainly in the first 6 months of treatment and were mild in severity; ISRs had a mean onset on the day of the injection and a mean duration of < 1 day. Among them, injection site pain, erythema, pruritus, swelling, induration, bruising, hypertrophy, inflammation and warmth were reported in 43.1% of patients treated with somatrogon compared to 25.2% of patients administered daily injections of somatropin.

In the long-term OLE of the clinical phase 3 study, local ISRs were similar in nature and severity, and reported early in subjects switching from somatropin to somatrogon treatment. ISRs were reported in 18.3% of patients originally treated with somatrogon in the main study and continuing treatment in the OLE portion of the study, and likewise, 37% were reported among patients originally treated with somatropin that were switched in the OLE portion of the study to treatment with somatrogon.

Immunogenicity
In the pivotal safety and efficacy study, among 109 subjects treated with somatrogon, 84 (77.1%) tested positive for anti-drug antibodies (ADAs). There were no clinical or safety effects observed with the formation of antibodies.

Other adverse drug reactions for somatropin may be considered class effects, such as:
- Neoplasms benign and malignant: (see section 4.4).
- Metabolism and nutrition disorders: diabetes mellitus type 2 (see section 4.4).
- Nervous system disorders: benign intracranial hypertension (see section 4.4), paraesthesia.
- Musculoskeletal, connective tissue, and bone disorders: myalgia.
- Reproductive system and breast disorders: gynaecomastia.
- Skin and subcutaneous tissue disorders: skin rash, urticaria and pruritus.
- General disorders and administration site conditions: peripheral oedema, facial oedema.
- Gastrointestinal disorders: pancreatitis (see section 4.4).

Metacresol
This medicinal product contains metacresol which may contribute to painful injections (see section 4.4).

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

Single doses of somatrogon higher than 0.66 mg/kg/week have not been studied.

Based on experience with daily growth hormone medicinal products, short-term overdose could lead initially to hypoglycaemia and subsequently to hyperglycaemia. Long-term overdose could result in signs and symptoms of gigantism and/or acromegaly consistent with the effects of growth hormone excess.

Treatment of overdose with somatrogon should consist of general supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pituitary and hypothalamic hormones and analogues, somatropin and somatropin agonists, ATC code: H01AC08.

Mechanism of action

Somatrogon is a glycoprotein comprised of the amino acid sequence of hGH with one copy of the of C-terminal peptide (CTP) from the beta chain of human chorionic gonadotropin (hCG) at the N-terminus and two copies of CTP (in tandem) at the C-terminus. The glycosylation and CTP domains account for the half-life of somatrogon, which allows for weekly dosing.

Somatrogon binds to the GH receptor and initiates a signal transduction cascade culminating in changes in growth and metabolism. Consistent with GH signalling, somatrogon binding leads to activation of the STAT5b signalling pathway and increases the serum concentration of IGF-1. IGF-1 was found to increase in a dose-dependent manner during treatment with somatrogon partially mediating the clinical effect. As a result, GH and IGF-1 stimulate metabolic changes, linear growth and enhance growth velocity in paediatric patients with GHD.

Pharmacodynamic effects

In clinical studies, somatrogon increases IGF-1. Pharmacodynamic evaluations performed approximately 96 hours after dose administration in order to assess the mean IGF-1 standard deviation score (SDS) over the dosing interval showed IGF-1 values normalised in treated subjects at one month of treatment.

Water and mineral metabolism
Somatrogon induces the retention of phosphorus.

Clinical efficacy and safety

The safety and efficacy of somatrogon for the treatment of children and adolescents from 3 years of age with GHD were evaluated in two multi-centre randomised, open-label controlled clinical studies.

Both studies included a 12-month main study period that compared once weekly somatrogon to somatropin administered once daily followed by a single arm OLE period during which all patients were administered somatrogon once weekly. The primary efficacy endpoint for both studies was annualised height velocity (HV) following 12 months of treatment. Other endpoints reflective of catch-up growth such as change in height SDS from baseline and height SDS were also evaluated in both studies.

The pivotal phase 3 multi-centre non-inferiority study evaluated the safety and efficacy of 0.66 mg/kg/week dose of somatrogon compared to 0.034 mg/kg/day of somatropin in 224 pre-pubertal paediatric patients with GHD. The mean age across the treatment groups was 7.7 years (min 3.01, max 11.96), 40.2% of patients were > 3 years to ≤ 7 years, 59.8% were > 7 years. 71.9% of patients were male and 28.1% were female. In this study, 74.6% of patients were White, 20.1% were Asian; 0.9% were Black. Baseline disease characteristics were balanced across both treatment groups. Approximately 68% of patients had peak plasma GH levels of ≤ 7 ng/mL, and the mean height was below -2 SDS.

Once weekly somatrogon was non-inferior based on HV at 12 months compared to somatropin administered once daily (see Table 2). Once weekly somatrogon also produced an increase in IGF-1 SDS values, from a mean of -1.95 at baseline to a mean of 0.65 at 12 months.

Table 2. Efficacy of somatrogon compared to somatropin in paediatric patients with GHD at month 12

Treatment parameter	Treatment group		LSM difference (95% CI)
	Somatrogon (N=109)	Somatropin (N=115)	
	LSM estimate	LSM estimate	
Height velocity (cm/yr)	10.10	9.78	0.33 (-0.24, 0.89)
Height standard deviation score	-1.94	-1.99	0.05 (-0.06, 0.16)
Change in height standard deviation score from baseline	0.92	0.87	0.05 (-0.06, 0.16)

Abbreviations: CI=confidence interval; GHD=growth hormone deficiency; LSM=least square mean; N=number of patients randomised and treated.

In the open-label extension of the pivotal phase 3 study, 91 patients received 0.66 mg/kg/week of somatrogon for at least 2 years and provided height data. A progressive gain in height SDS from baseline was observed at 2 years [cumulative change in height SDS mean (SD) = 1.38 (0.78), median = 1.19 (range: 0.2, 4.9)].

In the phase 2, multi-centre safety and dose-finding study, 31 patients received up to 0.66 mg/kg/week of somatrogon for up to 7.7 years. At the last assessment, height SDS [mean (SD)] was -0.39 (0.95) and cumulative change in height SDS [mean (SD)] from baseline was 3.37 (1.27).

Treatment burden
In a phase 3 randomised, open-label, crossover study in 87 paediatric patients with GHD, the impact of somatrogon administered once weekly (0.66 mg/kg/week) on treatment burden was compared to daily somatropin. Somatrogon administered once weekly demonstrated significant improvement (reduction) in treatment burden for the patient, improved (reduced) treatment burden for the caregiver, greater patient convenience, greater intent to comply and greater patient preference.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Ngenla in all subsets of the paediatric population for the long-term treatment of paediatric patients with growth disturbance due to insufficient secretion of growth hormone (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Somatrogon pharmacokinetics (PK) was assessed using a population PK approach for somatrogon in 42 paediatric patients (age range 3-15.5 years) with GHD.

Absorption

Following subcutaneous injection, serum concentrations increased slowly, peaking 6 to 18 hours after dosing.

In paediatric patients with GHD, somatrogon exposure increases in a dose-proportional manner for doses of 0.25 mg/kg/week, 0.48 mg/kg/week and 0.66 mg/kg/week. There is no accumulation of somatrogon after once weekly administration. In paediatric patients with GHD, the population PK estimated steady-state peak concentrations following 0.66 mg/kg/week was 636 ng/mL. Patients who tested positive for ADA had an approximately 45% higher steady-state average concentration.

Distribution

In paediatric patients with GHD, the population PK estimated apparent central volume of distribution was 0.728 L/kg and apparent peripheral volume of distribution was 0.165 L/kg.

Biotransformation

The metabolic fate of somatrogon is believed to be classical protein catabolism, with subsequent reclamation of the amino acids and return to the systemic circulation.

Elimination

In paediatric patients with GHD, the population PK estimated apparent clearance was 0.0317 L/h/kg. Patients who tested positive for ADA had an approximately 25.8% decrease in apparent clearance. With a population PK estimated effective half-life of 28.2 hours, somatrogon will be present in the circulation for about 6 days after the last dose.

Special populations

Age, race, gender, body weight
Based on population PK analyses, age, sex, race and ethnicity do not have a clinically meaningful effect on the pharmacokinetics of somatrogon in paediatric patients with GHD. The exposure of somatrogon decreases with an increase in body weight. However, the somatrogon dose of 0.66 mg/kg/week provides adequate systemic exposure to safely achieve efficacy over the weight range evaluated in the clinical studies.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeat-dose toxicity.

Reproductive and developmental toxicity studies were conducted in rats with somatrogon administered subcutaneously at doses up to 30 mg/kg (associated with exposures levels approximately 14 times the maximum recommended human dose based on AUC).

Somatrogon induced an increase in oestrous cycle length, copulatory interval, and number of corpora lutea in female rats but no effects on mating indices, fertility or early embryonic development.

No effects of somatrogon were observed on embryo-foetal development.

In a pre-postnatal development study somatrogon elicited an increase in first generation (F1) mean body weights (both sexes) as well as an increase in the mean copulatory interval in F1 females at the highest dose (30 mg/kg), which was consistent with a longer oestrous cycle length; however, there were no associated effects on mating indices.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trisodium citrate dihydrate
Citric acid monohydrate
L-Histidine
Sodium chloride
m-Cresol
Poloxamer 188
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

Before first use

3 years at 2 °C to 8 °C.

Prior to the first use store Ngenla in a refrigerator. The unopened pre-filled pen may temporarily be held for up to 4 hours at temperatures up to 32 °C.

After first use

28 days.
Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Keep Ngenla with the pen cap attached in order to protect from light.

Ngenla may be held at room temperature (up to 32 °C) for up to 4 hours with each injection for a maximum of 5 times. Return Ngenla to the refrigerator again after each use. Do not expose Ngenla to temperatures above 32 °C or leave at room temperature for more than 4 hours with each use. The Ngenla pen should be discarded if it has been used 5 times, if it has been exposed to temperatures higher than 32 °C or if it has been removed from the refrigerator for more than 4 hours with each use.

Chemical and physical in-use stability has been demonstrated for 28 days from the date of first use of the pre-filled pen, when the pre-filled pen has been stored at 2 °C to 8 °C in between each use.

6.4 Special precautions for storage

Store in a refrigerator (2 °C to 8 °C). Do not freeze. Keep Ngenla in the outer carton in order to protect from light.

For storage conditions after first use of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Ngenla 24 mg solution for injection in pre-filled pen

This multi-dose disposable pre-filled pen, which consists of a cartridge (Type I clear glass) permanently sealed in a plastic pen, contains 1.2 mL of somatrogon. 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 rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The pen cap, dose button and label on the pen are coloured lilac.

Pack size of 1 pre-filled pen.

Ngenla 60 mg solution for injection in pre-filled pen

This multi-dose disposable pre-filled pen, which consists of a cartridge (Type I clear glass) permanently sealed in a plastic pen, contains 1.2 mL of somatrogon. 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 rubber stopper (Type I rubber closures) shaped as a disc and sealed with an aluminium cap. The pen cap, dose button and label on the pen are coloured blue.

Pack size of 1 pre-filled pen.

6.6 Special precautions for disposal and other handling

The solution should appear clear and colourless to slightly light yellow solution and be free of particles. Do not inject the medicinal product if it is cloudy, dark yellow, or contains particulate matter. Do not shake, shaking can damage the medicinal product.

Each Ngenla pre-filled pen is for use by a single patient. A Ngenla pre-filled pen must never be shared between patients, even if the needle is changed.

The pre-filled pen should only be used up to 28 days after first use and before the expiry date.

Do not freeze the medicinal product. Do not expose to heat (above 32 °C). Do not use Ngenla if it has been frozen or exposed to heat, discard.

Dose preparation

The pen may be used straight from the refrigerator. For a more comfortable injection, the pre-filled pen containing the sterile solution of somatrogon may be allowed to reach room temperature up to 32 °C for up to 30 minutes. The solution in the pen should be inspected for flakes, particles and colouration. The pen should not be shaken. If flakes, particles or discolouration are observed, the pen should not be used.

Administration

The designated injection site should be prepared as instructed in the Instructions for Use. It is recommended to rotate the injection site at each administration. When in use, always replace the pen cap on the pre-filled pen after each injection. Return Ngenla to the refrigerator again after each use. A new needle must always be attached before use. Needles must not be re-used. The injection needle should be removed after each injection and the pen should be stored without a needle attached. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.

In the event of blocked needles (i.e. liquid does not appear at the needle tip), patients must follow the instructions described in the Instructions for Use accompanying the package leaflet.

Sterile needles are required for administration but are not included. Ngenla can be administered with a needle from 4 mm to 8 mm and between 30G and 32G.

Instructions for the preparation and administration of the product are given in the package leaflet and Instructions For Use.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. If the pre-filled pen is empty, has been exposed to temperatures higher than 32 °C, has been removed from the refrigerator for more than 4 hours with each use, has been used 5 times, or it has been more than 28 days after first use, it should be disposed of even if it contains unused medicinal product. A small amount of the sterile somatrogon solution may remain in the pen after all doses have been correctly given. Patients should be instructed not to use the remaining solution, but to properly discard the pen.

7. MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1617/001
EU/1/21/1617/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 February 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Pfizer Ireland Pharmaceuticals Unlimited Company
Grange Castle Business Park
Nangor Road
Dublin 22
D22 V8F8
Ireland

Name and address of the manufacturer responsible for batch release

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Ngenla 24 mg solution for injection in pre-filled pen
somatrogon

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One mL of solution contains 20 mg of somatrogon. Each pre-filled pen contains 24 mg of somatrogon in 1.2 mL of solution.

3. LIST OF EXCIPIENTS

Trisodium citrate dihydrate
Citric acid monohydrate
L-Histidine
Sodium chloride
Poloxamer 188
m-Cresol
Water for injections

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled pen
1.2 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Once weekly
For subcutaneous use
Read the package leaflet before use.

Pull to open

Tuck in flap to close

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

Discard the pen 28 days after first use, even if it contains unused medicine.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep Ngenla in the outer carton in order to protect from light.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1617/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Ngenla 24 mg

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

PRE-FILLED PEN LABEL

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

Ngenla 24 mg solution for injection in pre-filled pen
somatrogon
Subcutaneous use

2. METHOD OF ADMINISTRATION

Once weekly

3. EXPIRY DATE

EXP
Date of first use
Discard 28 days after first use

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.2 mL

6. OTHER

Store in a refrigerator.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Ngenla 60 mg solution for injection in pre-filled pen
somatrogon

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One mL of solution contains 50 mg of somatrogon. Each pre-filled pen contains 60 mg of somatrogon in 1.2 mL of solution.

3. LIST OF EXCIPIENTS

Trisodium citrate dihydrate
Citric acid monohydrate
L-Histidine
Sodium chloride
Poloxamer 188
m-Cresol
Water for injections

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled pen
1.2 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Once weekly
For subcutaneous use
Read the package leaflet before use.

Pull to open

Tuck in flap to close

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

Discard the pen 28 days after first use, even if it contains unused medicine.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep Ngenla in the outer carton in order to protect from light.

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

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1617/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Ngenla 60 mg

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

PRE-FILLED PEN LABEL

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

Ngenla 60 mg solution for injection in pre-filled pen
somatrogon
Subcutaneous use

2. METHOD OF ADMINISTRATION

Once weekly

3. EXPIRY DATE

EXP
Date of first use
Discard 28 days after first use

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.2 mL

6. OTHER

Store in a refrigerator.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Ngenla 24 mg solution for injection in pre-filled pen
somatrogon

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, pharmacist or nurse.
- This medicine has been prescribed for you or the child in your care only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours or those of the child in your care.
- If you or the child in your care get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ngenla is and what it is used for
2. What you need to know before you use Ngenla
3. How to use Ngenla
4. Possible side effects
5. How to store Ngenla
6. Contents of the pack and other information

1. What Ngenla is and what it is used for

Ngenla contains the active substance somatrogon, a modified form of human growth hormone. Natural human growth hormone is needed for bones and muscles to grow. It also helps your fat and muscle tissues to develop in the right amounts. Ngenla is used to treat children and adolescents from 3 years of age who do not have enough growth hormone and are not growing at the normal rate.

The active substance in Ngenla is made by 'recombinant DNA technology'. This means that it is grown in cells that have been modified in the laboratory so that they can produce it.

2. What you need to know before you use Ngenla

Do not use Ngenla
- If you or the child in your care are allergic to somatrogon (see Warnings and precautions) or any of the other ingredients of this medicine (listed in section 6).
- If you or the child in your care have an active tumour (cancer). Tell your doctor if you or the child in your care have or have had an active tumour. Tumours must be inactive, and you or the child in your care must have finished your anti-tumour treatment before starting treatment with Ngenla.
- If you or the child in your care have stopped growing because of closure of the growth plates (closed epiphyses) meaning that you or the child in your care have been told by your doctor that your bones have stopped growing.
- If you or the child in your care are seriously ill (for example, complications following open heart surgery, abdominal surgery, acute respiratory failure, multiple accidental trauma or similar conditions). If you or the child in your care are about to have, or have had, a major operation, or

go into hospital for any reason, tell your doctor and remind the other doctors you are seeing that you use growth hormone.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Ngenla:
- If you or the child in your care develop a serious allergic reaction, stop using Ngenla, talk to your doctor right away. Sometimes serious allergic reactions such as hypersensitivity, including anaphylaxis or angioedema (difficulties breathing or swallowing, or swelling of the face, lips, throat or tongue) have occurred. If you or the child in your care have any of the following symptoms of a serious allergic reaction:
    - breathing problems
    - swelling of your face, mouth, and tongue
    - hives (nettle rash, lumps rising under the skin)
    - rash
    - fever
- If you or the child in your care have replacement therapy with corticosteroid medicines (glucocorticoids) you or the child in your care should consult your doctor regularly as you or the child in your care may need adjustment of your glucocorticoid dose.
- Your doctor should check at intervals how well the thyroid gland is working in you or the child in your care and if necessary may prescribe treatment or adjust the dose of existing treatment as this may be needed for Ngenla to work properly.
- If you or the child in your care have Prader-Willi syndrome, you or the child should not be treated with Ngenla unless you or the child in your care has growth hormone deficiency.
- Your doctor should monitor you or the child in your care for high blood sugar levels (hyperglycaemia) during treatment with Ngenla. If you or the child in your care are treated with insulin or other diabetes medicines, your doctor may need to adjust the insulin dose. If you or the child in your care have diabetes and associated severe/worsening eye disease you or the child in your care should not be treated with Ngenla.
- If you or the child in your care have ever had any kind of tumour (cancer).
- If you or the child in your care experience changes in vision, severe or frequent headaches, associated with feeling sick (nausea), vomiting, or experience lack of muscle control or coordination of voluntary movements, such as walking or picking up objects, difficulty with speech, eye movement or swallowing, especially at the start of treatment, tell your doctor immediately. These could be signs of a temporary increase in pressure within the brain (intracranial hypertension).
- If you or the child in your care are seriously ill (for example, complications following open heart surgery, abdominal surgery, acute respiratory failure, multiple accidental trauma or similar conditions). If you or the child in your care are about to have, or have had, a major operation, or go into hospital for any reason, tell your doctor and remind the other doctors you are seeing that you or the child in your care use growth hormone.
- If you or the child in your care develop a severe stomach ache during treatment with Ngenla as this could be a symptom of inflammation of the pancreas.
- If you or the child in your care notice a sideways curvature in your spine (scoliosis), you or the child in your care will need to be checked often by your doctor.
- If during growing you or the child in your care develop a limp or hip or knee pain, you or the child in your care should consult your doctor right away. These could be symptoms of bone disorders in your hip as this may happen during periods of rapid growth.
- If you or the child in your care are taking or stop taking oral contraception or hormonal replacement therapy with oestrogen, your doctor may recommend the dose of Ngenla to be adjusted.

Other medicines and Ngenla
Tell your doctor, pharmacist or nurse if you or the child in your care are using, have recently used or might use any other medicines.
- If you or the child in your care take replacement therapy with corticosteroid medicines (glucocorticoids), as these may reduce the effect of Ngenla on growth. You or the child in your

care should consult your doctor regularly, as you or the child in your care may need adjustment of your glucocorticoid dose.
- If you or the child in your care are treated with insulin or other diabetes medicines, you should consult with your doctor as you or your doctor may need to adjust the dose.
- If you or the child in your care are receiving treatment with thyroid hormones, your doctor may need to adjust the dose.
- If you or the child in your care are receiving oestrogen taken orally, you should consult your doctor as you or the child may need to adjust your dose of Ngenla.
- If you or the child in your care are receiving ciclosporin (a medicine that weakens the immune system after transplantation), you should consult your doctor as your doctor may need to adjust the dose.
- If you or the child in your care are receiving medicines to control epilepsy (anticonvulsants), you should consult your doctor as your doctor may need to adjust the dose.

Pregnancy and breast-feeding
If you or the child in your care are pregnant or breast-feeding, think you or the child in your care may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Ngenla has not been tested in pregnant women and it is not known if this medicine can harm your unborn baby. It is therefore preferable to avoid Ngenla during pregnancy. If you are able to get pregnant, you should not use Ngenla unless you are also using reliable contraception.

It is not known whether somatrogon can pass into breast milk. Tell your doctor or the doctor of the child in your care, if you or the child in your care are breast-feeding or plan to do so. Your doctor will then help you or the child in your care decide whether to stop breast-feeding, or whether to stop taking Ngenla, considering the benefit of breast-feeding to the baby and the benefit of Ngenla to you or the child in your care.

Driving and using machines
Ngenla does not affect the ability to drive and use machines.

Ngenla contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

Ngenla contains metacresol
Ngenla contains a preservative called metacresol. In very rare cases the presence of metacresol can cause inflammation (swelling) in muscles. If you or the child in your care experience muscle pain or pain at the injection site, inform your doctor.

3. How to use Ngenla

This medicine will only be prescribed by a doctor who has experience with growth hormone treatment and who has confirmed your diagnosis or that of the child in your care.

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

The dose of Ngenla to be injected will be decided by your doctor.

How much to use
Your doctor will work out your dose of Ngenla from your body weight in kilograms. The recommended dose is 0.66 mg per kg body weight and is given once weekly. If you or the child in

your care have been previously treated with daily growth hormone injections, your doctor will tell you to wait before taking the first dose of Ngenla until the day after your last daily injection and then continue with Ngenla once each week.

Do not change your dose unless your doctor has told you to.

How Ngenla is given
- Ngenla is available as a pre-filled pen in 2 different sizes (Ngenla 24 mg and Ngenla 60 mg). Based on the recommended dose your doctor or the doctor of the child in your care will prescribe the most appropriate pen size (see section 6 “Contents of the pack and other information”).
- Before you or the child in your care use the pen for the first time, your/their doctor or nurse will show you how to use it. Ngenla is given as an injection under the skin (subcutaneous injection) using a pre-filled pen. Do not inject it into a vein or muscle.
- The best place to give Ngenla is in the abdomen (belly), thighs, buttocks or upper arms. Injections to the upper arms and buttocks should be given by the caregiver.
- Fatty tissue below the skin can shrink at the site of injection (see section 4). To avoid this, use a different injection site each time.
- If more than one injection is required to deliver a complete dose, each should be administered at a different injection site.

Detailed instructions for use of the pre-filled pen are at the end of this leaflet.

When to use Ngenla
You or the child in your care should use this medicine once a week on the same day each week.

You or the child in your care should record which day of the week you use Ngenla to help you or the child in your care remember to inject this medicine once a week.

If necessary you or the child in your care can change the day of your/their weekly injection as long as it has been at least 3 days since you or the child in your care had your/their last injection. After selecting a new dosing day, continue giving yourself or the child in your care the injection on that day each week.

If you use more Ngenla than you should
If you or the child in your care have injected more Ngenla than you should have been given, contact your doctor straight away as your/their blood sugar levels may need to be checked.

If you forget to use Ngenla
If you or the child in your care forgot to inject a dose and:
- It is 3 days or less since you or the child in your care should have used Ngenla, use it as soon as you remember. Then inject your/their next dose on your/their usual injection day.
- It is more than 3 days since you or the child in your care should have used Ngenla, skip the missed dose. Then inject your/their next dose as usual on your/their next scheduled day. A regular dosing day should be maintained.

Do not use a double dose to make up for a forgotten dose.

If you stop using Ngenla
Do not stop using this medicine without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common: may affect more than 1 in 10 people
- Headache
- Bleeding, inflammation, itching, pain, redness, soreness, stinging, tenderness, or warmth at the injection site (injection site reactions)
- Fever (pyrexia)

Common: may affect up to 1 in 10 people
- Decrease in the number of red blood cells in the blood (anaemia)
- Increase in the number of eosinophils in the blood (eosinophilia)
- Decrease in the blood level of thyroid hormone (hypothyroidism)
- Allergic inflammation of the conjunctiva, the clear layer over the outside of the eye (allergic conjunctivitis)
- Joint pain (arthralgia)
- Pain in arms or legs

Uncommon: may affect up to 1 in 100 people
- The adrenal glands do not make enough steroid hormones (adrenal insufficiency)
- Rash

Not known: frequency cannot be estimated from the available data
- Localised loss of fat below the skin (lipoatrophy)
- Problems with hip joint which may cause hip or knee pain or limp (epiphysiolysis, including slipped capital femoral epiphysis)

Other possible side effects not seen with Ngenla but which have been reported in other growth hormone medicines treatment may include the following:
- Tissue growth (non cancerous or cancer)
- Type 2 diabetes
- Increased intracranial pressure (which causes symptoms such as strong headache, visual disturbances or vomiting)
- Numbness or tingling
- Joint or muscle pain
- Breast enlargement in boys and men
- Skin rash, reddening and itching
- Water retention (which shows as puffy fingers or swollen ankles)
- Facial swelling
- Pancreatitis (which causes symptoms of stomach pain, nausea, vomiting or diarrhoea)

In very rare cases the presence of metacresol can cause inflammation (swelling) in muscles. If you or the child in your care experience muscle pain or pain at the injection site, inform your doctor.

Reporting of side effects
If you or the child in your care get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via 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 Ngenla

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 pen label and on the carton after 'EXP'. The expiry date refers to the last day of that month.

The pre-filled pen should not be used more than 28 days after first use.

Before first use of Ngenla
- Store in a refrigerator (2 °C - 8 °C).
- Keep Ngenla in the outer carton in order to protect from light.
- Remove Ngenla from the refrigerator prior to use. Ngenla may be held at room temperature (up to 32 °C) for up to 4 hours.
- Do not use this medicine if you notice that the solution is cloudy or dark yellow. Do not use the medicine if it has flakes or particles.
- Do not shake the pen. Shaking can damage the medicine.

After first use of Ngenla
- Use within 28 days after first use. Store in a refrigerator (2 °C - 8 °C). Do not freeze.
- Keep Ngenla with the pen cap on in order to protect from light.
- Do not store the pre-filled pen with a needle attached.
- Discard the pen after last dose, even if it contains unused medicine.
- Ngenla may be held at room temperature (up to 32 °C) for up to 4 hours with each injection for a maximum of 5 times. Return Ngenla to the refrigerator again after each use.
- Do not leave at room temperature for more than 4 hours with each use.
- Do not put the pen anywhere that the temperature goes above 32 °C.
- If it has been more than 28 days after first use of your pen, get rid of it even if it contains unused medicine. If your pen or the pen of the child in your care has been exposed to temperatures higher than 32 °C, or has been removed from the refrigerator for more than 4 hours with each use or if it has been used a total of 5 times, get rid of it even if it contains unused medicine.

To help you remember when to dispose of your pen you can write the date of first use on the pen label.

A small amount of medicine may remain in the pen after all doses have been correctly given. Do not try to use any remaining medicine. After the last dose is given, the pen must be properly thrown away.

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 Ngenla contains
- The active substance is somatrogon.

Ngenla 24 mg solution for injection in pre-filled pen
One mL of solution contains 20 mg of somatrogon.
Each pre-filled pen contains 24 mg somatrogon in 1.2 mL of solution. Each pre-filled pen delivers doses from 0.2 mg to 12 mg in a single injection in 0.2 mg increments.

Ngenla 60 mg solution for injection in pre-filled pen
One mL of solution contains 50 mg of somatrogon.
Each pre-filled pen contains 60 mg somatrogon in 1.2 mL solution. Each pre-filled pen delivers doses from 0.5 mg to 30 mg in a single injection in 0.5 mg increments.

- The other ingredients are: trisodium citrate dihydrate, citric acid monohydrate, L-Histidine, sodium chloride (see section 2 “Ngenla contains sodium”), poloxamer 188, m-Cresol, water for injections.

What Ngenla looks like and contents of the pack
Ngenla is a clear and colourless to slightly light yellow solution for injection (injection) in a pre-filled pen.

Ngenla 24 mg solution for injection is available in a pack size containing 1 pre-filled pen. The pen cap, dose button, and label on the pen are coloured lilac.

Ngenla 60 mg solution for injection is available in a pack size containing 1 pre-filled pen. The pen cap, dose button, and label on the pen are coloured blue.

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Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

Manufacturer
Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for use
Ngenla 24 mg Pen

Injection for subcutaneous (under the skin) use only

Keep this leaflet. These instructions show step-by-step directions on how to prepare and give a Ngenla injection.

Important information about your Ngenla pen

- Ngenla for injection is a multi-dose pre-filled pen containing 24 mg of medicine.
- Ngenla for injection can be given by a patient, caregiver, doctor, nurse or pharmacist. **Do not** try to inject Ngenla yourself until you are shown the right way to give the injections and read and understand the Instructions for Use. If your doctor, nurse or pharmacist decides that you or a caregiver may be able to give your injections of Ngenla at home, you should receive training on the right way to prepare and inject Ngenla. It is important that you read, understand, and follow these instructions so that you inject Ngenla the right way. It is important to talk to your doctor, nurse or pharmacist to be sure you understand your Ngenla dosing instructions.
- To help you remember when to inject Ngenla, you can mark your calendar ahead of time. Call your doctor, nurse or pharmacist if you or your caregiver have any questions about the right way to inject Ngenla.
- Each turn (click) of the dose knob increases the dose by 0.2 mg of medicine. You can give from 0.2 mg to 12 mg in a single injection. If your dose is more than 12 mg, you will need to give more than 1 injection. Each injection should be given at a different injection site.
- A small amount of the medicine may remain in the pen after all doses have been correctly given. This is normal. Patients should not try to use the remaining solution but get rid of the pen in the correct way.
- **Do not** share your pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.
- Always use a new sterile needle for each injection. This will reduce the risk of contamination, infection, leakage of medicine, and blocked needles leading to the wrong dose.
- **Do not** shake your pen. Shaking can damage the medicine.
- The pen is **not recommended** for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product.

Supplies you will need each time you inject

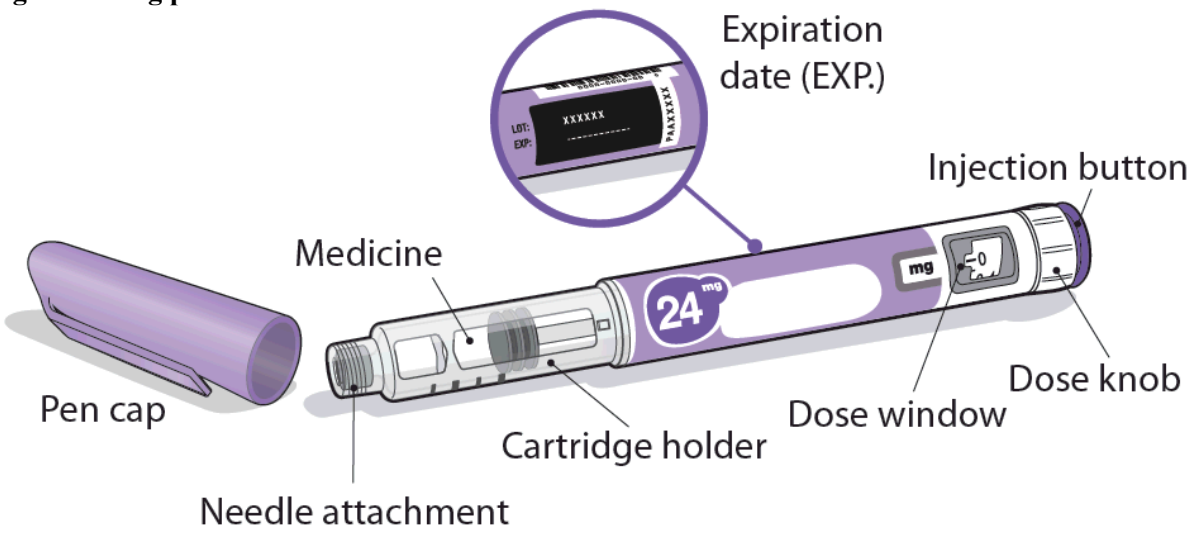
Included in the carton:

- 1 Ngenla 24 mg pen.

Not included in the carton:

- 1 new sterile needle for each injection.
- Alcohol swabs.
- Cotton balls or gauze pads.
- Adhesive bandage.
- A suitable sharps disposal container for disposal of pen needles and pens.

Ngenla 24 mg pen:

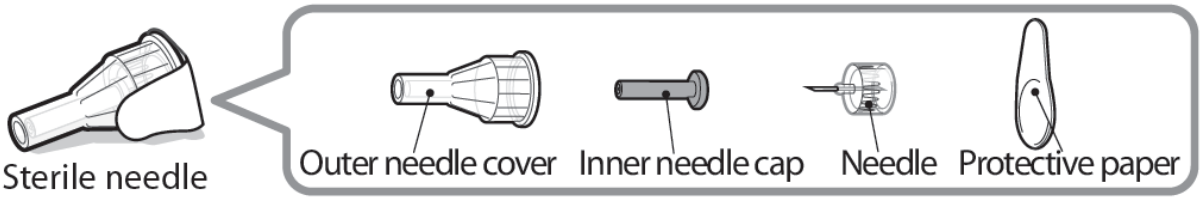


Needles to use

Pen needles are **not included** with your Ngenla pen. You can use pen needles from 4 mm to 8 mm and between 30G and 32G.

- The following needles have been shown to be compatible with your Ngenla pen:
  - 32G (Novo Nordisk®, NovoFine® Plus)
  - 31G (Novo Nordisk®, NovoFine®)
  - 31G (Becton, Dickinson and Company, BD Ultra-Fine™ or BD Micro-Fine™)
- The following needles with safety shield have been shown to be compatible with your Ngenla pen:
  - 30G (Becton, Dickinson and Company, AutoShield Duo™)
  - 30G (Novo Nordisk®, NovoFine® AutoCover®)
- Talk with your doctor, nurse or pharmacist about the right needle for you.

Sterile needle (example) not supplied:



Note: Needles with safety shield do not have an inner needle cap. Steps 5, 6 and 11 within these instructions relating to the inner needle cap may not apply when using a needle with safety shield. Refer to the needle manufacturer's instructions for use for more information.

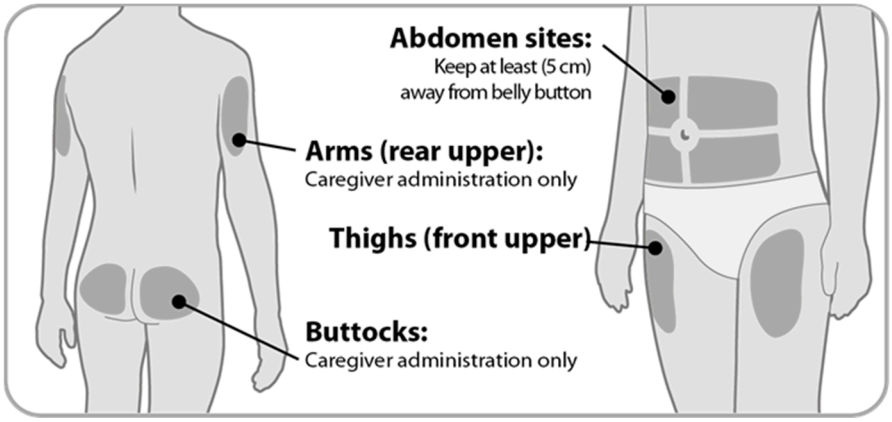
Caution: Never use a bent or damaged needle. Always handle pen needles with care to make sure you do not prick yourself (or anyone else) with the needle. **Do not** attach a new needle to your pen until you are ready for your injection.

Preparing for your injection

Step 1 Getting ready

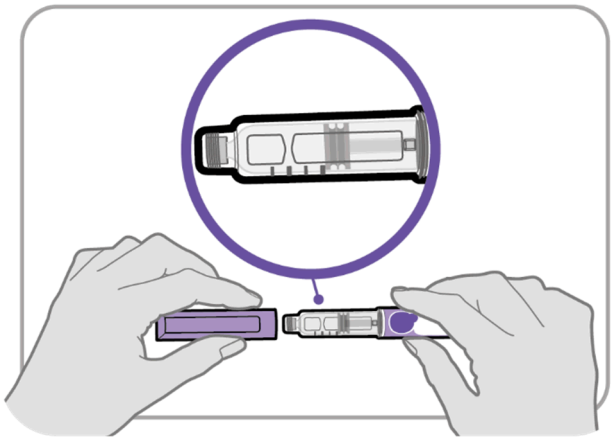
- Wash and dry your hands.
- You can use your pen straight from the refrigerator. For a more comfortable injection, leave your pen at room temperature for up to 30 minutes. **(See section 5 "How to store Ngenla" of the Ngenla 24 mg pre-filled pen Package Leaflet).**
- Check the name, strength, and label of your pen to make sure it is the medicine your doctor has prescribed for you.
- Check the expiry date on the pen label. **Do not** use if the expiry date has passed.
- **Do not** use your pen if:
    - it has been frozen or exposed to heat (above 32 °C) or it has been more than 28 days after first use of the pen. **(See section 5 "How to store Ngenla" of the Ngenla 24 mg pre-filled pen Package Leaflet).**
    - it has been dropped
    - it looks broken or damaged
- **Do not** remove the pen cap from your pen - until you are ready to inject.

Step 2 Choose and clean your injection site



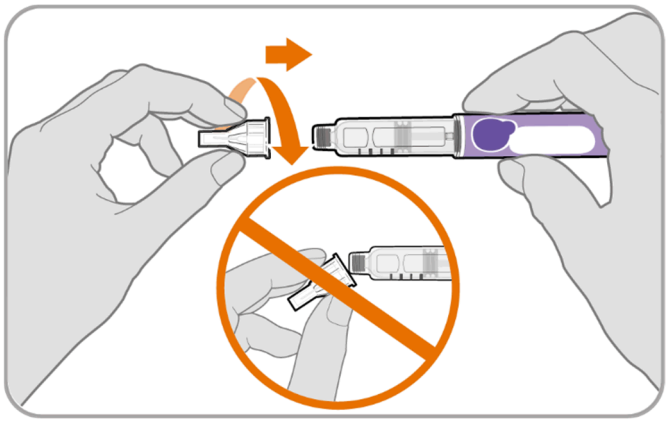
- Ngenla can be given in the abdomen (belly), thighs, buttocks, or upper arms.
- Choose the best place to inject, as recommended by your doctor, nurse or pharmacist. Choose a different injection site for each injection.
- If more than 1 injection is needed to complete your full dose, each injection should be given in a different injection site.
- **Do not** inject into bony areas, areas that are bruised, red, sore or hard, and areas that have scars or skin conditions.
- Clean the injection site with an alcohol swab.
- Allow the injection site to dry.
- **Do not** touch injection site after cleaning.

Step 3 Check medicine



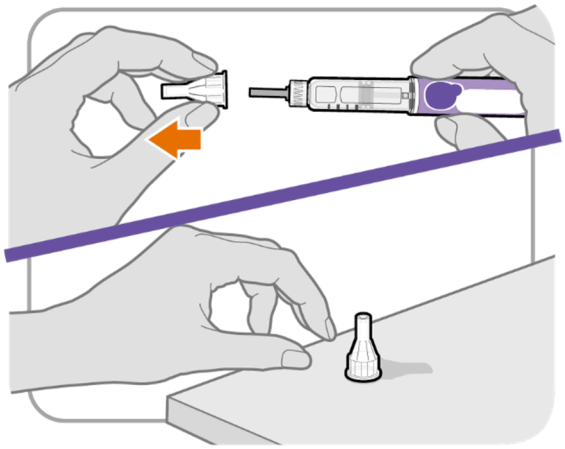
- Pull off the pen cap and keep it for after your injection.
- Check the medicine inside the cartridge holder.
- Make sure the medicine is clear and colourless to slightly light yellow. **Do not** inject the medicine if it is cloudy or dark yellow.
- Make sure the medicine is free of flakes or particles. **Do not** inject the medicine if it has flakes or particles.
  Note: It is normal to see one or more bubbles in the medicine.

Step 4 Attach needle



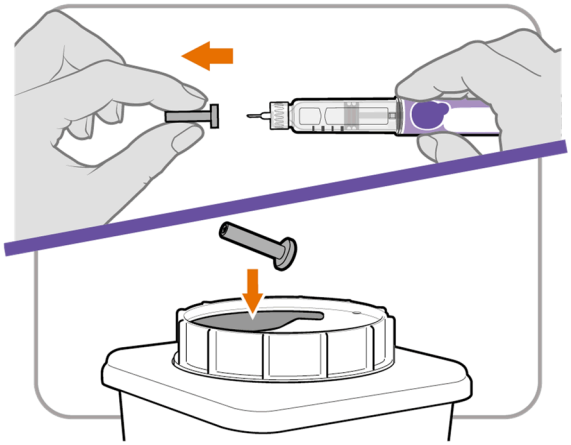
- Take a new needle and pull off the protective paper.
- Line the needle up with your pen keeping them both straight.
- Gently push and then screw the needle onto your pen.
  Do not over tighten.
  Note: Be careful not to attach the needle at an angle. This may cause the pen to leak.
  Caution: Needles have sharp tips at both ends. Handle with care to make sure you do not prick yourself (or anyone else) with the needle.

Step 5 Pull off outer needle cover

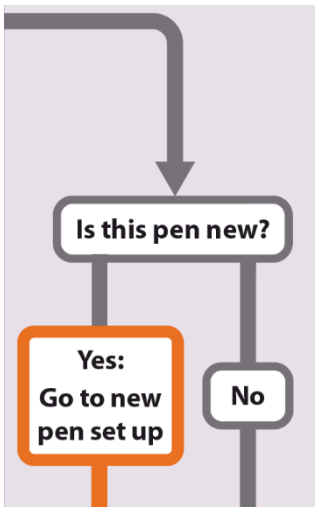


- Pull off the outer needle cover.
- Make sure you keep the outer needle cover. You will need it later to remove the needle.
  Note: You should see an inner needle cap after you have removed the outer cover. If you do not see this, try to attach the needle again.
  Note: If using needle with safety shield, refer to the manufacturer's instructions for use.

Step 6 Pull off inner needle cap



- Pull off the inner needle cap carefully to show the needle.
- Throw away the inner needle cap in a sharps container. It is not needed again.
  Note: If using needle with safety shield, refer to the manufacturer's instructions for use.



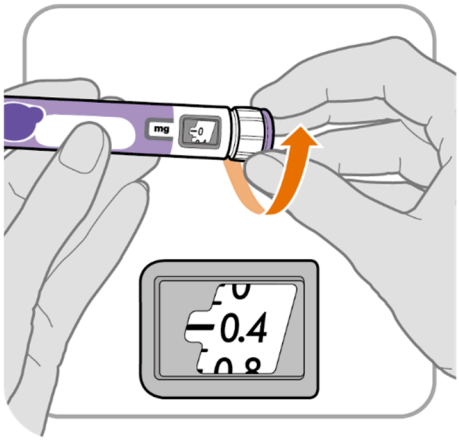
('Yes: Go to new pen set up' has an arrow directing to 'New pen set up (priming)' and 'No' has an arrow directing to 'Setting your prescribed dose')

New pen set up (priming) – for the first use of a new pen only

You must set up each new pen (priming) before using it for the first time

- New pen set up is done before each new pen is used for the first time.
- The purpose of setting up a new pen is to remove air bubbles and make sure you get the correct dose.
  Important: Skip Step-A through to Step-C if you have already set up your pen.

Step-A: Set knob to 0.4

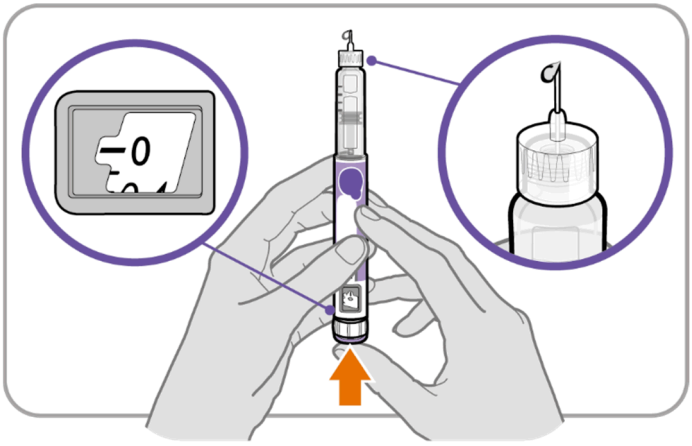


- Turn the dose knob to **0.4**.
  Note: If you turn the dose knob too far, you can turn it back.

Step-B: Tap cartridge holder

- Hold the pen with the needle pointing up so that the air bubbles can rise.
- **Tap** the cartridge holder gently to float any air bubbles to the top.
  Important: Follow Step-B even if you do not see air bubbles.

Step-C: Press button and check for liquid

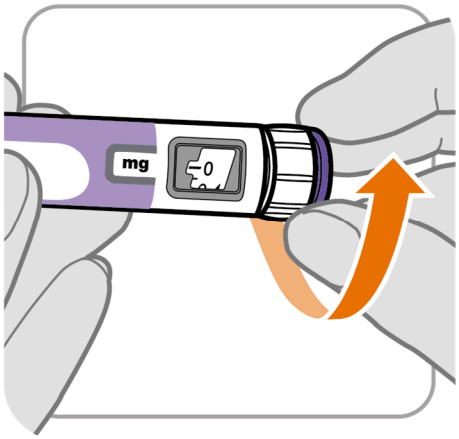


- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.
- **Check** for liquid at the needle tip. If liquid appears, your pen is set up.
- Always make sure that a drop of liquid appears before you inject. If liquid has not appeared, repeat Step-A through to Step-C.
  - If liquid does not appear after you have repeated Step-A through Step-C five (5) times, attach a new needle and try one (1) more time.

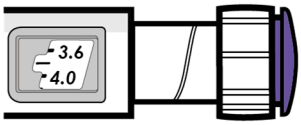
  Do not use the pen if a drop of liquid still does not appear. Contact your doctor, nurse or pharmacist, and use a new pen.

Setting your prescribed dose

Step 7 Set your dose

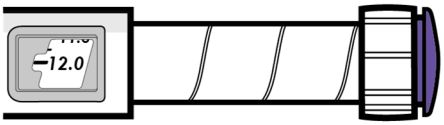


Example A:



3.8 mg shown in the dose window

Example B:



12.0 mg shown in the dose window

- Turn the dose knob to set your dose.
  - The dose can be increased or decreased by turning the dose knob in either direction.
  - The dose knob turns 0.2 mg at a time.
  - Your pen contains 24 mg of medicine but you can only set a dose of up to 12 mg for a single injection.
  - The dose window shows the dose in mg. See **Examples A and B**.
- **Always check the dose window to make sure you have set the correct dose.**
  Important: Do not press the injection button while setting your dose.

What should I do if I cannot set the dose I need?

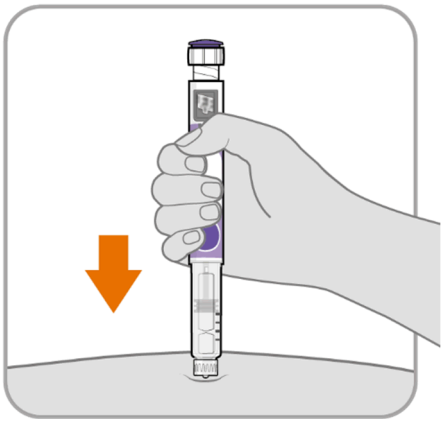
- If your dose is more than 12 mg you will need more than 1 injection.
- You can give from 0.2 mg to 12 mg in a single injection.
  - If you need help dividing up your dose the right way, ask your doctor, nurse or pharmacist.
  - Use a new needle for each injection **(See Step 4: Attach needle)**.
  - If you normally need to give 2 injections for your full dose, be sure to give your second dose.

What should I do if I do not have enough medicine left in my pen?

- If your pen contains less than 12 mg of medicine, the dose knob will stop with the remaining amount of medicine shown in the dose window.
- If there is not enough medicine left in your pen for your full dose, you may either:
  - inject the amount left in your pen, then prepare a new pen to complete your dose in full.
    Remember to subtract the dose you have already received. For example, if the dose is 3.8 mg and you can only set the dose knob to 1.8 mg, you should inject another 2.0 mg with a new pen.
  - or get a new pen and inject the full dose.

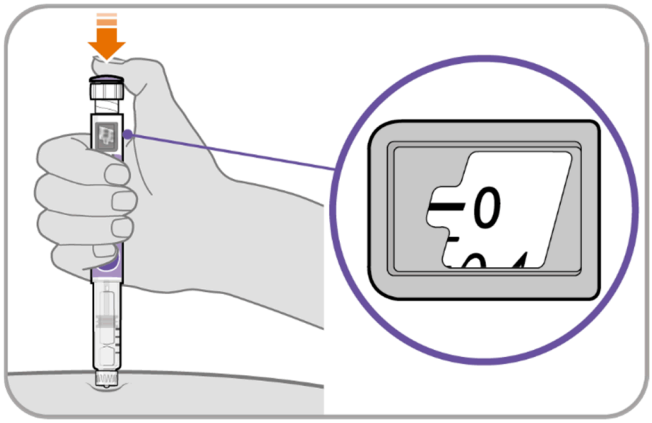
Injecting your dose

Step 8 Insert the needle



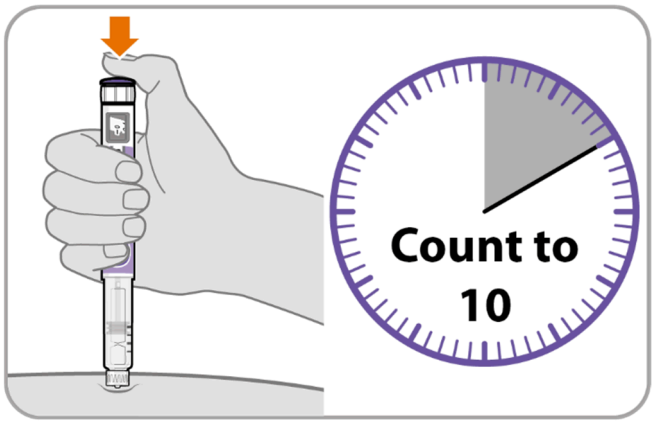
- Hold your pen so you can see the numbers in the dose window.
- Insert the needle straight into your skin.

Step 9 Inject your medicine



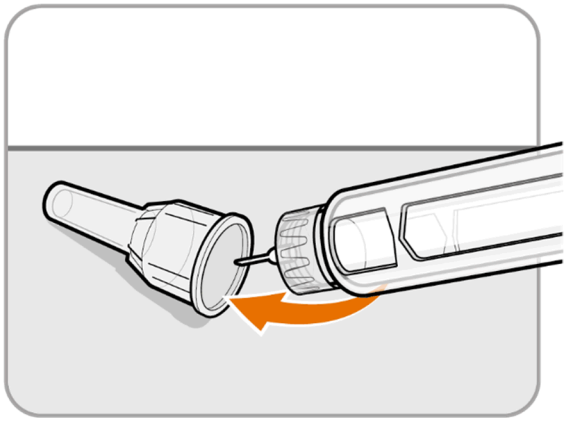
- Keep holding the needle in the same position in your skin.
- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.

Step 10 Count to 10



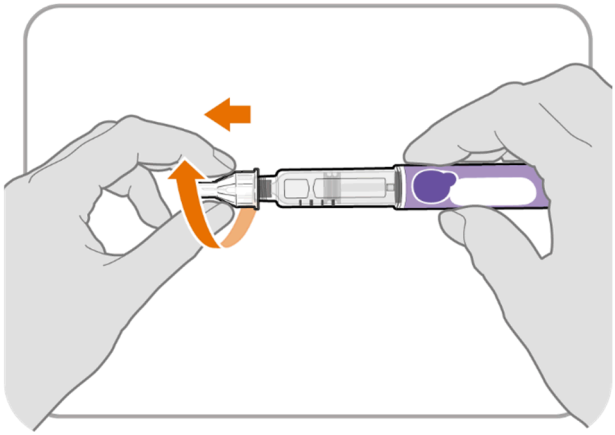
- **Continue to press the injection button while counting to 10**. Counting to 10 will allow the full dose of medicine to be given.
- After counting to 10, let go of the injection button and slowly remove the pen from the injection site by pulling the needle **straight out.**
  Note: You may see a drop of medicine at the needle tip. This is normal and does not affect the dose you just received.

Step 11 Attach outer needle cover



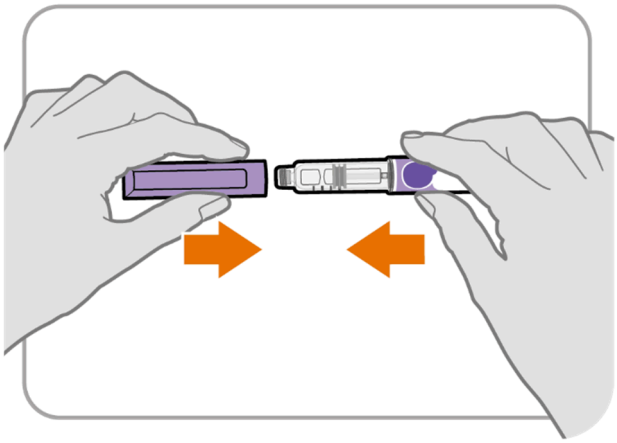
- Carefully place the outer needle cover back on the needle.
- Press on the outer needle cover until it is secure.
  Caution: Never try to put the inner needle cap back on the needle. You may prick yourself with the needle.
  Note: If using needle with safety shield, refer to manufacturer's instructions for use.

Step 12 Remove the needle



- Unscrew the needle from the pen.
- Gently pull until the needle comes off.
  Note: If the needle is still on, replace the outer needle cover and try again. Be sure to apply pressure when unscrewing the needle.
  Dispose of your used pen needles in a sharps container as instructed by your doctor, nurse or pharmacist and in accordance with local health and safety laws. Keep the sharps container out of the reach of children. **Do not** reuse needles.

Step 13 Replace the pen cap



- Replace the pen cap back onto your pen.
- **Do not** recap the pen with a needle attached.
- If there is any medicine left in your pen, store in the refrigerator between uses. **(See section 5 "How to store Ngenla" of the Ngenla 24 mg pre-filled pen Package Leaflet)**.

Step 14 After your injection

- Press lightly on the injection site with a clean cotton ball or gauze pad, and hold for a few seconds.
- **Do not** rub the injection site. You may have slight bleeding. This is normal.
- You may cover the injection site with a small adhesive bandage, if needed.
- If your pen is empty or it has been **more than 28 days** after first use, throw it away even if it contains unused medicine. Throw away your pen in the sharps container.
- To help you remember when to dispose of your pen you can write the date of first use on the pen label and below:

Date of first use _____ / _____ / _____

Package leaflet: Information for the patient

Ngenla 60 mg solution for injection in pre-filled pen
somatrogon

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, pharmacist or nurse.
- This medicine has been prescribed for you or the child in your care only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours or those of the child in your care.
- If you or the child in your care get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ngenla is and what it is used for
2. What you need to know before you use Ngenla
3. How to use Ngenla
4. Possible side effects
5. How to store Ngenla
6. Contents of the pack and other information

1. What Ngenla is and what it is used for

Ngenla contains the active substance somatrogon, a modified form of human growth hormone. Natural human growth hormone is needed for bones and muscles to grow. It also helps your fat and muscle tissues to develop in the right amounts. Ngenla is used to treat children and adolescents from 3 years of age who do not have enough growth hormone and are not growing at the normal rate.

The active substance in Ngenla is made by 'recombinant DNA technology'. This means that it is grown in cells that have been modified in the laboratory so that they can produce it.

2. What you need to know before you use Ngenla

Do not use Ngenla
- If you or the child in your care are allergic to somatrogon (see Warnings and precautions) or any of the other ingredients of this medicine (listed in section 6).
- If you or the child in your care have an active tumour (cancer). Tell your doctor if you or the child in your care have or have had an active tumour. Tumours must be inactive, and you or the child in your care must have finished your anti-tumour treatment before starting treatment with Ngenla.
- If you or the child in your care have stopped growing because of closure of the growth plates (closed epiphyses) meaning that you or the child in your care have been told by your doctor that your bones have stopped growing.
- If you or the child in your care are seriously ill (for example, complications following open heart surgery, abdominal surgery, acute respiratory failure, multiple accidental trauma or similar conditions). If you or the child in your care are about to have, or have had, a major operation, or

go into hospital for any reason, tell your doctor and remind the other doctors you are seeing that you use growth hormone.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Ngenla:
- If you or the child in your care develop a serious allergic reaction, stop using Ngenla, talk to your doctor right away. Sometimes serious allergic reactions such as hypersensitivity, including anaphylaxis or angioedema (difficulties breathing or swallowing, or swelling of the face, lips, throat or tongue) have occurred. If you or the child in your care have any of the following symptoms of a serious allergic reaction:
    - breathing problems
    - swelling of your face, mouth, and tongue
    - hives (nettle rash, lumps rising under the skin)
    - rash
    - fever
- If you or the child in your care have replacement therapy with corticosteroid medicines (glucocorticoids) you or the child in your care should consult your doctor regularly as you or the child in your care may need adjustment of your glucocorticoid dose.
- Your doctor should check at intervals how well the thyroid gland is working in you or the child in your care and if necessary may prescribe treatment or adjust the dose of existing treatment as this may be needed for Ngenla to work properly.
- If you or the child in your care have Prader-Willi syndrome, you or the child should not be treated with Ngenla unless you or the child in your care has growth hormone deficiency.
- Your doctor should monitor you or the child in your care for high blood sugar levels (hyperglycaemia) during treatment with Ngenla. If you or the child in your care are treated with insulin or other diabetes medicines, your doctor may need to adjust the insulin dose. If you or the child in your care have diabetes and associated severe/worsening eye disease you or the child in your care should not be treated with Ngenla.
- If you or the child in your care have ever had any kind of tumour (cancer).
- If you or the child in your care experience changes in vision, severe or frequent headaches, associated with feeling sick (nausea), vomiting, or experience lack of muscle control or coordination of voluntary movements, such as walking or picking up objects, difficulty with speech, eye movement or swallowing, especially at the start of treatment, tell your doctor immediately. These could be signs of a temporary increase in pressure within the brain (intracranial hypertension).
- If you or the child in your care are seriously ill (for example, complications following open heart surgery, abdominal surgery, acute respiratory failure, multiple accidental trauma or similar conditions). If you or the child in your care are about to have, or have had, a major operation, or go into hospital for any reason, tell your doctor and remind the other doctors you are seeing that you or the child in your care use growth hormone.
- If you or the child in your care develop a severe stomach ache during treatment with Ngenla as this could be a symptom of inflammation of the pancreas.
- If you or the child in your care notice a sideways curvature in your spine (scoliosis), you or the child in your care will need to be checked often by your doctor.
- If during growing you or the child in your care develop a limp or hip or knee pain, you or the child in your care should consult your doctor right away. These could be symptoms of bone disorders in your hip as this may happen during periods of rapid growth.
- If you or the child in your care are taking or stop taking oral contraception or hormonal replacement therapy with oestrogen, your doctor may recommend the dose of Ngenla to be adjusted.

Other medicines and Ngenla
Tell your doctor, pharmacist or nurse if you or the child in your care are using, have recently used or might use any other medicines.
- If you or the child in your care take replacement therapy with corticosteroid medicines (glucocorticoids), as these may reduce the effect of Ngenla on growth. You or the child in your

care should consult your doctor regularly, as you or the child in your care may need adjustment of your glucocorticoid dose.
- If you or the child in your care are treated with insulin or other diabetes medicines, you should consult with your doctor as you or your doctor may need to adjust the dose.
- If you or the child in your care are receiving treatment with thyroid hormones, your doctor may need to adjust the dose.
- If you or the child in your care are receiving oestrogen taken orally, you should consult your doctor as you or the child may need to adjust your dose of Ngenla.
- If you or the child in your care are receiving ciclosporin (a medicine that weakens the immune system after transplantation), you should consult your doctor as your doctor may need to adjust the dose.
- If you or the child in your care are receiving medicines to control epilepsy (anticonvulsants), you should consult your doctor as your doctor may need to adjust the dose.

Pregnancy and breast-feeding
If you or the child in your care are pregnant or breast-feeding, think you or the child in your care may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Ngenla has not been tested in pregnant women and it is not known if this medicine can harm your unborn baby. It is therefore preferable to avoid Ngenla during pregnancy. If you are able to get pregnant, you should not use Ngenla unless you are also using reliable contraception.

It is not known whether somatrogon can pass into breast milk. Tell your doctor or the doctor of the child in your care, if you or the child in your care are breast-feeding or plan to do so. Your doctor will then help you or the child in your care decide whether to stop breast-feeding, or whether to stop taking Ngenla, considering the benefit of breast-feeding to the baby and the benefit of Ngenla to you or the child in your care.

Driving and using machines
Ngenla does not affect the ability to drive and use machines.

Ngenla contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

Ngenla contains metacresol
Ngenla contains a preservative called metacresol. In very rare cases the presence of metacresol can cause inflammation (swelling) in muscles. If you or the child in your care experience muscle pain or pain at the injection site, inform your doctor.

3. How to use Ngenla

This medicine will only be prescribed by a doctor who has experience with growth hormone treatment and who has confirmed your diagnosis or that of the child in your care.

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

The dose of Ngenla to be injected will be decided by your doctor.

How much to use
Your doctor will work out your dose of Ngenla from your body weight in kilograms. The recommended dose is 0.66 mg per kg body weight and is given once weekly. If you or the child in

your care have been previously treated with daily growth hormone injections, your doctor will tell you to wait before taking the first dose of Ngenla until the day after your last daily injection and then continue with Ngenla once each week.

Do not change your dose unless your doctor has told you to.

How Ngenla is given
- Ngenla is available as a pre-filled pen in 2 different sizes (Ngenla 24 mg and Ngenla 60 mg). Based on the recommended dose your doctor or the doctor of the child in your care will prescribe the most appropriate pen size (see section 6 “Contents of the pack and other information”).
- Before you or the child in your care use the pen for the first time, your/their doctor or nurse will show you how to use it. Ngenla is given as an injection under the skin (subcutaneous injection) using a pre-filled pen. Do not inject it into a vein or muscle.
- The best place to give Ngenla is in the abdomen (belly), thighs, buttocks or upper arms. Injections to the upper arms and buttocks should be given by the caregiver.
- Fatty tissue below the skin can shrink at the site of injection (see section 4). To avoid this, use a different injection site each time.
- If more than one injection is required to deliver a complete dose, each should be administered at a different injection site.

Detailed instructions for use of the pre-filled pen are at the end of this leaflet.

When to use Ngenla
You or the child in your care should use this medicine once a week on the same day each week.

You or the child in your care should record which day of the week you use Ngenla to help you or the child in your care remember to inject this medicine once a week.

If necessary you or the child in your care can change the day of your/their weekly injection as long as it has been at least 3 days since you or the child in your care had your/their last injection. After selecting a new dosing day, continue giving yourself or the child in your care the injection on that day each week.

If you use more Ngenla than you should
If you or the child in your care have injected more Ngenla than you should have been given, contact your doctor straight away as your/their blood sugar levels may need to be checked.

If you forget to use Ngenla
If you or the child in your care forgot to inject a dose and:
- It is 3 days or less since you or the child in your care should have used Ngenla, use it as soon as you remember. Then inject your/their next dose on your/their usual injection day.
- It is more than 3 days since you or the child in your care should have used Ngenla, skip the missed dose. Then inject your/their next dose as usual on your/their next scheduled day. A regular dosing day should be maintained.

Do not use a double dose to make up for a forgotten dose.

If you stop using Ngenla
Do not stop using this medicine without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common: may affect more than 1 in 10 people
- Headache
- Bleeding, inflammation, itching, pain, redness, soreness, stinging, tenderness, or warmth at the injection site (injection site reactions)
- Fever (pyrexia)

Common: may affect up to 1 in 10 people
- Decrease in the number of red blood cells in the blood (anaemia)
- Increase in the number of eosinophils in the blood (eosinophilia)
- Decrease in the blood level of thyroid hormone (hypothyroidism)
- Allergic inflammation of the conjunctiva, the clear layer over the outside of the eye (allergic conjunctivitis)
- Joint pain (arthralgia)
- Pain in arms or legs

Uncommon: may affect up to 1 in 100 people
- The adrenal glands do not make enough steroid hormones (adrenal insufficiency)
- Rash

Not known: frequency cannot be estimated from the available data
- Localised loss of fat below the skin (lipoatrophy)
- Problems with hip joint which may cause hip or knee pain or limp (epiphysiolysis, including slipped capital femoral epiphysis)

Other possible side effects not seen with Ngenla but which have been reported in other growth hormone medicines treatment may include the following:
- Tissue growth (non cancerous or cancer)
- Type 2 diabetes
- Increased intracranial pressure (which causes symptoms such as strong headache, visual disturbances or vomiting)
- Numbness or tingling
- Joint or muscle pain
- Breast enlargement in boys and men
- Skin rash, reddening and itching
- Water retention (which shows as puffy fingers or swollen ankles)
- Facial swelling
- Pancreatitis (which causes symptoms of stomach pain, nausea, vomiting or diarrhoea)

In very rare cases the presence of metacresol can cause inflammation (swelling) in muscles. If you or the child in your care experience muscle pain or pain at the injection site, inform your doctor.

Reporting of side effects
If you or the child in your care get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via 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 Ngenla

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 pen label and on the carton after 'EXP'. The expiry date refers to the last day of that month.

The pre-filled pen should not be used more than 28 days after first use.

Before first use of Ngenla
- Store in a refrigerator (2 °C - 8 °C).
- Keep Ngenla in the outer carton in order to protect from light.
- Remove Ngenla from the refrigerator prior to use. Ngenla may be held at room temperature (up to 32 °C) for up to 4 hours.
- Do not use this medicine if you notice that the solution is cloudy or dark yellow. Do not use the medicine if it has flakes or particles.
- Do not shake the pen. Shaking can damage the medicine.

After first use of Ngenla
- Use within 28 days after first use. Store in a refrigerator (2 °C - 8 °C). Do not freeze.
- Keep Ngenla with the pen cap on in order to protect from light.
- Do not store the pre-filled pen with a needle attached.
- Discard the pen after last dose, even if it contains unused medicine.
- Ngenla may be held at room temperature (up to 32 °C) for up to 4 hours with each injection for a maximum of 5 times. Return Ngenla to the refrigerator again after each use.
- Do not leave at room temperature for more than 4 hours with each use.
- Do not put the pen anywhere that the temperature goes above 32 °C.
- If it has been more than 28 days after first use of your pen, get rid of it even if it contains unused medicine. If your pen or the pen of the child in your care has been exposed to temperatures higher than 32 °C, or has been removed from the refrigerator for more than 4 hours with each use or if it has been used a total of 5 times, get rid of it even if it contains unused medicine.

To help you remember when to dispose of your pen you can write the date of first use on the pen label.

A small amount of medicine may remain in the pen after all doses have been correctly given. Do not try to use any remaining medicine. After the last dose is given, the pen must be properly thrown away.

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 Ngenla contains
- The active substance is somatrogon.

Ngenla 24 mg solution for injection in pre-filled pen
One mL of solution contains 20 mg of somatrogon.
Each pre-filled pen contains 24 mg somatrogon in 1.2 mL of solution. Each pre-filled pen delivers doses from 0.2 mg to 12 mg in a single injection in 0.2 mg increments.

Ngenla 60 mg solution for injection in pre-filled pen
One mL of solution contains 50 mg of somatrogon.
Each pre-filled pen contains 60 mg somatrogon in 1.2 mL solution. Each pre-filled pen delivers doses from 0.5 mg to 30 mg in a single injection in 0.5 mg increments.

- The other ingredients are: trisodium citrate dihydrate, citric acid monohydrate, L-Histidine, sodium chloride (see section 2 “Ngenla contains sodium”), poloxamer 188, m-Cresol, water for injections.

What Ngenla looks like and contents of the pack
Ngenla is a clear and colourless to slightly light yellow solution for injection (injection) in a pre-filled pen.

Ngenla 24 mg solution for injection is available in a pack size containing 1 pre-filled pen. The pen cap, dose button, and label on the pen are coloured lilac.

Ngenla 60 mg solution for injection is available in a pack size containing 1 pre-filled pen. The pen cap, dose button, and label on the pen are coloured blue.

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Manufacturer
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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for use
Ngenla 60 mg Pen

Injection for subcutaneous (under the skin) use only

Keep this leaflet. These instructions show step-by-step directions on how to prepare and give a Ngenla injection.

Important information about your Ngenla pen

- Ngenla for injection is a multi-dose pre-filled pen containing 60 mg of medicine.
- Ngenla for injection can be given by a patient, caregiver, doctor, nurse or pharmacist. **Do not** try to inject Ngenla yourself until you are shown the right way to give the injections and read and understand the Instructions for Use. If your doctor, nurse or pharmacist decides that you or a caregiver may be able to give your injections of Ngenla at home, you should receive training on the right way to prepare and inject Ngenla. It is important that you read, understand, and follow these instructions so that you inject Ngenla the right way. It is important to talk to your doctor, nurse or pharmacist to be sure you understand your Ngenla dosing instructions.
- To help you remember when to inject Ngenla, you can mark your calendar ahead of time. Call your doctor, nurse or pharmacist if you or your caregiver have any questions about the right way to inject Ngenla.
- Each turn (click) of the dose knob increases the dose by 0.5 mg of medicine. You can give from 0.5 mg to 30 mg in a single injection. If your dose is more than 30 mg, you will need to give more than 1 injection. Each injection should be given at a different injection site.
- A small amount of the medicine may remain in the pen after all doses have been correctly given. This is normal. Patients should not try to use the remaining solution but get rid of the pen in the correct way.
- **Do not** share your pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.
- Always use a new sterile needle for each injection. This will reduce the risk of contamination, infection, leakage of medicine, and blocked needles leading to the wrong dose.
- **Do not** shake your pen. Shaking can damage the medicine.
- The pen is **not recommended** for use by the blind or visually impaired without the assistance of a person trained in the proper use of the product.

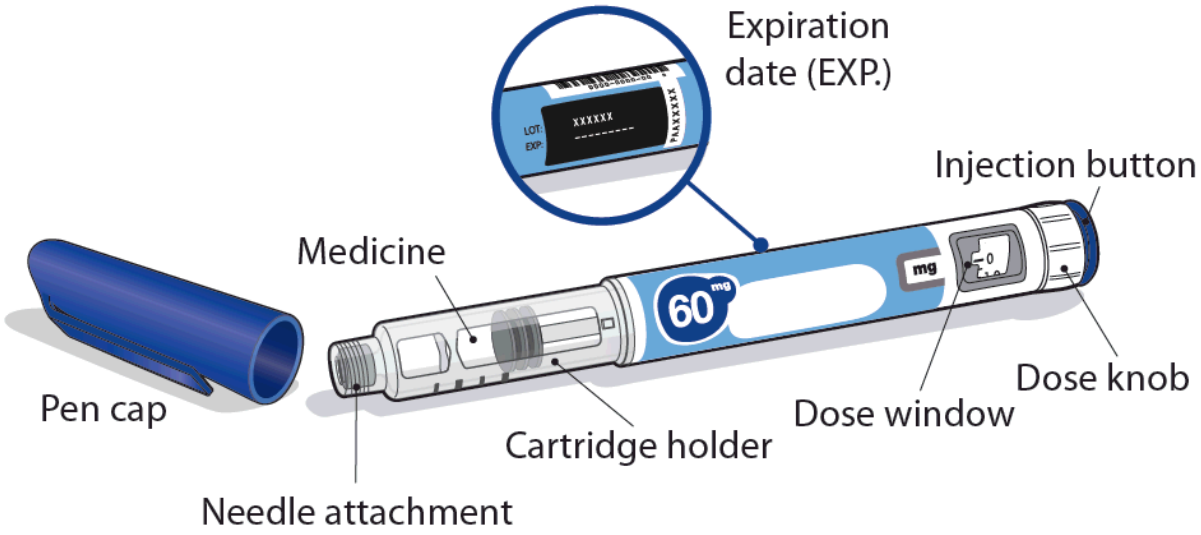
Supplies you will need each time you inject
Included in the carton:

- 1 Ngenla 60 mg pen.

Not included in the carton:

- 1 new sterile needle for each injection.
- Alcohol swabs.
- Cotton balls or gauze pads.
- Adhesive bandage.
- A suitable sharps disposal container for disposal of pen needles and pens.

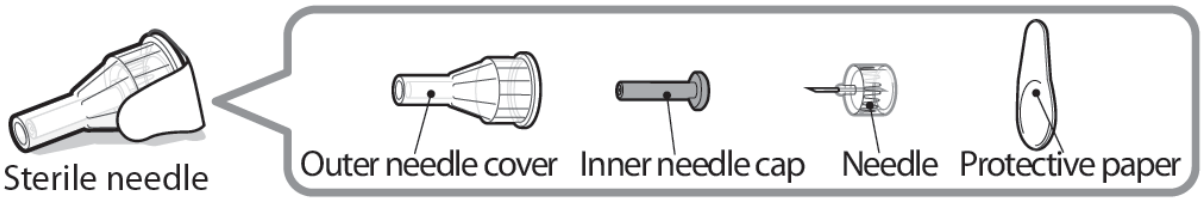
Ngenla 60 mg pen:



Needles to use
Pen needles are **not included** with your Ngenla pen. You can use pen needles from 4 mm to 8 mm and between 30G and 32G.

- The following needles have been shown to be compatible with your Ngenla pen:
  - 32G (Novo Nordisk®, NovoFine® Plus)
  - 31G (Novo Nordisk®, NovoFine®)
  - 31G (Becton, Dickinson and Company, BD Ultra-Fine™ or BD Micro-Fine™)
- The following needles with safety shield have been shown to be compatible with your Ngenla pen:
  - 30G (Becton, Dickinson and Company, AutoShield Duo™)
  - 30G (Novo Nordisk®, NovoFine® AutoCover®)
- Talk with your doctor, nurse or pharmacist about the right needle for you.

Sterile needle (example) not supplied:



Note: Needles with safety shield do not have an inner needle cap. Steps 5, 6 and 11 within these instructions relating to the inner needle cap may not apply when using a needle with safety shield. Refer to the needle manufacturer's instructions for use for more information.

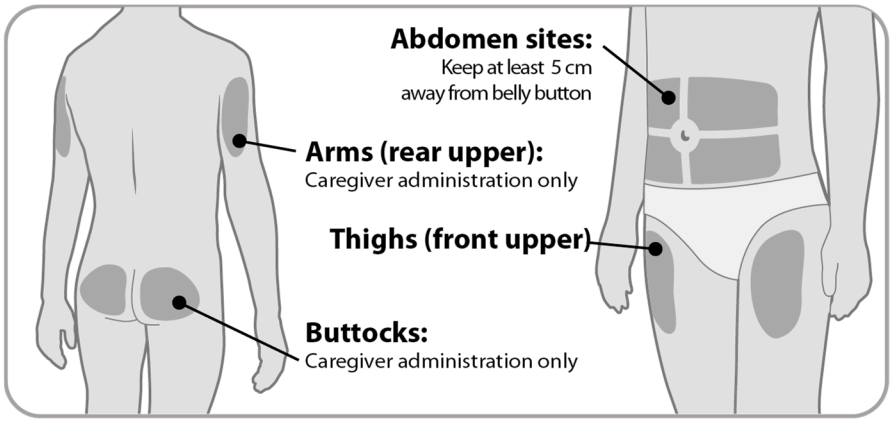
Caution: Never use a bent or damaged needle. Always handle pen needles with care to make sure you do not prick yourself (or anyone else) with the needle. **Do not** attach a new needle to your pen until you are ready for your injection.

Preparing for your injection

Step 1 Getting ready

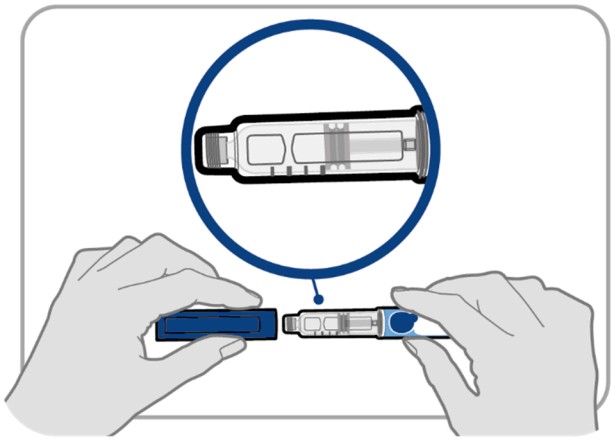
- Wash and dry your hands.
- You can use your pen straight from the refrigerator. For a more comfortable injection, leave your pen at room temperature for up to 30 minutes. **(See section 5 "How to store Ngenla" of the Ngenla 60 mg pre-filled pen Package Leaflet)**.
- Check the name, strength, and label of your pen to make sure it is the medicine your doctor has prescribed for you.
- Check the expiry date on the pen label. **Do not** use if the expiry date has passed.
- **Do not** use your pen if:
  - it has been frozen or exposed to heat (above 32 °C) or it has been more than 28 days after first use of the pen. **(See section 5 "How to store Ngenla" of the Ngenla 60 mg pre-filled pen Package Leaflet)**.
  - it has been dropped
  - it looks broken or damaged
- **Do not** remove the pen cap from your pen - until you are ready to inject.

Step 2 Choose and clean your injection site



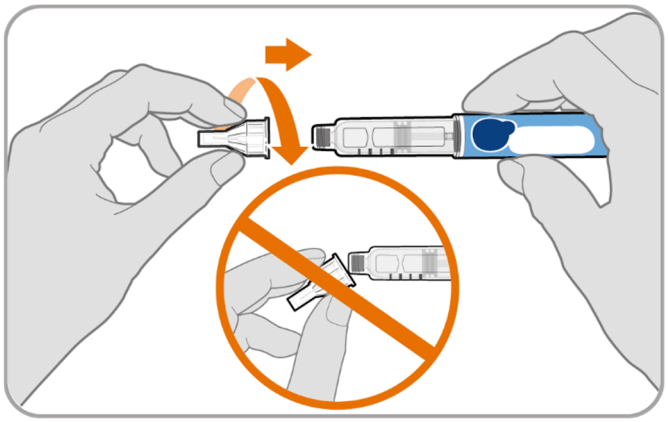
- Ngenla can be given in the abdomen (belly), thighs, buttocks, or upper arms.
- Choose the best place to inject, as recommended by your doctor, nurse or pharmacist. Choose a different injection site for each injection.
- If more than 1 injection is needed to complete your full dose, each injection should be given in a different injection site.
- **Do not** inject into bony areas, areas that are bruised, red, sore or hard, and areas that have scars or skin conditions.
- Clean the injection site with an alcohol swab.
- Allow the injection site to dry.
- **Do not** touch injection site after cleaning.

Step 3 Check medicine



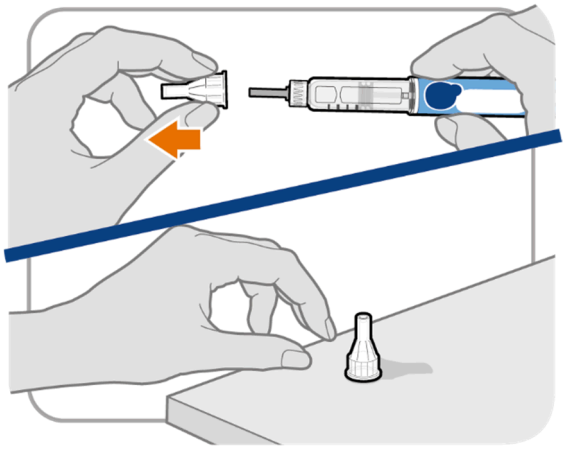
- Pull off the pen cap and keep it for after your injection.
- Check the medicine inside the cartridge holder.
- Make sure the medicine is clear and colourless to slightly light yellow. **Do not** inject the medicine if it is cloudy or dark yellow.
- Make sure the medicine is free of flakes or particles. **Do not** inject the medicine if it has flakes or particles.
  Note: It is normal to see one or more bubbles in the medicine.

Step 4 Attach needle



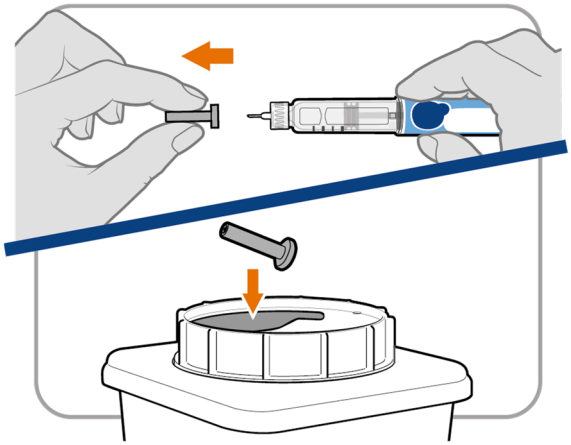
- Take a new needle and pull off the protective paper.
- Line the needle up with your pen keeping them both straight.
- Gently push and then screw the needle onto your pen.
  Do not over tighten.
  Note: Be careful not to attach the needle at an angle. This may cause the pen to leak.
  Caution: Needles have sharp tips at both ends. Handle with care to make sure you do not prick yourself (or anyone else) with the needle.

Step 5 Pull off outer needle cover

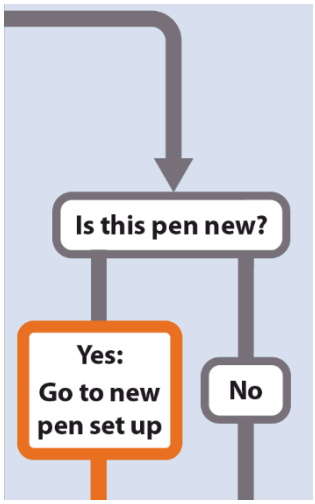


- Pull off the outer needle cover.
- Make sure you keep the outer needle cover. You will need it later to remove the needle.
  Note: You should see an inner needle cap after you have removed the outer cover. If you do not see this, try to attach the needle again.
  Note: If using needle with safety shield, refer to the manufacturer's instructions for use.

Step 6 Pull off inner needle cap



- Pull off the inner needle cap carefully to show the needle.
- Throw away the inner needle cap in a sharps container. It is not needed again.
  Note: If using needle with safety shield, refer to the manufacturer's instructions for use.



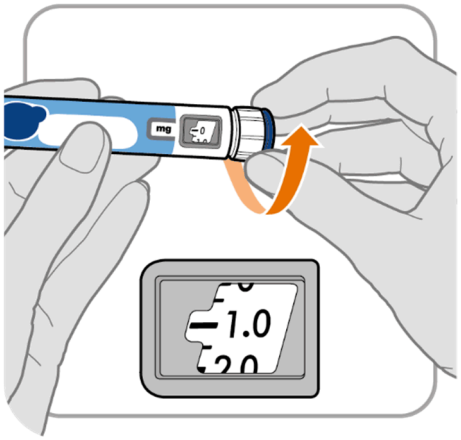
('Yes: Go to new pen set up' has an arrow directing to 'New pen set up (priming)' and 'No' has an arrow directing to 'Setting your prescribed dose')

New pen set up (priming) – for the first use of a new pen only

You must set up each new pen (priming) before using it for the first time

- New pen set up is done before each new pen is used for the first time.
- The purpose of setting up a new pen is to remove air bubbles and make sure you get the correct dose.
  Important: Skip Step-A through to Step-C if you have already set up your pen.

Step-A: Set knob to 1.0

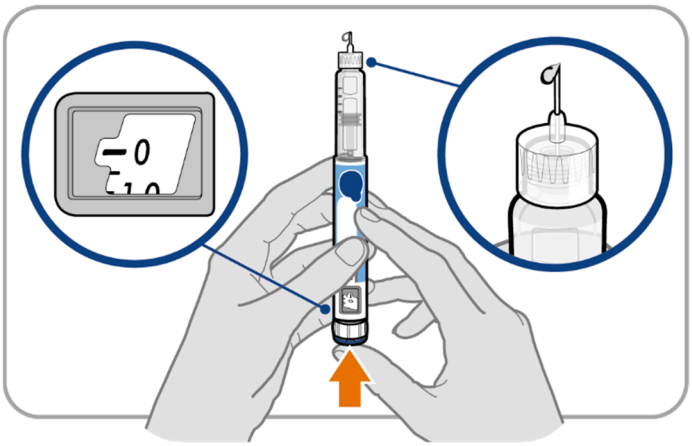


- Turn the dose knob to **1.0**.
  Note: If you turn the dose knob too far, you can turn it back.

Step-B: Tap cartridge holder

- Hold the pen with the needle pointing up so that the air bubbles can rise.
- **Tap** the cartridge holder gently to float any air bubbles to the top.
  Important: Follow Step-B even if you do not see air bubbles.

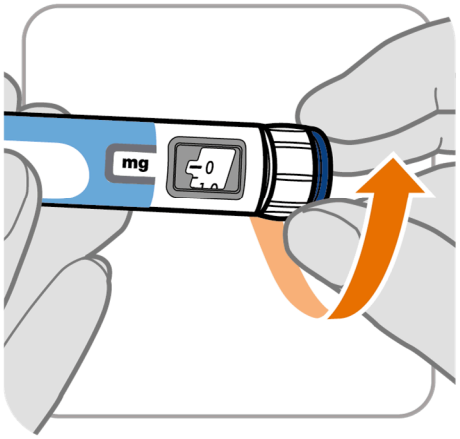
Step-C: Press button and check for liquid



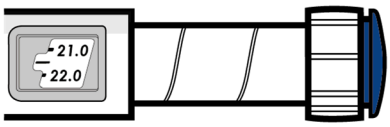
- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.
- **Check** for liquid at the needle tip. If liquid appears, your pen is set up.
- Always make sure that a drop of liquid appears before you inject. If liquid has not appeared, repeat Step-A through to Step-C.
  - If liquid does not appear after you have repeated Step-A through Step-C five (5) times, attach a new needle and try one (1) more time.
    Do not use the pen if a drop of liquid still does not appear. Contact your doctor, nurse or pharmacist, and use a new pen.

Setting your prescribed dose

Step 7 Set your dose

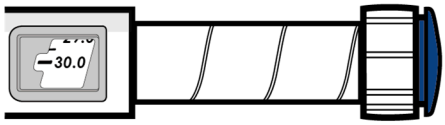


Example A:



21.5 mg shown in the dose window

Example B:



30.0 mg shown in the dose window

- Turn the dose knob to set your dose.
  - The dose can be increased or decreased by turning the dose knob in either direction.
  - The dose knob turns 0.5 mg at a time.
  - Your pen contains 60 mg of medicine but you can only set a dose of up to 30 mg for a single injection.
  - The dose window shows the dose in mg. See **Examples A and B**.
- **Always check the dose window to make sure you have set the correct dose.**
  Important: Do not press the injection button while setting your dose.

What should I do if I cannot set the dose I need?

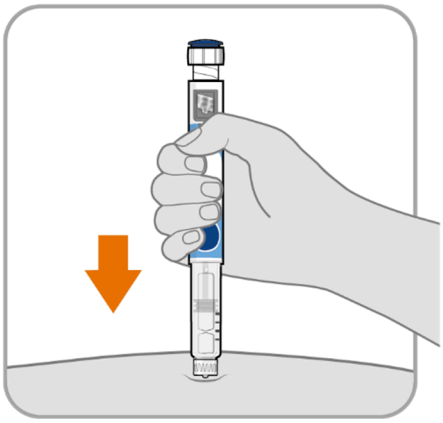
- If your dose is more than 30 mg you will need more than 1 injection.
- You can give from 0.5 mg to 30 mg in a single injection.
  - If you need help dividing up your dose the right way, ask your doctor, nurse or pharmacist.
  - Use a new needle for each injection **(See Step 4: Attach needle)**.
  - If you normally need to give 2 injections for your full dose, be sure to give your second dose.

What should I do if I do not have enough medicine left in my pen?

- If your pen contains less than 30 mg of medicine, the dose knob will stop with the remaining amount of medicine shown in the dose window.
- If there is not enough medicine left in your pen for your full dose, you may either:
  - inject the amount left in your pen, then prepare a new pen to complete your dose in full.
    Remember to subtract the dose you have already received. For example, if the dose is 21.5 mg and you can only set the dose knob to 17 mg, you should inject another 4.5 mg with a new pen.
  - or get a new pen and inject the full dose.

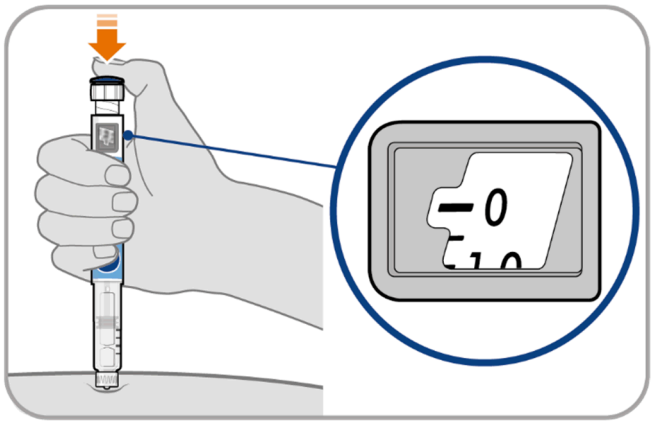
Injecting your dose

Step 8 Insert the needle



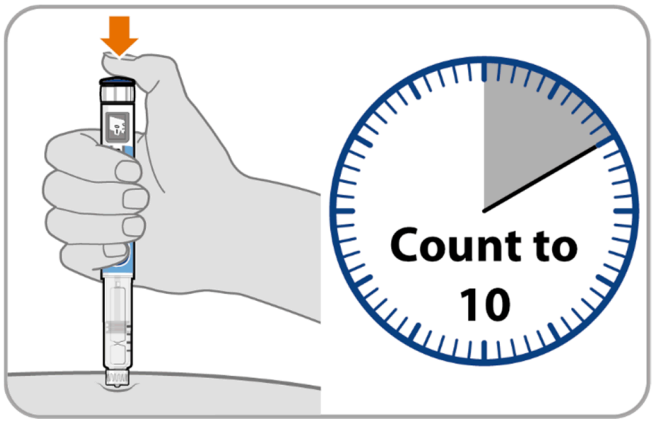
- Hold your pen so you can see the numbers in the dose window.
- Insert the needle straight into your skin.

Step 9 Inject your medicine



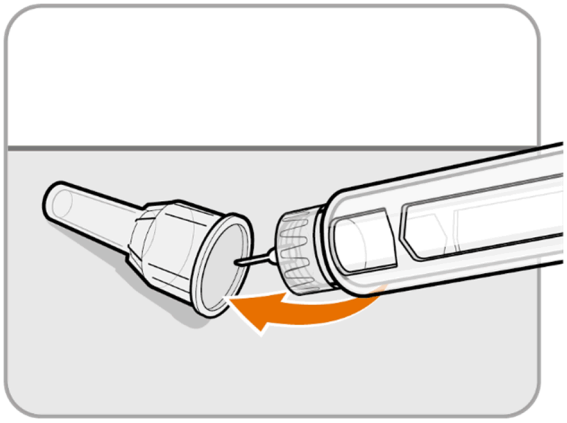
- Keep holding the needle in the same position in your skin.
- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.

Step 10 Count to 10



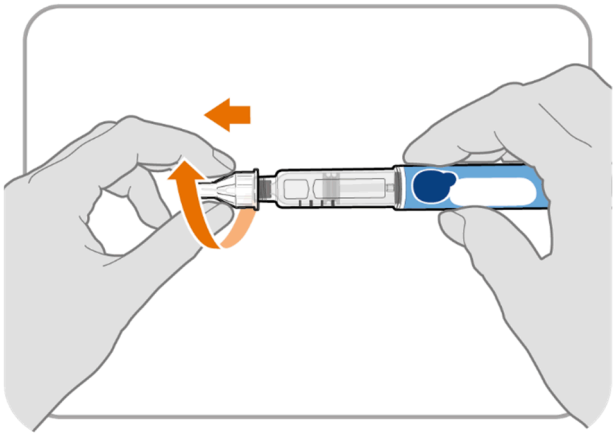
- **Continue to press the injection button while counting to 10**. Counting to 10 will allow the full dose of medicine to be given.
- After counting to 10, let go of the injection button and slowly remove the pen from the injection site by pulling the needle **straight out.**
  Note: You may see a drop of medicine at the needle tip. This is normal and does not affect the dose you just received.

Step 11 Attach outer needle cover



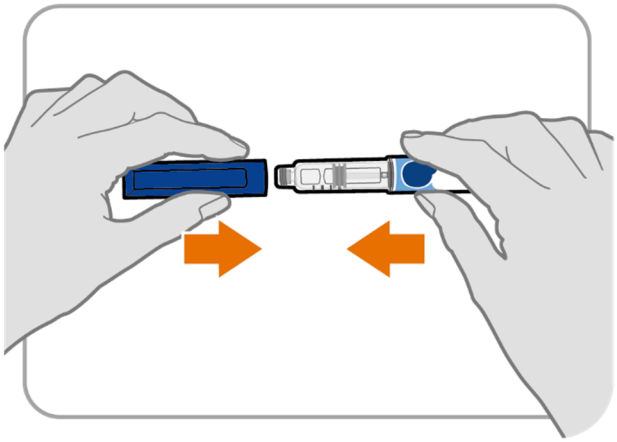
- Carefully place the outer needle cover back on the needle.
- Press on the outer needle cover until it is secure.
  Caution: Never try to put the inner needle cap back on the needle. You may prick yourself with the needle.
  Note: If using needle with safety shield, refer to the manufacturer's instructions for use.

Step 12 Remove the needle



- Unscrew the needle from the pen.
- Gently pull until the needle comes off.
  Note: If the needle is still on, replace the outer needle cover and try again. Be sure to apply pressure when unscrewing the needle.
- Dispose of your used pen needles in a sharps container as instructed by your doctor, nurse or pharmacist and in accordance with local health and safety laws. Keep the sharps container out of the reach of children. **Do not** reuse needles.

Step 13 Replace the pen cap



- Replace the pen cap back onto your pen.
- **Do not** recap the pen with a needle attached.
- If there is any medicine left in your pen, store in the refrigerator between uses. **(See section 5 "How to store Ngenla" of the Ngenla 60 mg pre-filled pen Package Leaflet)**.

Step 14 After your injection

- Press lightly on the injection site with a clean cotton ball or gauze pad, and hold for a few seconds.
- **Do not** rub the injection site. You may have slight bleeding. This is normal.
- You may cover the injection site with a small adhesive bandage, if needed.
- If your pen is empty or it has been **more than 28 days** after first use, throw it away even if it contains unused medicine. Throw away your pen in the sharps container.
- To help you remember when to dispose of your pen you can write the date of first use on the pen label and below:

Date of first use _____ / _____ / _____