For the use only of a Registered Medical Practitioner (Endocrinologist), or a Hospital or a Laboratory

Somatrogon Solution for Injection in Pre-filled Pen

GENRYZON®

1. GENERIC NAME

Somatrogon

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Somatrogon 24 mg/1.2 ml 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.

Somatrogon 60 mg/1.2 ml 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.

List of Excipients

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

3. DOSAGE FORM AND STRENGTH

Solution for injection
Somatrogon 24 mg/1.2 ml solution for injection in pre-filled pen
Somatrogon 60 mg/1.2 ml solution for injection in pre-filled pen

All strengths/presentations mentioned in this document might not be available in the market.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Somatrogon 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 Contraindications). 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. 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.

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

Somatrogon 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).

Somatrogon 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 8.4 (Storage and Handling Instructions) and at the end of the package leaflet.

4.3 Contraindications

Hypersensitivity to somatrogon (see section 4.4 Special Warnings and Precautions for Use) or to any of the excipients listed in section 2 (Qualitative and Quantitative Composition).

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 Special Warnings and Precautions for Use).

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 Special Warnings and Precautions for Use).

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 Contraindications).

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 Drugs Interactions). 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 Drugs Interactions).

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 Drugs Interactions and 4.8 Undesirable Effects).

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 Drugs Interactions).

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. 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 Posology and Method of Administration). 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 Drugs Interactions).

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 Drugs Interactions

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 Special Warnings and Precautions for Use).

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 Special Warnings and Precautions for Use).

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 Special Warnings and Precautions for Use).

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 Special Warnings and Precautions for Use).

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 Use in Special Populations

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 Pharmacokinetic Properties).

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 Pharmacokinetic Properties). Somatrogon is not recommended during pregnancy and in women of childbearing potential not using contraception.

Lactation

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.

4.7 Effects on Ability to Drive and Use Machines

Somatrogon 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 Mechanism of Action). The data reflect exposure of 265 patients to somatrogon administered once weekly (0.66 mg/kg/week).

Table 1 presents the adverse reactions 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					
Eye disorders		Conjunctivitis allergic				
Skin and subcutaneous tissue disorders			Rash generalised			
Musculoskeletal and connective tissue disorders		Arthralgia Pain in extremity				
General disorders and administration site conditions	Injection site reactions[a] Pyrexia					

[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 Special Warnings and Precautions for Use).
- Metabolism and nutrition disorders: diabetes mellitus type 2 (see section 4.4 Special Warnings and Precautions for Use).
- Nervous system disorders: benign intracranial hypertension (see section 4.4 Special Warnings and Precautions for Use), 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 Special Warnings and Precautions for Use).

Metacresol
This medicinal product contains metacresol which may contribute to painful injections (see section 4.4 Special Warnings and Precautions for Use).

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.

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 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.

5.2 Pharmacodynamic Properties

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

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 HT 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 somatrogon 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 Posology and Method of Administration for information on paediatric use).

5.3 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.

6. NONCLINICAL PROPERTIES

6.1. Animal Toxicology or Pharmacology

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.

7. DESCRIPTION

Solution for injection (injection).

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

Somatrogon 24 mg solution for injection in pre-filled pen

Pack size of 1 pre-filled pen.

Somatrogon 60 mg solution for injection in pre-filled pen

Pack size of 1 pre-filled pen.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

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

8.2 Shelf -life

36 months

8.3 Packaging Information

Somatrogon 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.

Somatrogon 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.

All pack presentation may not available for market in India

8.4 Storage and Handling Instructions

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

Before first use

3 years at 2 °C to 8 °C.
Prior to the first use store somatrogon 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 somatrogon with the pen cap attached in order to protect from light.

Somatrogon 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 somatrogon to the refrigerator again after each use. Do not expose somatrogon to temperatures above 32 °C or leave at room temperature for more than 4 hours with each use. The somatrogon 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.

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 Somatrogon pre-filled pen is for use by a single patient. A somatrogon 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 Somatrogon 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 somatrogon 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.

Sterile needles are required for administration but are not included. Somatrogon can be administered with a needle from 4 mm to 8 mm and 31 or 32G.

Instructions for the preparation and administration of the product are given in the 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.

Instructions for use
Somatrogon 24 mg Pen Injection for subcutaneous (under the skin) use only

These instructions show step-by-step directions on how to prepare and give a Somatrogon injection.

Important information about your Somatrogon pen

- Somatrogon for injection is a multi-dose pre-filled pen containing 24 mg of medicine.
- Somatrogon for injection can be given by a patient, caregiver, doctor, nurse or pharmacist. Do not try to inject Somatrogon 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 Somatrogon at home, you should receive training on the right way to prepare and inject Somatrogon. It is important that you read, understand, and follow these instructions so that you inject Somatrogon the right way. It is important to talk to your doctor, nurse or pharmacist to be sure you understand your Somatrogon dosing instructions.
- To help you remember when to inject Somatrogon, 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 Somatrogon.
- 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.
- 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

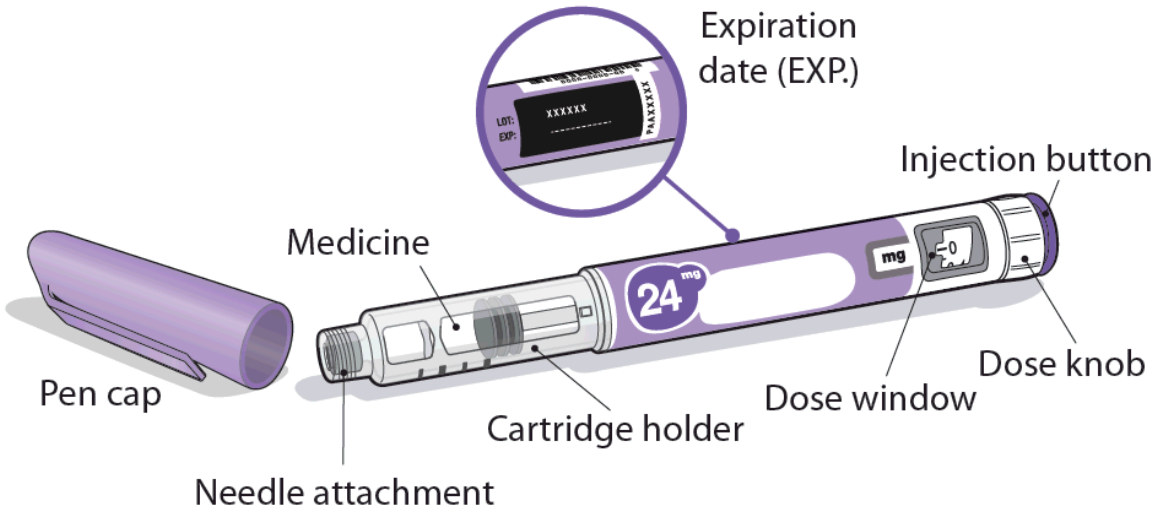
Included in the carton:

- 1 Somatrogon 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.

Somatrogon 24 mg pen:

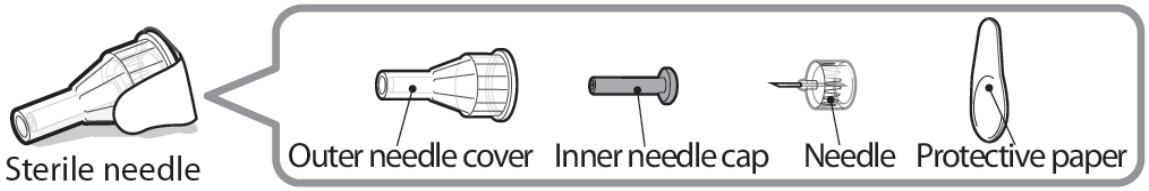


Needles to use

Pen needles are not included with your Somatrogon pen. You can use pen needles from 4 mm to 8 mm.

- Needles to use with your Somatrogon pen:
  - 31G or 32G
- Talk with your doctor, nurse or pharmacist about the right needle for you.

Sterile needle (example) not supplied:



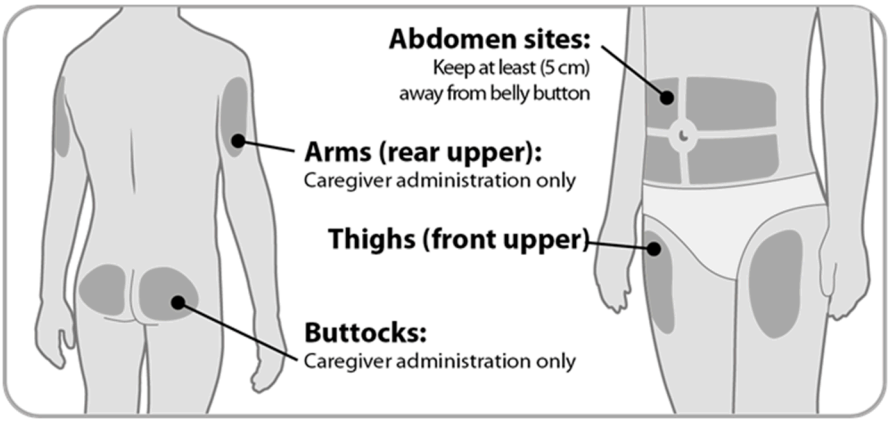
Caution: Never use a bent or damaged needle. Always handle pen needles with care to make sure you do not prick yourself (or anyone else) with the needle. **Do not** attach a new needle to your pen until you are ready for your injection.

Preparing for your injection

Step 1 Getting ready

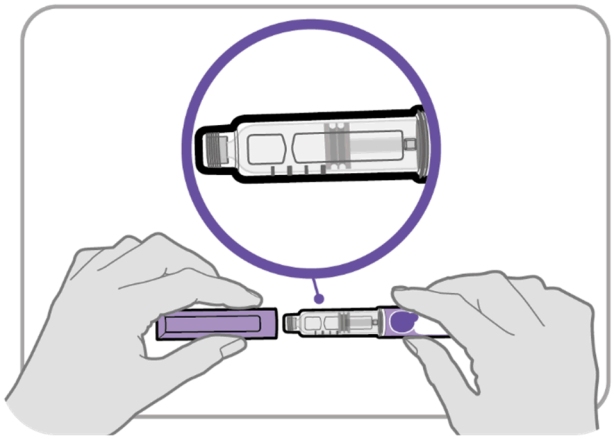
- Wash and dry your hands.
- You can use your pen straight from the refrigerator. For a more comfortable injection, leave your pen at room temperature for up to 30 minutes. (**See section 8.4 "How to store Somatrogon" of the Somatrogon 24 mg pre-filled pen Package Leaflet**).
- Check the name, strength, 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 8.4 "How to store Somatrogon" of the Somatrogon 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



- Somatrogon 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.
- 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.

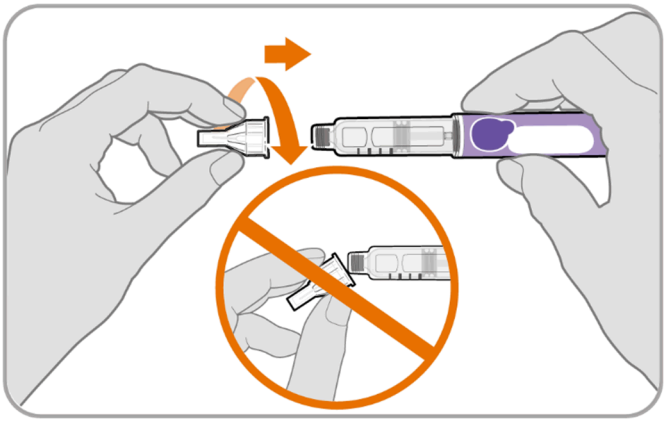
Step 3 Check medicine



- 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



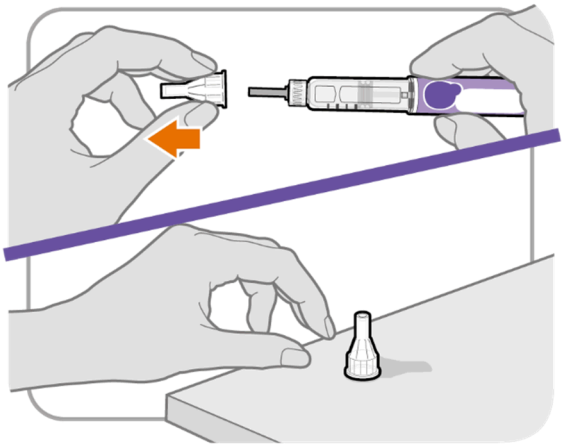
- Take a new needle and pull off the protective paper.
- Line the needle up with your pen keeping them both straight.
- Gently push and then screw the needle onto your pen.

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.

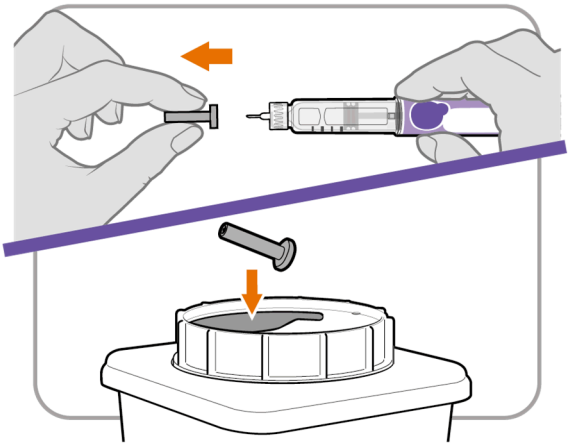
Step 5 Pull off outer needle cover



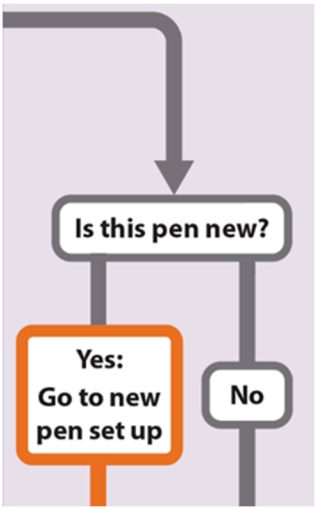
- Pull off the outer needle cover.
- Make sure you keep the outer needle cover. You will need it later to remove the needle.

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.

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.



('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')

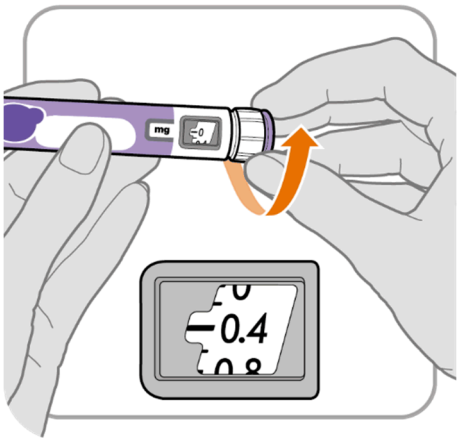
New pen set up (priming) – for the first use of a new pen only

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.

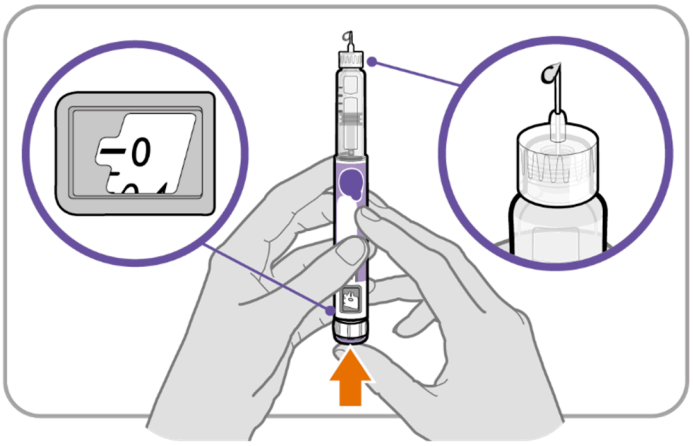
Note: If you turn the dose knob too far, you can turn it back.

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

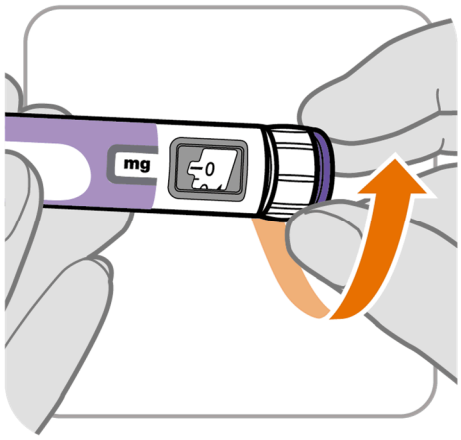


- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.
- **Check** for liquid at the needle tip. If liquid appears, your pen is set up.
- Always make sure that a drop of liquid appears before you inject. If liquid has not appeared, repeat Step-A through 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.

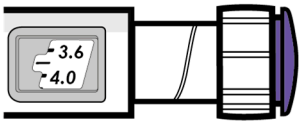
Do not use the pen if a drop of liquid still does not appear. Contact your doctor, nurse or pharmacist, and use a new pen.

Setting your prescribed dose

Step 7 Set your dose

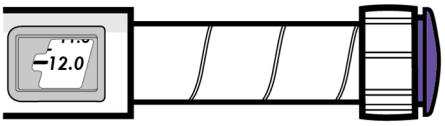


Example A:



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?

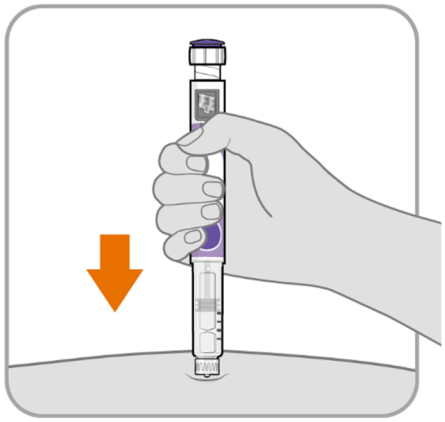
- If your pen contains less than 12 mg of medicine, the dose knob will stop with the remaining amount of medicine shown in the dose window.
- If there is not enough medicine left in your pen for your full dose, you may either:
  - inject the amount left in your pen, then prepare a new pen to complete 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.

- o or get a new pen and inject the full dose.

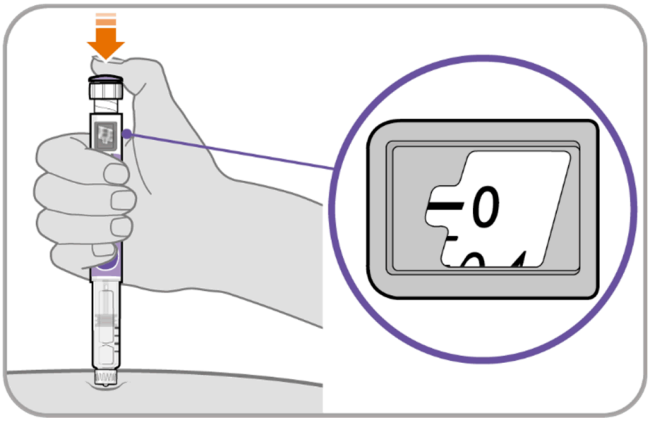
Injecting your dose

Step 8 Insert the needle



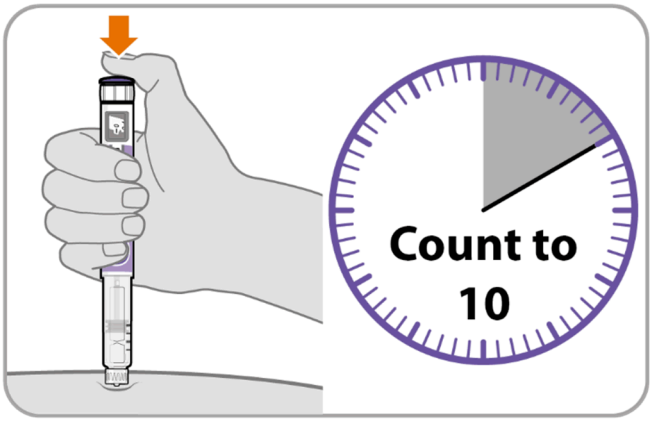
- Hold your pen so you can see the numbers in the dose window.
- Insert the needle straight into your skin.

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.

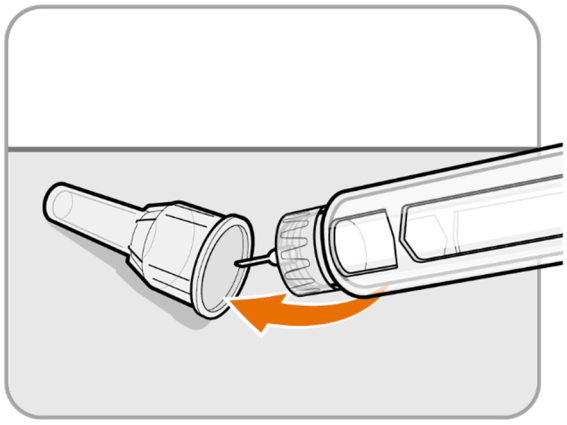
Step 10 Count to 10



- **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.

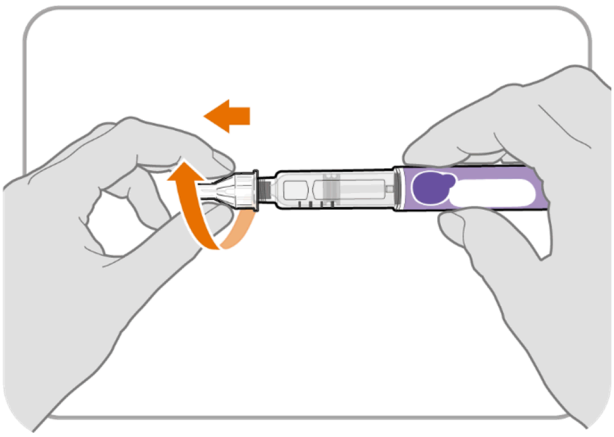
Step 11 Attach outer needle cover



- 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.

Step 12 Remove the needle

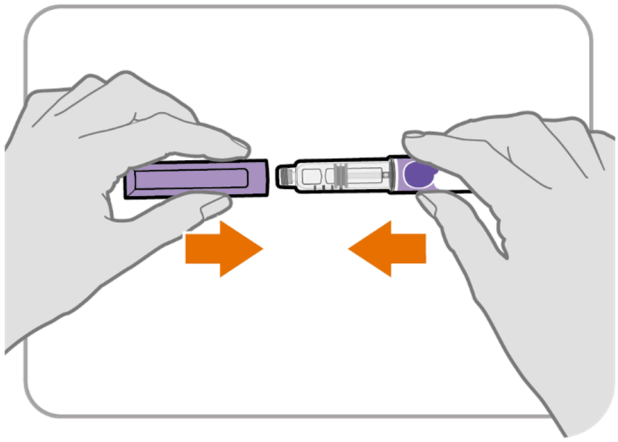


- Unscrew the capped needle from the pen.
- Gently pull until the capped needle comes off.

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 8.4 "How to store Somatrogon" of the Somatrogon 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 _____ / _____ / _____

Instructions for use
Somatrogon 60 mg Pen Injection for subcutaneous (under the skin) use only
These instructions show step-by-step directions on how to prepare and give a Somatrogon injection.

Important information about your Somatrogon pen

- Somatrogon for injection is a multi-dose pre-filled pen containing 60 mg of medicine.
- Somatrogon for injection can be given by a patient, caregiver, doctor, nurse or pharmacist. **Do not** try to inject Somatrogon 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 Somatrogon at home, you should receive training on the right way to prepare and inject Somatrogon. It is important that you read, understand, and follow these instructions so that you inject Somatrogon the right way. It is important to talk to your doctor, nurse or pharmacist to be sure you understand your Somatrogon dosing instructions.
- To help you remember when to inject Somatrogon, 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 Somatrogon.
- 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.
- 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

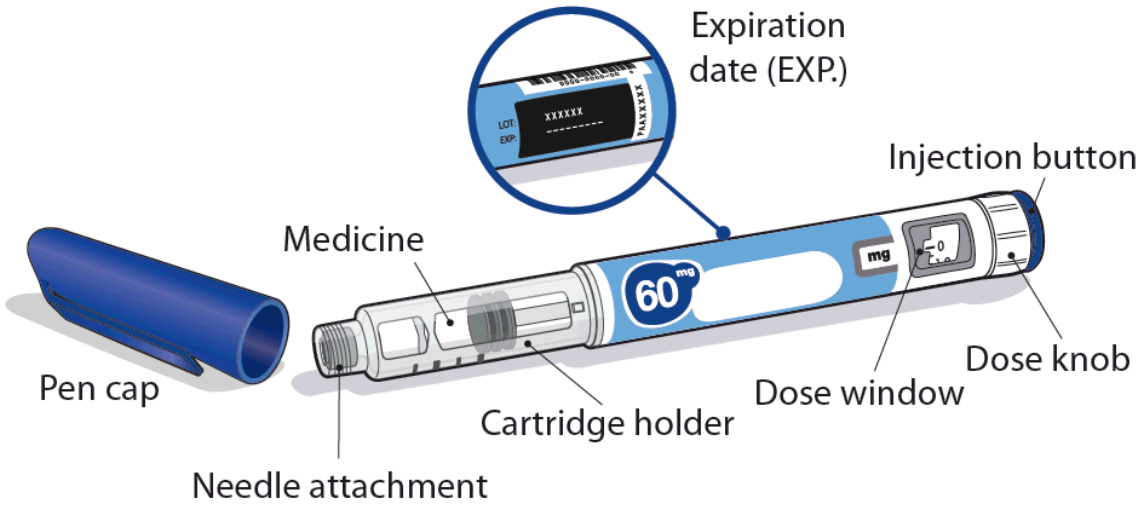
Included in the carton:

- 1 Somatrogon 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.

Somatrogon 60 mg pen:

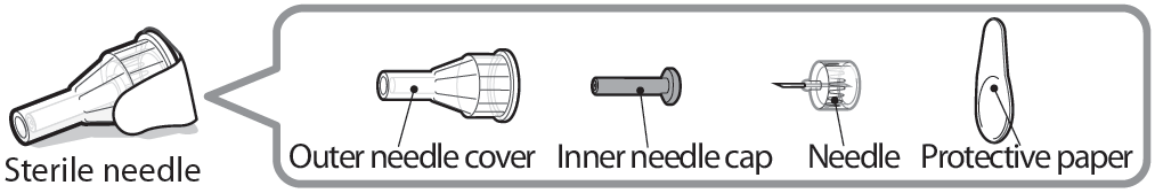


Needles to use

Pen needles are **not included** with your Somatrogon pen. You can use pen needles from 4 mm to 8 mm.

- Needles to use with your Somatrogon pen:
  - 31G or 32G
- Talk with your doctor, nurse or pharmacist about the right needle for you.

Sterile needle (example) not supplied:



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

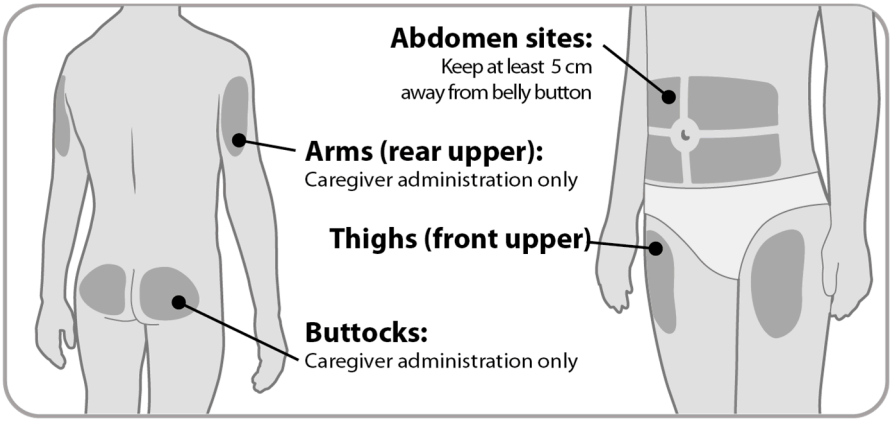
Step 1 Getting ready

- 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 Somatrogon" of the Somatrogon 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 8.4 "How to store Somatrogon" of the Somatrogon 60 mg pre filled pen Package Leaflet**).
- it has been dropped
- it looks broken or damaged

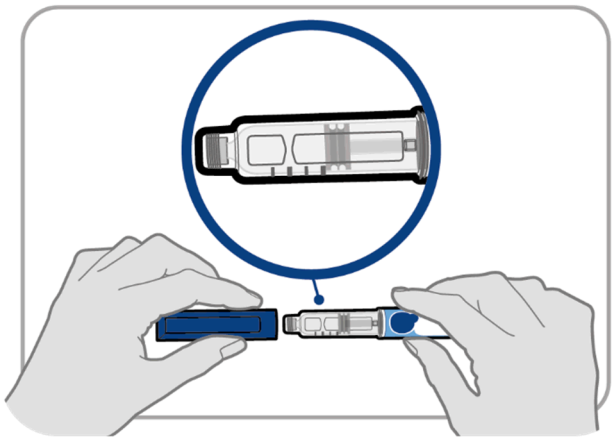
- **Do not** remove the pen cap from your pen - until you are ready to inject.

Step 2 Choose and clean your injection site



- Somatrogon 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.
- 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

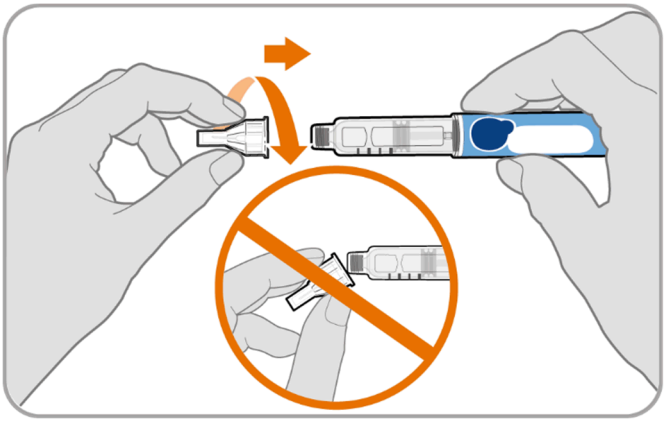


- Pull off the pen cap and keep it for after your injection.
- Check the medicine inside the cartridge holder.

- 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



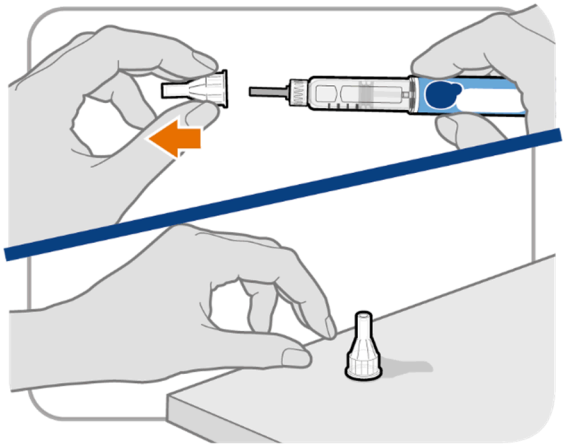
- Take a new needle and pull off the protective paper.
- Line the needle up with your pen keeping them both straight.
- Gently push and then screw the needle onto your pen.

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.

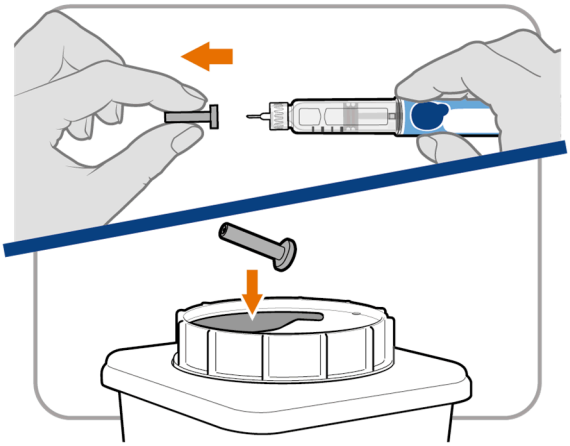
Step 5 Pull off outer needle cover



- 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.

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.

('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')

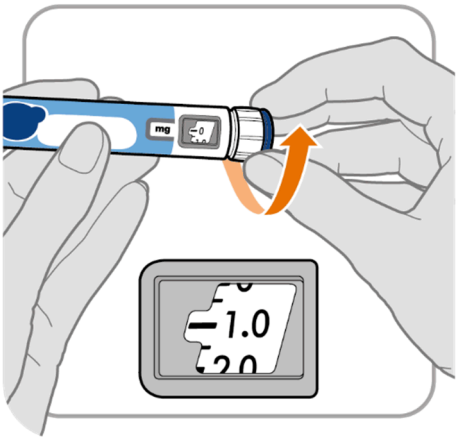
New pen set up (priming) – for the first use of a new pen only

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**.

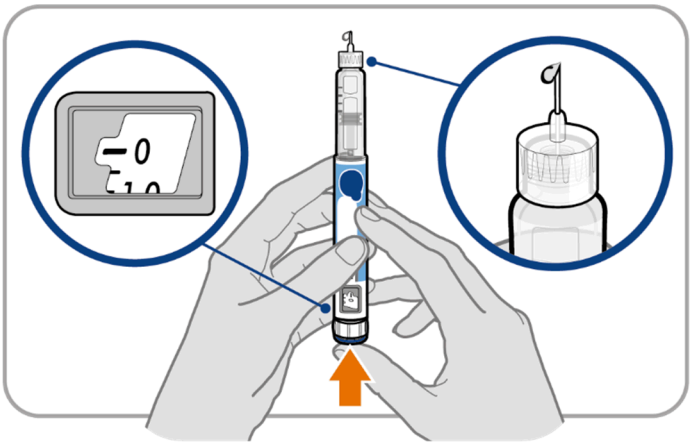
Note: If you turn the dose knob too far, you can turn it back.

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

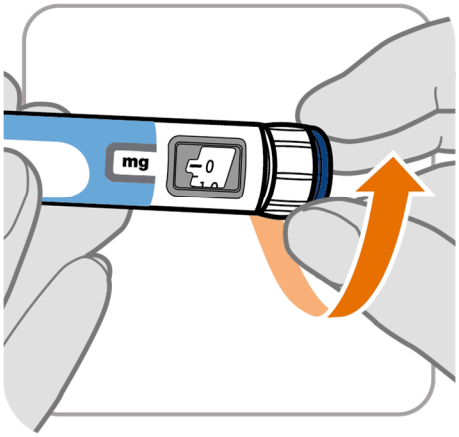


- **Press the injection button** until it cannot go any further and **"0"** is shown in the dose window.
- **Check** for liquid at the needle tip. If liquid appears, your pen is set up.
- Always make sure that a drop of liquid appears before you inject. If liquid has not appeared, repeat Step-A through 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.

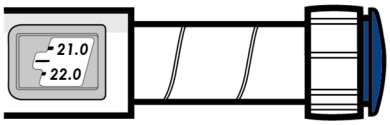
Do not use the pen if a drop of liquid still does not appear. Contact your doctor, nurse or pharmacist, and use a new pen.

Setting your prescribed dose

Step 7 Set your dose

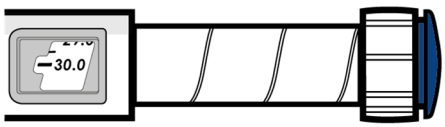


Example A:



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?

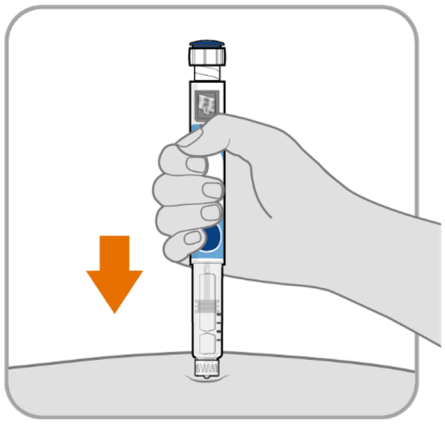
- If your dose is more than 30 mg you will need more than 1 injection.
- You can give from 0.5 mg to 30 mg in a single injection.
  - If you need help dividing up your dose the right way, ask your doctor, nurse or pharmacist.
  - Use a new needle for each injection (**See Step 4: Attach needle**).
 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

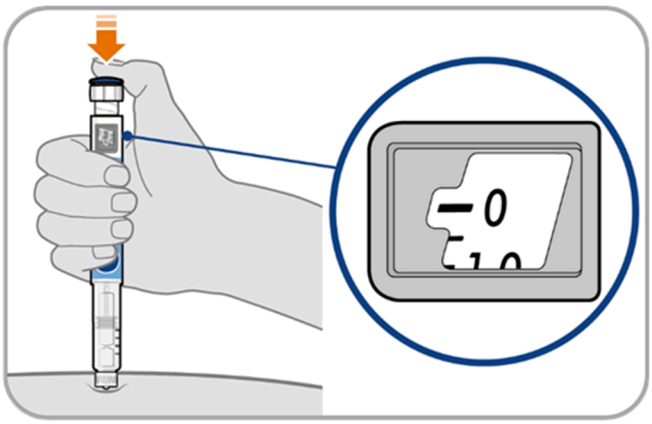
Injecting your dose

Step 8 Insert the needle



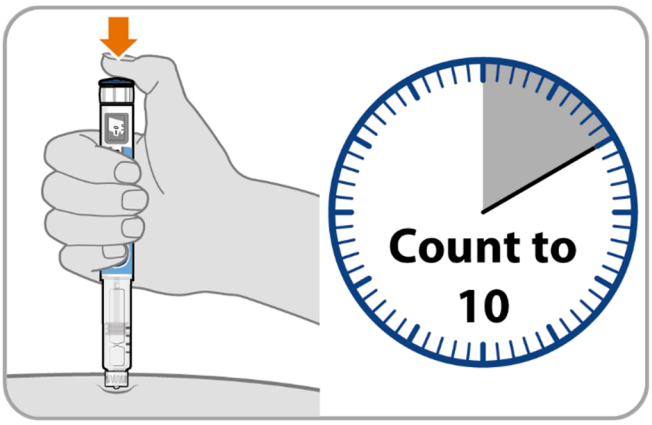
- Hold your pen so you can see the numbers in the dose window.
- Insert the needle straight into your skin.

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.

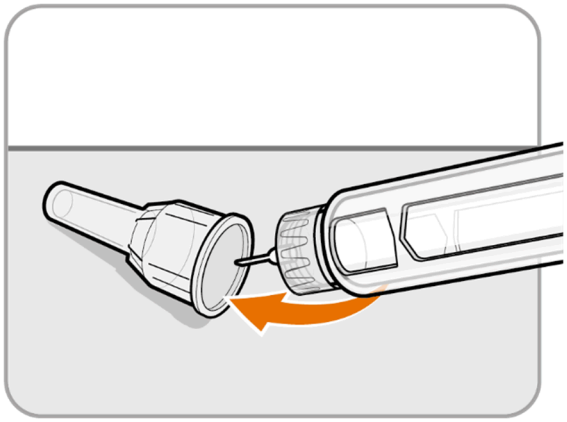
Step 10 Count to 10



- **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.

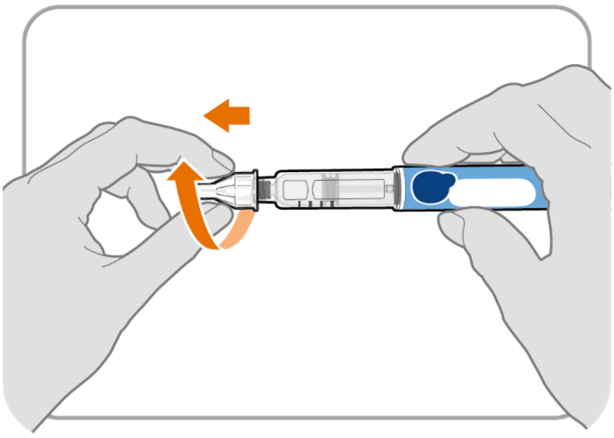
Step 11 Attach outer needle cover



- 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.

Step 12 Remove the needle

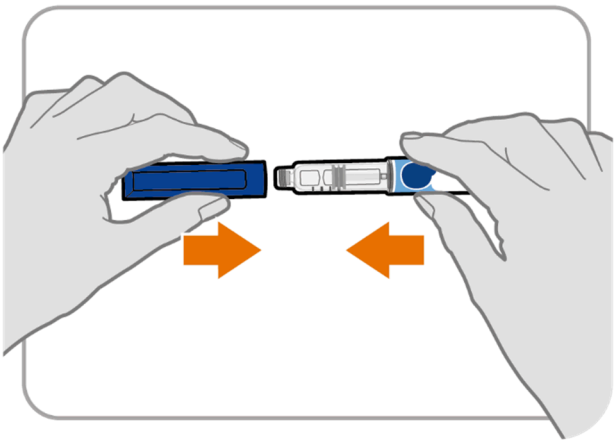


- Unscrew the capped needle from the pen.
- Gently pull until the capped needle comes off.

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 8.4 "How to store somatrogon" of the somatrogon 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 _____ / _____ / _____

9. PATIENT COUNSELLING INFORMATION

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 Special Warnings and Precautions for Use).

The patient should receive training to ensure understanding of the administration procedure to support self-administration. The patient should also receive information regarding storage of the product.

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

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

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 Undesirable Effects).

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

10. DETAILS OF MANUFACTURER

M/s. Pfizer manufacturing Belgium NV, Rijksweg 12, 2870, Purrs, Belgium

Imported by:

Pfizer Products India Pvt. Ltd., The Capital-B wing, 1802,18th Floor, Plot No. C-70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai, India

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

IMP/BIO/22/000055 dated 12 -August- 2022

12. DATE OF REVISION

January 2023