PT. Pfizer Indonesia
Local Product Document

Product Document Title: Recombinant Somatropin
Trade Name: Genotropin GoQuick
CDS Effective Date: August 12, 2019
Supersedes: July 20, 2018

COMPOSITION

Genotropin GoQuick: A two compartment cartridge, the front part content includes recombinant somatropin 5.3 mg, glycine 2.0 mg, mannitol 41 mg, sodium dihydrogen phosphate anhydr. 0.29 mg and disodium phosphate 0.28 mg; and the rear part content includes m-cresol 3.0 mg and water for injection to 1 mL. The two compartment cartridge is sealed in a disposable multidose pre-filled pen.

PROPERTIES

Genotropin GoQuick contains somatropin, human growth hormone, produced by recombinant DNA-technology. Contents and sequence of amino acids are identical with human hypophyseal growth hormone. Somatropin promotes growth partly by stimulating somatomedin and protein synthesis. In subcutaneous injection approx. 80% is absorbed. Maximal plasma concentration is obtained after approx. 5 hours. The half-life is approx. 4 hours.

Somatropin is synthesized in *E. coli* bacteria. The synthesis takes place via a pre-hormone consisting of growth hormone linked to a signal peptide occurring naturally in the bacterium. The pre-hormone is split in the inner cell wall of the bacterium, releasing growth hormone into the periplasmic space. Growth hormone is then harvested through careful disruption of the outer cell wall of the bacterium. The inner cell wall remains in the principle intact.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Somatropin is a potent metabolic hormone of importance for the metabolism of lipids, carbohydrates and proteins. In children with inadequate endogenous growth hormone, somatropin stimulates linear growth and increases growth rate. In adults, as well as in children, somatropin maintains a normal body composition by increasing nitrogen retention and stimulation of skeletal muscle growth, and by mobilisation of body fat. Visceral adipose tissue is particularly responsive to somatropin. In addition to enhanced lipolysis, somatropin decreases the uptake of triglycerides into body fat stores. Serum concentrations of IGF-I (Insulin-like Growth Factor-I) and IGFBP3 (Insulin-like Growth Factor Binding Protein 3) are increased by somatropin. In addition, the following actions have been demonstrated:

– Lipid metabolism: Somatropin induces hepatic LDL cholesterol receptors, and affects the profile of serum lipids and lipoproteins. In general, administration of somatropin to growth

hormone deficient patients results in reductions in serum LDL and apolipoprotein B. A reduction in serum total cholesterol may also be observed.

– Carbohydrate metabolism: Somatropin increases insulin but fasting blood glucose is commonly unchanged. Children with hypopituitarism may experience fasting hypoglycaemia. This condition is reversed by somatropin.

– Water and mineral metabolism: Growth hormone deficiency is associated with decreased plasma and extracellular volumes. Both are rapidly increased after treatment with somatropin. Somatropin induces the retention of sodium, potassium and phosphorus.

– Bone metabolism: Somatropin stimulates the turnover of skeletal bone. Long-term administration of somatropin to growth hormone deficient patients with osteopenia results in an increase in bone mineral content and density at weight-bearing sites.

– Physical capacity: Muscle strength and physical exercise capacity are improved after long-term treatment with somatropin. Somatropin also increases cardiac output, but the mechanism has yet to be clarified. A decrease in peripheral vascular resistance may contribute to this effect.

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

Pharmacokinetic Properties

Absorption
The bioavailability of subcutaneously administered somatropin is approximately 80% in both healthy subjects and growth hormone deficient patients. A subcutaneous dose of 0.035 mg/kg of somatropin results in plasma C_{max} and t_{max} values in the range of 13-35 ng/mL and 3-6 hours, respectively.

Following a 0.03 mg/kg subcutaneous (SC) injection in the thigh of 1.3 mg/mL GENOTROPIN GoQuick to adult GHD patients, approximately 80% of the dose was systemically available as compared with that available following intravenous dosing. Results were comparable in both male and female patients. Similar bioavailability has been observed in healthy adult male subjects.

In healthy adult males, following an SC injection in the thigh of 0.03 mg/kg, the extent of absorption (AUC) of a concentration of 5.3 mg/mL GENOTROPIN GoQuick was 35% greater than that for 1.3 mg/mL GENOTROPIN GoQuick. The mean (±standard deviation) peak (C_{max}) serum levels were 23.0 (±9.4) ng/mL and 17.4 (±9.2) ng/mL, respectively.

In a similar study involving pediatric GHD patients, 5.3 mg/mL GENOTROPIN GoQuick yielded a mean AUC that was 17% greater than that for 1.3 mg/mL GENOTROPIN GoQuick. The mean C_{max} levels were 21.0 ng/mL and 16.3 ng/mL, respectively.

Adult GHD patients received two single SC doses of 0.03 mg/kg of GENOTROPIN GoQuick at a concentration of 1.3 mg/mL, with a one- to four-week washout period between injections. Mean C_{max} levels were 12.4 ng/mL (first injection) and 12.2 ng/mL (second injection), achieved at approximately six hours after dosing.

There are no data on the bioequivalence between the 12-mg/mL formulation and either the 1.3-mg/mL or the 5.3-mg/mL formulations.

Distribution
The mean volume of distribution of GENOTROPIN GoQuick following administration to GHD adults was estimated to be 1.3 (±0.8) L/kg.

Metabolism
The metabolic fate of GENOTROPIN GoQuick involves classical protein catabolism in both the liver and kidneys. In renal cells, at least a portion of the breakdown products are returned to the systemic circulation. The mean terminal half-life of intravenous GENOTROPIN GoQuick in normal adults is 0.4 hours, whereas subcutaneously administered GENOTROPIN GoQuick has a half-life of 3.0 hours in GHD adults. The observed difference is due to slow absorption from the subcutaneous injection site.

Excretion
The mean clearance of subcutaneously administered GENOTROPIN GoQuick in 16 GHD adult patients was 0.3 (±0.11) L/hrs/kg.

Special Populations
Pediatric: The pharmacokinetics of GENOTROPIN GoQuick are similar in GHD pediatric and adult patients.

Gender: No gender studies have been performed in pediatric patients; however, in GHD adults, the absolute bioavailability of GENOTROPIN GoQuick was similar in males and females.

Race: No studies have been conducted with GENOTROPIN GoQuick to assess pharmacokinetic differences among races.

Renal or hepatic insufficiency: Information about the pharmacokinetics of somatropin in patients with renal or hepatic insufficiency is either lacking or incomplete.

Elimination: The mean terminal half-life of somatropin after intravenous administration in growth hormone deficient adults is about 0.4 hours. However, after subcutaneous administration, half-lives of 2-3 hours are achieved. The observed difference is likely due to slow absorption from the injection site following subcutaneous administration.

Sub-populations: The absolute bioavailability of somatropin seems to be similar in males and females following s.c. administration.

Information about the pharmacokinetics of somatropin in geriatric and paediatric populations, in different races and in patients with renal, hepatic or cardiac insufficiency is either lacking or incomplete.

Preclinical Safety Data

In studies regarding general toxicity, local tolerance and reproduction toxicity no clinically relevant effects have been observed.

In vitro and *in vivo* genotoxicity studies on gene mutations and induction of chromosome aberrations have been negative.

An increased chromosome fragility has been observed in one *in-vitro* study on lymphocytes taken from patients after long-term treatment with somatropin and following the addition of the radiomimetic drug bleomycin. The clinical significance of this finding is unclear.

In another study, no increase in chromosomal abnormalities was found in the lymphocytes of patients who had received long-term somatropin therapy.

INDICATION

Somatropin is indicated for the long-term treatment of children with growth disturbance due to the following conditions:

- Insufficient secretion of growth hormone.
- Turner syndrome.
- Chronic renal insufficiency.
- Born small for gestational age.
- Prader-Willi syndrome.
- Pre Pubertas idiopathic short stature.

Somatropin is also indicated for improvement of body composition in children with Prader-Willi syndrome.

Somatropin is indicated for replacement therapy in adults with growth hormone deficiency.

CONTRAINDICATION

Somatropin is contraindicated in patients who have evidence of neoplastic activity and in patients with uncontrolled growth of benign intracranial tumors. Anti-tumor therapy must be completed prior to starting somatropin.

Somatropin is contraindicated in patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma, or acute respiratory failure. Two placebo-controlled clinical trials (N=522), conducted in adult patients to evaluate the effects of somatropin 5.3 or 8 mg (16 or 24 IU) on length of stay in intensive care units, showed significantly higher mortality (41.9% versus 19.3%) in patients treated with somatropin compared with those who received placebo (see **SPECIAL WARNINGS AND PRECAUTIONS FOR USE** in patients who are receiving somatropin for growth hormone replacement).

Somatropin is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment (see **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

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

Somatropin is contraindicated in patients with acute catabolism, including pre- and post-operative treatment, critically ill patients and burn patients.

Hypersensitivity to the active substance or to any of the excipients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

There have been reports of fatalities associated with the use of growth hormone in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of respiratory impairment or sleep apnea, or unidentified respiratory infection. Another possible risk factor may be male gender. Patients with Prader-Willi syndrome should be evaluated for upper airway obstruction, sleep apnoea, or respiratory inspections before initiation of treatment with somatropin. If during treatment with somatropin patients show signs of upper airway obstruction (including onset of or increased snoring), treatment should be interrupted. All patients with Prader-Willi syndrome should be evaluated for sleep apnea and monitored if sleep apnea is suspected. These patients should also have effective weight control and be monitored for signs of respiratory infections, which should be diagnosed as early as possible and treated aggressively.

Myositis is a very rare adverse event that may be related to the preservative m-cresol. If myalgia or disproportionate pain at injection site develops, myositis should be considered and, if confirmed, a presentation of somatropin without m-cresol should be used.

Somatropin reduces insulin sensitivity and therefore patients should be observed for evidence of glucose intolerance. In rare cases, therapy with somatropin may produce sufficient glucose intolerance to meet the diagnostic criteria for Type 2 diabetes mellitus. The risk of developing diabetes during treatment with somatropin is greatest in those patients with other risk factors for Type 2 diabetes mellitus, such as obesity, family history of diabetes, treatment with steroids, or prior impaired glucose tolerance. In patients with pre-existing diabetes mellitus, the dose of anti-diabetic therapy might require adjustment when somatropin is instituted.

In general, peripheral thyroid hormone levels remain within the normal reference range during treatment with somatropin. However, there is an enhanced conversion of T4 to T3 that may result in a reduction in serum T4 and an increase in serum T3 concentrations. This effect may be of clinical relevance for patients with central subclinical hypothyroidism in whom hypothyroidism may theoretically develop. Conversely, mild hyperthyroidism may occur in patients receiving replacement therapy with thyroxin. It is therefore advisable to test thyroid function shortly after the start of treatment with somatropin, and after dose adjustments.

Introduction of somatropin treatment may result in inhibition of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD-1) and reduced serum cortisol concentrations. In patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked and glucocorticoid replacement may be required. In addition, patients treated with glucocorticoid replacement therapy for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses, following initiation of somatropin treatment (see **Interactions**).

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

In patients with growth hormone deficiency secondary to treatment of malignant disease, it is recommended to monitor for signs of relapse of the malignancy.

Therapy with Genotropin GoQuick should be directed by physicians who are experienced in the diagnosis and management of patients with growth hormone deficiency.

Excessive glucocorticoid therapy will inhibit the growth promoting effect of human growth hormone.

Patients with co-existing ACTH deficiency should have their glucocorticoid replacement dose carefully adjusted to avoid an inhibitory effect on growth.

In patients with endocrine disorders, including growth hormone deficiency, slipped epiphyses of the hip may occur more frequently than in the general population. Children who develop a limp during treatment with somatropin should be evaluated. (see **UNDESIRABLE EFFECTS**).

In case of severe or recurrent headache, visual problems, nausea, or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed, a diagnosis of benign intracranial hypertension should be considered and, if appropriate, growth hormone treatment should be discontinued. At present, there is insufficient evidence to guide the decision of whether or not to reintroduce growth hormone therapy in patients with resolved intracranial hypertension. If growth hormone treatment is restarted, careful monitoring for symptoms of intracranial hypertension is necessary.

Progression of scoliosis can occur in patients who experience rapid growth. Because growth hormone increases growth rate, physicians should be alert to this abnormality, which may manifest during growth hormone therapy. Scoliosis is commonly seen in patients with Prader-Willi syndrome.

In patients with chronic renal insufficiency, renal function should be below 50% of normal before institution of therapy with somatropin. To verify growth disturbance, growth should be followed for a year preceding institution of therapy. Conservative treatment for renal insufficiency should have been established and should be maintained during therapy with growth hormone. Somatropin should be discontinued at renal transplantation. To date, no data on final height in patients with chronic renal insufficiency treated with Genotropin GoQuick are available. If patients who are receiving growth hormone replacement therapy become acutely critically ill, the potential benefit of continued treatment with somatropin should be weighed against the potential risk (see **CONTRAINDICATION**).

Somatropin is ineffective for growth promotion in children with closed epiphyses.

In short children born SGA other medical reasons or treatments that could explain growth disturbance should be ruled out before starting treatment. Experience with prolonged treatment in adults and in patients with PWS is limited.

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

In SGA children it is recommended to measure the IGF-I level before start of treatment and twice a year thereafter. If on repeated measurements IGF-I levels exceed +2SD compared to references for age and pubertal status, the IGF-I/IGFBP-3 ratio could be taken into account to consider dose adjustment.

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

Clinical studies indicated that the treatment of Genotropin GoQuick for the “acute catabolism, including pre and post-operative treatment, critically ill patients and burn patients”, has been reported that the side effect of Jacob-Creutzfeldt Syndrome (subacute spongioform encephalopathy), which is slow-virus disease in the Central Nervous System, characterized by the progressive dementia, myoclonic convulsion which attacked adults and old aged, and can cause death. Therefore, Genotropin GoQuick is not recommended to use for those indications.

Fertility, pregnancy and lactation
Animal reproduction studies have not shown evidence of harmful effects on the fetus. Treatment with Somatropin should be interrupted if pregnancy occurs. There are, however, no studies in pregnant women. Because animal reproduction studies are not always predictive of human response, somatropin should be used during pregnancy only if clearly needed.

During normal pregnancy, the levels of pituitary growth hormone markedly fall after week 20 of gestation, being replaced almost entirely by placental growth hormone by week 30. Therefore, it is unlikely that continued replacement therapy with somatropin would be necessary in growth hormone deficient women during the third trimester of pregnancy.

It is not known if somatropin is excreted into breast milk, but absorption of intact protein from the gastrointestinal tract of the infant is extremely unlikely.

Effects on ability to drive and use machines
No effects on the ability to drive and use machines have been observed.

UNDESIRABLE EFFECTS

Patients with growth hormone deficiency are characterized by extracellular volume deficit. When treatment with somatropin is started, this deficit is rapidly corrected. In general, in adult patients, adverse effects related to fluid retention, such as oedema peripheral, face oedema, musculoskeletal stiffness, arthralgia, myalgia and paraesthesia are mild to moderate, arise within the first months

of treatment, and subside spontaneously or with dose-reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

Tabulated list of adverse reactions

Table 1 shows the adverse reactions ranked under headings of System Organ Class and frequency for children and adults separately, 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); not known (cannot be estimated from the available data).

Table 1: Tabulated List of Adverse Reactions

System Organ Class	Very Common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Very Rare (<1/10,000)	Frequency Not Known (Cannot be estimated from the available data)
Neoplasms Benign, Malignant, and Unspecified (Including cysts and polyps)				(Children) leukaemia		
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders		(Adults) paraesthesia	(Children) paraesthesia	(Children) benign intracranial hypertension		(Adults) benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders			(Children) rash*, pruritus*, urticaria*			(Adults) rash*, pruritus*, urticaria*
Musculoskeletal and Connective Tissue Disorders	(Adults) arthralgia	(Adults) myalgia (Children) arthralgia (Adults) musculoskeletal stiffness		(Children) myalgia		(Children) musculoskeletal stiffness
General Disorders and Administration Site Conditions	(Adults) oedema peripheral	(Children) injection-site reactions	(Children) oedema peripheral			(Adults) injection-site reaction, (Adults & Children)

Table 1: Tabulated List of Adverse Reactions

System Organ Class	Very Common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Very Rare (<1/10,000)	Frequency Not Known (Cannot be estimated from the available data)
						face oedema
Investigations						Blood cortisol decreased

* ADR identified post-marketing

Transient injection site reactions in children have been reported.

Somatropin has been reported to reduce serum cortisol levels, possibly by affecting carrier proteins or by increased hepatic clearance. The clinical relevance of these findings may be limited. Nevertheless, corticosteroid replacement therapy should be optimised before initiation of Genotropin GoQuick therapy. Carpal tunnel syndrome is an uncommon event among adults.

Somatropin has given rise to the formation of antibodies in approximately 1% of patients. The binding capacity of these antibodies has been low and no clinical changes have been associated with their formation.

Rare cases of leukaemia have been reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Reactions at the site of injection have been reported, such as itching; lumps, redness and lipoatrophy.

Genotropin GoQuick has given rise to the formation of antibodies to growth hormone and *E. coli* protein in a small number of patients.

The binding capacity of these antibodies has been low and without clinical significance. Investigation of eventual formation of antibodies should be performed if expected effect on the growth does not take place.

In the post-marketing experience rare cases of sudden death have been reported in patients affected by Prader-Willi syndrome treated with somatropin, although no causal relationship has been demonstrated.

Slipped capital femoral epiphysis and Legg-Calve-Perthes disease have been reported in children treated with growth hormone. No causal relationship has been demonstrated with somatropin.

Interactions

Concomitant treatment with glucocorticoids inhibits the growth-promoting effects of somatropin containing products. 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 **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Administration of somatropin may increase the clearance of compounds metabolized by cytochrome P4503A4 (e.g., sex steroids, corticosteroids, anticonvulsants, and cyclosporin). The clinical significance of this potential interaction is unknown.

In women on oral oestrogen replacement, a higher dose of growth hormone may be required to achieve the treatment goal (see **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Overdose
Acute overdosage could lead initially to hypoglycaemia and subsequently to hyperglycaemia. Long-term overdosage could result in signs and symptoms consistent with the effects of human growth hormone excess.

DOSAGE AND ADMINISTRATION
The dosage and administration schedule should be individualized. Somatropin should be given subcutaneously and the injection site varied to prevent lipoatrophy.

Table 2: Dosage Recommendations for Pediatric Patients

Indication	Daily Dose			
	mg/kg body weight	IU/kg body weight	mg/m² body surface area	IU/m² body surface area
Growth hormone deficiency	0.025 – 0.035	0.07 - 0.10	0.7 - 1.0	2.1 - 3.0
Turner syndrome	0.045 - 0.050	0.14	1.4	4.3
Chronic renal insufficiency	0.045 - 0.050	0.14	1.4	4.3
Prader-Willi syndrome	0.035	0.10	1.0	3.0
Small for gestational age	0.035 – 0.067	0.10 – 0.20	1.0 – 2.0	3.0 - 6.0
Pre-pubertas idiopathic short stature	Up to 0.067	Up to 0.20	Up to 2.0	Up to 6.0

Dosage Recommendations for Adult Patients with Growth Hormone Deficiency
The recommended starting dose is 0.15 to 0.30 mg (0.45 to 0.90 IU) per day. The final dose should be individually titrated as needed with respect to age and gender. The daily maintenance dose seldom exceeds 1.3 mg (4 IU) per day. Women may require higher doses than men. This means that there is a risk that women, especially those on oral oestrogen replacement may be under-treated. As normal physiological growth hormone production decreases with age, dose requirements may be reduced. Clinical response, side effects, and determination of IGF-I in serum may be used as guidance for dose titration.

SHELF LIFE AND STORAGE CONDITION

The product is assigned a shelf life of 36 months when stored at 2°C – 8°C and protect from light. Reconstituted solution of Genotropin GoQuick can be stored protected from light at 2°C – 8°C for 4 weeks.

PRESENTATION

Genotropin 5.3 mg (GoQuick), Box of two-compartment glass cartridge with separating rubber stoppers and sealed in a disposable multidose pre-filled pen, Reg. No. DKI0886101444A1

HARUS DENGAN RESEP DOKTER

Manufactured by:
Pfizer Manufacturing Belgium NV, Puurs, Belgium

Imported by:
PT. Pfizer Indonesia, Jakarta-Indonesia

GENOTROPIN GOQUICK

INSTRUCTIONS FOR USE

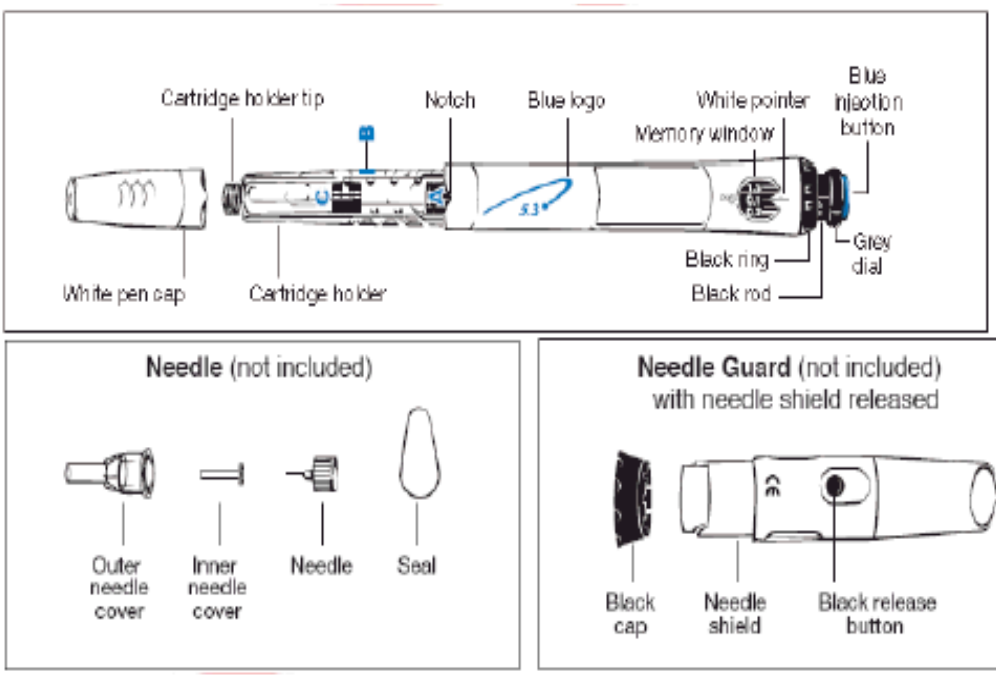
Important Information
Please read these instructions completely before using Genotropin GoQuick.

If you have any questions about your dose or your treatment with Genotropin, call your doctor or nurse.

About Genotropin GoQuick
Genotropin GoQuick is a prefilled, multidose, disposable injection pen that holds 5.3 mg of somatropin. The Genotropin in the pen is mixed only once, when you start a new pen. A single pen can be used up to 28 days after mixing. You never have to change cartridges. When the pen is empty, you just start a new pen.

The pen has dose memory. The dose is set once on a new pen. The pen then gives the same dose for each injection. You can use the pen with or without the optional needle guard.

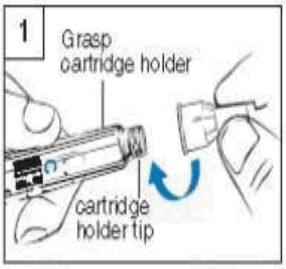
Before You Use Genotropin GoQuick
- Get training from your doctor or nurse.
- Know your dose. Know the pen parts.
- Make sure you have the pen with the blue injection button.
- Wash your hands.



Setting Up and Using a New Genotropin GoQuick

Step 1. Attach the Needle

a. Pull the white pen cap straight off the pen.
b. Peel the seal from a new needle.
c. Firmly grasp the cartridge holder. (Figure 1)
d. Push the needle onto the cartridge holder tip.
e. Gently screw the needle onto the pen. Do not overtighten.
f. Leave both needle covers on the needle.

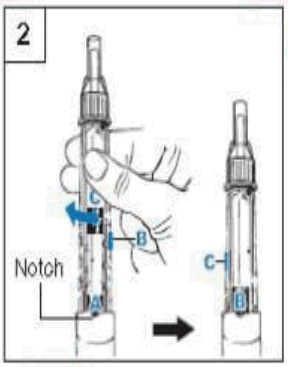


Step 2. Mix the Genotropin

a. Hold the pen with the needle-end pointing up and the **A** facing you. (Figure 2)
b. **Firmly** twist the cartridge holder into the pen until **B** clicks into the notch.
- Gently tilt the pen from side to side. Do not shake the pen. Shaking may damage the growth hormone.

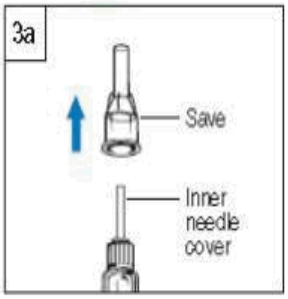
c. Check that the liquid in the cartridge is clear. All the powder should be dissolved.
- If not, gently tilt the pen from side to side a few more times.

d. Check the liquid again. Make sure it is clear.
- If the liquid is clear, go to Step 3. If the liquid is still cloudy or you see any powder, use a new pen.

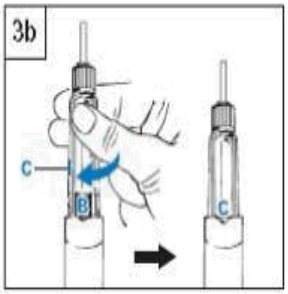


Step 3. Remove the Air

a. Pull the outer needle cover off. Save it to re-cap the needle. (Figure 3a)

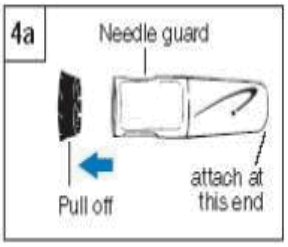


b. Leave the inner needle cover on.
c. Hold the pen with the needle-end pointing up. (Figure 3b)
d. Tap the cartridge holder gently to help any trapped air move to the top.
e. **Firmly,** twist the cartridge holder into the pen until **C** clicks into the notch.
- Some liquid may appear around the inner needle cover.



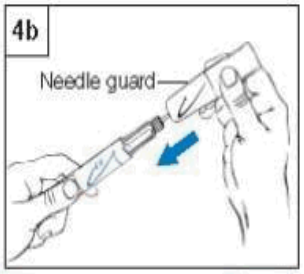
Step 4. Attach the Needle Guard (Optional)

a. Pull the black cap off the needle guard. (Figure 4a)
- If the needle shield slides out, push it back into the needle guard until it clicks into place.



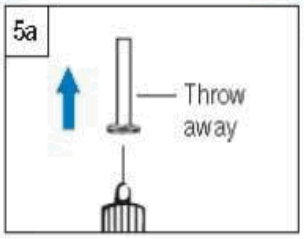
b. Hold the pen in one hand below the blue logo. With the other hand, hold the needle guard below the needle shield. (Figure 4b)

c. Line up the black logo on the needle guard with the blue logo on the pen. Carefully push the needle guard onto the pen until it snaps into place.

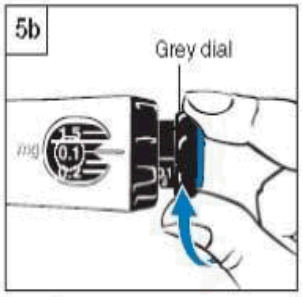


Step 5. Prime the Pen

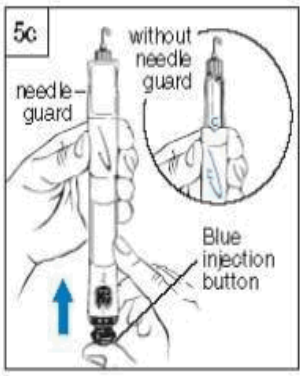
a. Pull the inner needle cover off. Throw it away. (Figure 5a)



b. Check that 0.1 mg is set in the memory window.



c. Turn the grey dial in the direction of the arrows until it stops clicking. (Figure 5b)



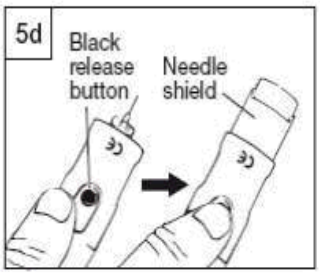
d. Hold the pen with the needle pointing up. (Figure 5c with and without needle guard)

e. Push the blue injection button until liquid appears.

f. If liquid does not appear at Step "e", repeat Steps b-e in this section up to two more times.

g. If liquid still does not appear, do not use the pen.

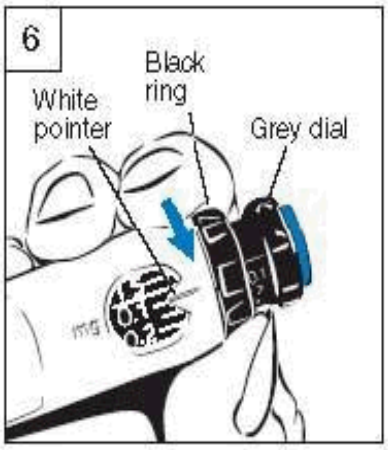
- See the Questions and Answers section below for more information.



h. If you use the needle guard, press the black button to release the needle shield. (Figure 5d)

Step 6. Set the Dose

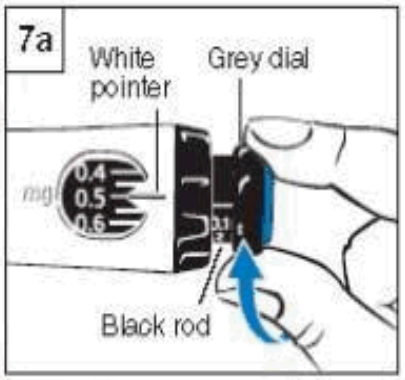
- Use the black ring to set the dose. Be careful not to turn the grey dial while setting the dose.



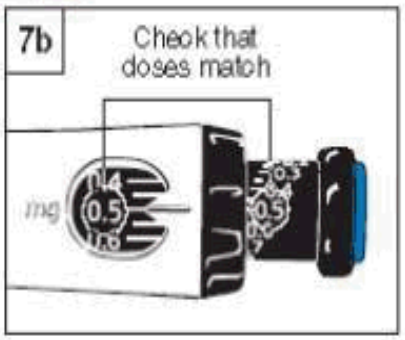
a. Hold the black ring as shown in Figure 6.
b. Turn the black ring until your dose lines up with the white pointer. Your doctor or nurse has told you your dose.
c. If you turn your dose past the white pointer, just turn the black ring back to set the correct dose.
d. Once you have set your dose, do not change it unless your doctor or nurse tells you.
Note: If you cannot turn the black ring, press in the blue injection button until it stops clicking. Then continue to set your dose using the black ring (for more information, see also the Questions and Answers section below).

Step 7. Draw Up a Dose

a. Turn the grey dial in the direction of the arrow until the clicking stops. (Figure 7a)



b. Your dose on the black rod should line up with the white pointer.
c. Check that the dose you drew up on the black rod is the same as the dose you set in the memory window. Figure 7b shows an example.
d. If the doses do not match, make sure you have turned the grey dial in the direction of the arrow until it does not click anymore.

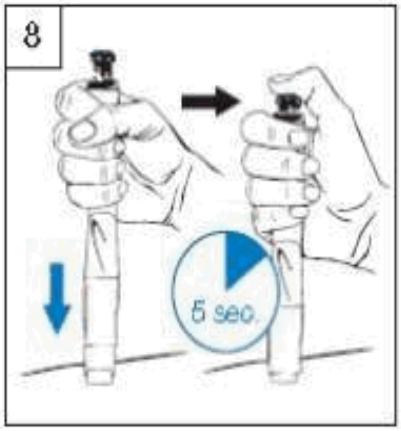


Step 8. Give the Injection

a. Prepare an injection site as your doctor or nurse has told you.
b. Hold the pen over the injection site.
c. Push the pen down to insert the needle into the skin.
d. Using your thumb, push the blue injection button down until it stops clicking. (Figure 8)

- Count for 5 seconds before you pull the needle out of the skin. Keep light pressure on the button with your thumb while you count.

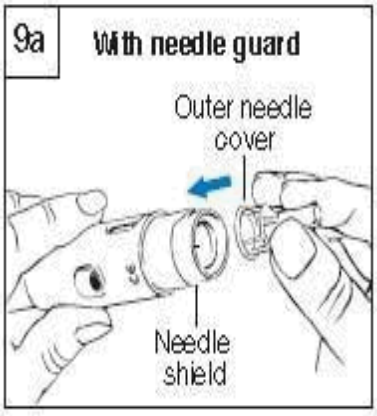
e. Pull the pen straight out from the skin.



Step 9. Remove the Needle; Cap and Store Your Pen

Step 9a: With needle guard

a. Place the outer needle cover into the end of the needle shield. (Figure 9a)

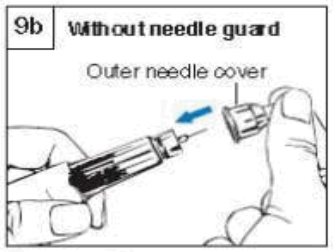


b. Use the needle cover to push in the needle shield until it locks into place.

c. Use the needle cover to unscrew the needle and put it in a proper container for used needles.

d. Leave the needle guard on the pen.

e. Place the black cap on the needle guard. Store your pen in the refrigerator.



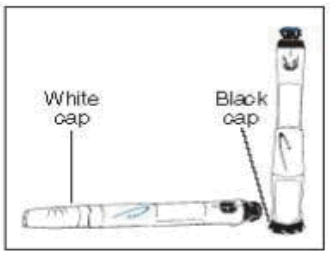
Step 9b: Without needle guard

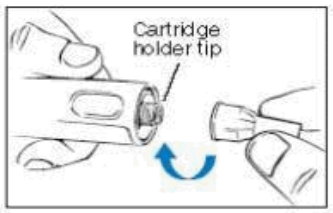
a. Do not touch the needle.

b. Carefully cap the needle with the outer needle cover. (Figure 9b)

c. Use the needle cover to unscrew the needle and put it in a proper container for used needles.

d. Place the white cap on the pen. Store your pen in the refrigerator.





Routine Use of Genotropin GoQuick

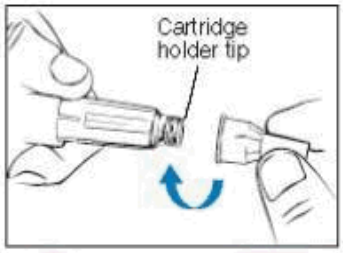
1 Pull the black cap from the needle guard or the white cap from the pen.

2 Attach a new needle.

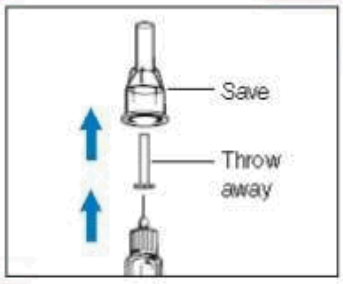
- With the needle guard:
- If the needle shield releases, push it back into place.
- Attach a new needle to the cartridge holder tip.

Without the needle guard:

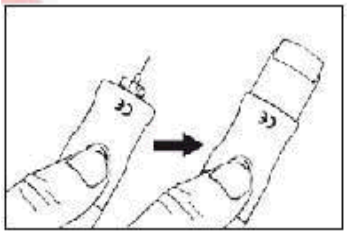
- Attach a new needle to the cartridge holder tip



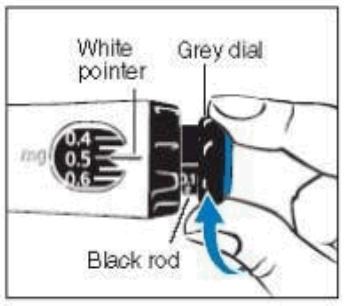
3. Remove both needle covers. Save the outer needle cover.



4. If you use the needle guard, press the black release button to extend the needle shield.

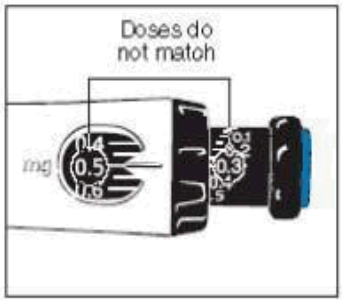


5. To draw up the dose, turn the grey dial until it stops clicking.

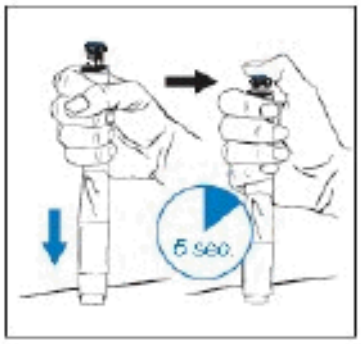


6. Check that the dose you drew up is the same as the dose you set in the memory window.

- If the dose you drew up is smaller, the pen does not have a full dose of Genotropin.
- Follow what your doctor or nurse told you to do when the pen does not have a full dose left.

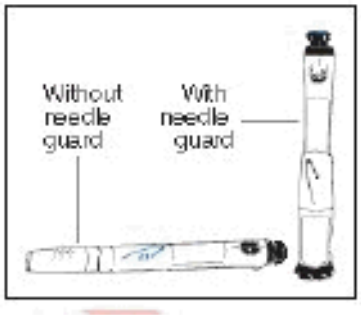


7. Prepare an injection site as your doctor or nurse has told you.



8. Give the injection.
   - Push the pen down to insert the needle into the skin.
   - Push the blue injection button down until it stops clicking.
   - Count for 5 seconds before you pull the needle out of the skin. Keep light pressure on the button with your thumb while you count.
   - Pull the pen straight out from the skin.

9. Remove the needle.
   - With the needle guard
   - Use the outer needle cover to push in the needle shield until it locks into place.
   - Without the needle guard
   - Carefully cap the needle with the outer needle cover.
   - Use the outer needle cover to unscrew the needle. Throw the needle away in a proper container for used needles.



10. Cap your needle guard or pen and store it in the refrigerator.

ADDITIONAL INFORMATION

Storage

- Refer to the patient information leaflet for how to store your Genotropin GoQuick.
- After <28 days>, dispose of the pen (or discard) even if there is some medicine left.
- Do not freeze or expose Genotropin GoQuick to frost.
- Do not use your Genotropin GoQuick after its expiry date.
- Follow your local health and safety laws to dispose of (or discard) your pen. Ask your doctor or nurse, if you are not sure what to do.

Handling

- Do not mix the powder and liquid of Genotropin GoQuick unless a needle is on the pen.
- Do not store your Genotropin GoQuick with the needle attached. The Genotropin may leak from the pen and air bubbles may form in the cartridge. Always remove the needle and attach the pen cap or needle guard cap before storing.
- Take care not to drop your Genotropin GoQuick.
- If you do drop the pen you must perform another prime as described in Step 5 (Setting Up and Using a New Genotropin GoQuick). But if any part of your Genotropin GoQuick appears broken or damaged, do not use the pen. Contact your doctor or nurse for another pen.
- Clean the pen and needle guard with a damp cloth. Do not put the pen in water.

Needles

- Always use a new needle for each injection.
- Put all used needles in an appropriate “sharps” container. Follow your local health and safety laws to dispose of your needles. Ask your doctor or nurse, if you are not sure what to do.
- Do not share your pen or needles.

General

- The numbers and lines on the cartridge holder can help you estimate how much GENOTROPIN is left in the pen.
- If in routine use Step 6 the pen does not have a full dose of Genotropin, the scale on the black rod indicates the amount of drug remaining in the pen.
- Patients who are blind or who do not see well should only use the Genotropin GoQuick with the help of someone trained to use the pen.
- Follow your doctor or nurse’s instructions for cleaning your hands and skin when you prepare and give the injection.
- Do not discard your needle guard, to remove it from the pen just twist it off. Save it to use with each new pen.
- If you have questions about how to use the Genotropin Go Quick, ask your doctor or nurse

QUESTIONS AND ANSWERS

Questions

What should I do if I see more than a small drop of liquid on the needle after giving my injection?

Is it a problem if I see air bubbles in the cartridge? What should I do if I see GENOTROPIN leaking from the pen?

What should I do if the pen that I am using was not put in the refrigerator overnight?

What should I do if I can't turn the black ring?

What if my doctor changes my dose when I've already started a pen?

What if I inject the wrong dose?

What if my pen will not prime (i.e. if liquid did not appear in step 5g)?

What doses can my pen deliver?

Answers

For your next injection wait the full time of 5 seconds before taking the needle from the skin. If you still see some liquid after you take out the needle, hold in for a little longer next time.

No, small amounts of air may be present in the cartridge during normal use.

Make sure that the needle has been attached correctly.

Discard the pen and use a new Genotropin GoQuick.

You have probably accidentally turned the grey dial. If you have turned the grey dial the pen will prevent you from turning the black ring so that your dose does not change during your injection.

To release the black ring, press in the blue injection button until it stops. Note that liquid will come out of the needle. Then continue to set your dose using the black ring.

Set the new dose by turning the black ring.

Call your doctor or nurse immediately and follow his/her instructions.

Call your doctor or nurse and follow his/her instructions.

The pen can deliver doses from 0.10 mg to 1.5 mg of Genotropin. Each click of the black ring changes the dose by 0.05 mg.