PT. Pfizer Indonesia
Local Product Document

Generic Name: 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 anhydrous. 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 is a white, sterile lyophilized powder in the front compartment and a clear solution in the rear compartment. The reconstituted solution is almost colorless and can be slightly opalescent. 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.

Clinical Trials

Japanese phase 3 study (body composition abnormality in Prader-Willi syndrome)
An open-label uncontrolled clinical study was conducted in patients with Prader Willi syndrome (20 adult patients, 6 GH naïve patients, and 7 GH treated patients). Dosage and administrations were that adult participants received 0.042 mg/kg/week for the first 4 weeks and then titrated to 0.084 mg/kg/week, and GH treated pediatric patients received 0.084 mg/kg/week. The doses of adults and GH treated pediatrics were adjusted with reference to symptoms and serum IGF-I levels, but the daily dose was not to exceed 1.6 mg. GH naïve patients received 0.245 mg/kg/week. All patients are received in 6 to 7 divided doses. The change from baseline to Month 12 in lean body mass (%) measured by DEXA for the adult cohort (point estimate of the least square mean [95% confidence interval]) was 3.09 [1,85, 4.33], and greater than the pre specified efficacy criterion of 0 (estimated by the mixed model for repeated measures including the baseline value, visit value, and baseline value-by-visit interaction covariates).

Item	Cohort	At the start of the study	At Month 12	Change from baseline
Lean body mass[d](%)	Adults cohort (n=20)	60.57±5.139 (n＝20)	63.57±4.704 (n＝19)	3.08±2.917 (n＝19)

	GH naïve cohort (n=6)	57.36±8.202 (n=6)	61.95±7.556 (n=6)	4.59±4.490 (n=6)
	GH treated cohort (n=7)	70.76±8.554 (n=7)	68.03±6.705 (n=6)	-1.34± 3.238 (n=6)

n: Number of patients. Values are expressed as mean±SD（n）
a) Measurement of lean body mass: DXA method

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.
- Pre Pubertas idiopathic short stature.

Somatropin is also indicated for improvement of body composition and short stature without closed epiphyses 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 pediatric patients with body composition abnormality and short stature without closed epiphyses in 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.

Body composition abnormality and short stature without closed epiphyses in Prader-Willi syndrome
For the patients with Prader-Willi syndrome should be confirmed by appropriate genetic testing.

The treatment of Prader-Willi syndrome is based on dietary therapy and exercise therapy. These therapies should be attempted before the initiation of growth hormone therapy.

In adults, perform tests periodically so that the serum IGF-I value does not exceed the upper limit of the reference range.

When this drug is co-administered with hormones other than this drug in adults, serum IGF-I concentration should be carefully monitored because the hormone to be used concomitantly may affect the serum IGF-I concentration.

Treatment should be given by physicians skilled in treatment of this disease (such as professionals in the field of endocrinology) or under the guidance of such physicians. The experience of long-term administration in adult patients is limited.

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

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)
General Disorders and Administration Site Conditions	(Adults) oedema peripheral	(Children) injection-site reactions	(Children) oedema peripheral			(Adults) injection-site reaction, (Adults & Children) 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.

Japanese phase 3 study (body composition abnormality in Prader-Willi syndrome)
Adverse reactions were reported in 9 (45.0%) adult patients and 3 GH naïve patients (50.0). None reported adverse reactions in the GH treated cohort. The common adverse reactions reported were glycosylated haemoglobin increased[3 (15.0%) adult and 1 (16.7%) GH naive] and IGF- I increased[2 (10.0%) adult and 1 (16.7%) GH naive].

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor lmpor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
JI. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext .1079
Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com
Website: www.pfizersafetyreporting.com

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
Body composition abnormality and short stature without closed epiphyses in Prader-Willi syndrome[a]	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

a: In pediatric patients without closed epiphyses, growth velocity should be assessed every year, and the dosage should be declined to 0.084 mg/kg/week and so on as adults if growth velocity ≥ 1 cm/year has not been satisfied or when the bone age reaches 17 years for males and 15 years for females.

Dosage Recommendations for Adult Patients with Body Composition Abnormality and Short Stature without Closed Epiphyses in Prader-Willi Syndrome

In adults, usually the initial dosage is 0.042 mg/kg/week as somatropin (genetical recombination) in 6 to 7 divided doses by subcutaneous route. The dosage is titrated by 0.084 mg/kg/week at a maximum according to the patient's clinical symptoms. The dosage may be adjusted according to patient's clinical symptoms and laboratory test results such as serum insulin-like growth factor-I (IGF-I) concentrations. However, the maximum daily dosage should not be higher than 1 mg/day.

It is recommended to measure the serum IGF-I concentration 4 weeks after the initiation of administration, and subsequently every 12 to 24 weeks. In case of onset of adverse reactions, etc., measure the serum IGF-I concentration as necessary and take appropriate measures such as dose reduction or discontinuation of this drug.

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.

STORAGE CONDITION

The product should be 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-Sint-Amands, Belgium

Imported by:
PT. Pfizer Indonesia, Jakarta-Indonesia

GENOTROPIN GOQUICK

INSTRUCTIONS FOR USE

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

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

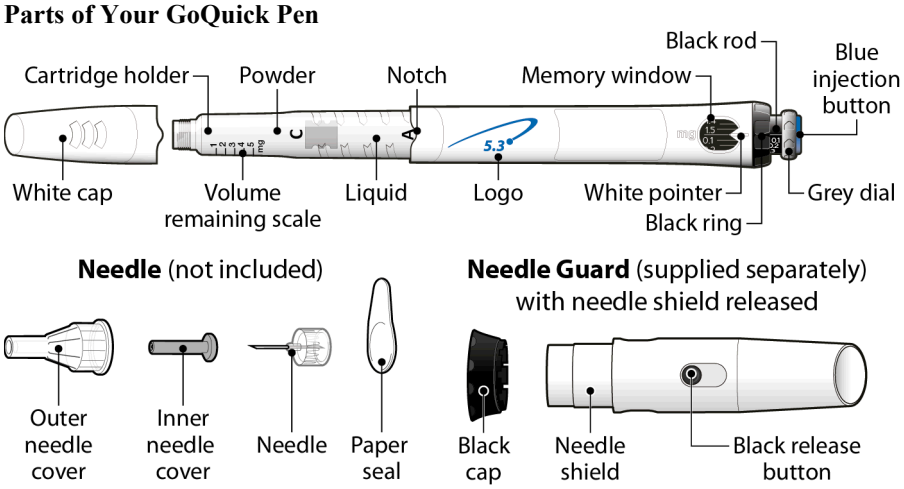
About GoQuick
GoQuick is a prefilled, multidose, disposable injection pen that holds 5.3 mg of somatropin. Your pen can deliver doses from 0.1 mg to 1.5 mg of Genotropin. Each click of the black ring changes the dose by 0.05 mg. The Genotropin in your pen is mixed only once, when you start a new pen. You never have to change cartridges. When your pen is empty, you just start a new pen.

Your pen has dose memory. The dose is set once on a new pen. Your pen then allows you to draw up the same set dose for each injection. This will prevent you from drawing more than your set dose.

Important Information
- **Do not** mix the powder and liquid of your pen unless a needle is on your pen.
- **Do not** store your pen with the needle attached. The Genotropin may leak from your pen and air bubbles may form in the cartridge. Always remove the needle and attach your pen cap or needle guard cap before storing.
- Take care not to drop your pen. If you drop your pen and any part of it appears broken or damaged, **do not** use it. Contact your doctor or nurse for another pen. If you drop your pen and it is not damaged or broken, you must perform another prime as described in Step 6 (Setting up and using a new GoQuick Pen).
- Clean your pen with a damp cloth. **Do not** put your pen in water.
- Always use a new needle for each injection. **Do not** share your pen needles.
- The volume remaining scale along the side of the cartridge holder is a guide to show the volume of Genotropin left in your pen.

Storage and Disposal
- Store your pen in the refrigerator (2°C to 8°C) in the outer carton to protect from light. **Do not** freeze or expose it to frost.
- **Do not** use your pen after its expiry date.
- 28 days after mixing, throw away (dispose of) your pen even if there is some medicine left.
- See the *other side of this* leaflet for how to store your GoQuick Pen.
- Follow your local health and safety laws to throw away (dispose of) your pen. Ask your doctor or nurse if you are not sure what to do.

Parts of Your GoQuick Pen

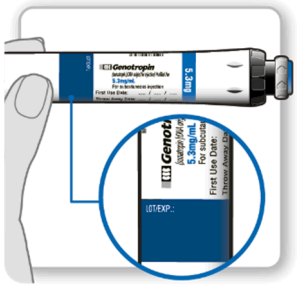


Pen needles are **not included** with your GoQuick Pen. You will need to get pen needles up to a length of 8 mm from your pharmacy.

- Needles to use with your GoQuick Pen:
  - 31G or 32G (Becton Dickinson and Company)
  - 31G or 32G (Novo Nordisk®)
  - 32.5G or 34G (Terumo)

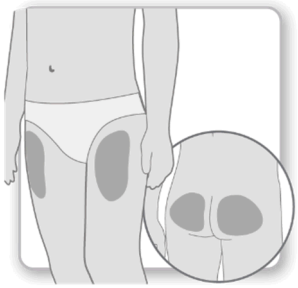
Setting up and using a new GoQuick Pen

Step 1 Preparation



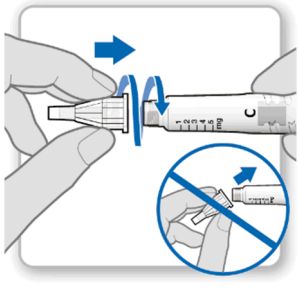
- **Wash and dry** your hands.
- **Gather** the following supplies on a clean flat surface:
    - A new GoQuick Pen
    - A new needle (not included)
    - Suitable sharps container (not included).
- **Check** the expiry date on your pen label. **Do not** use your pen if the pen has passed its expiry date.

Step 2 Choose Injection Site



- **Choose and clean** an injection site as recommended by your doctor or nurse. Choose a different site each time you give yourself an injection. Each new injection should be given at least 2 cm from the site you used before.
- Avoid areas that are bony, bruised, red, sore or hard, and areas of the skin that have scars or skin conditions.

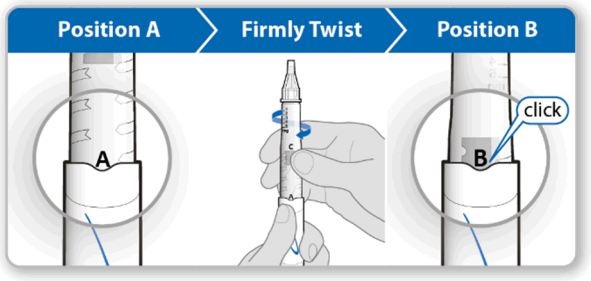
Step 3 Attach the Needle



- **Pull** the white cap straight off your pen.
- Take a new needle and peel off the paper seal
- **Gently push and then** screw the needle onto your pen. **Do not** overtighten.
- **Note:** Be careful not to attach the needle at an angle. This may cause your pen to leak.

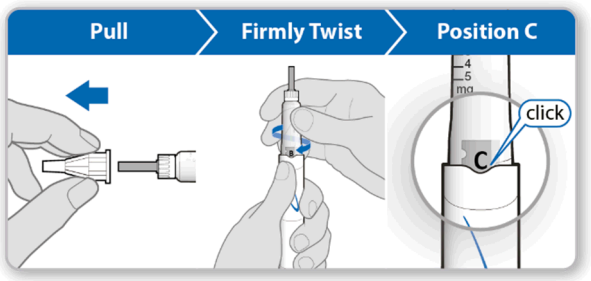
- Leave both needle covers on the needle.

Step 4 Mix the Genotropin



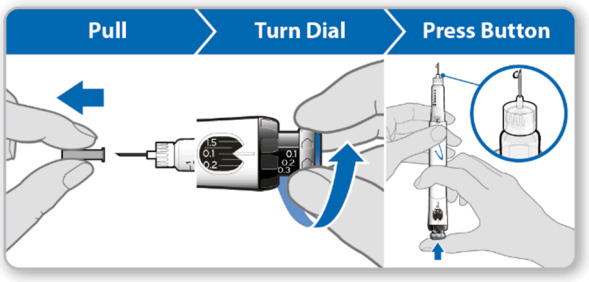
- **Hold** your pen with the needle-end pointing up and the **"A"** facing you.
- Firmly twist the cartridge holder into the pen until **"B"** clicks into the notch.
- **Gently tilt** your pen from side to side to help dissolve the powder completely. **Do not** shake the pen. Shaking can damage the growth hormone.
- **Check** that the liquid in the cartridge is clear and all the powder is dissolved.
    - If the liquid is cloudy or you see any powder, gently tilt your pen from side to side a few more times.
    - If the liquid is still cloudy or you see any powder, **do not** use the pen and try again with a new pen.

Step 5 Remove the Air from Your Pen



- **Pull** the outer needle cover off. Keep it to remove the needle after your injection.
- Leave the inner needle cover on.
  Note: You should see an inner needle cover after you have removed the outer cover. If you do not see this, try to attach the needle again.
- **Hold** your pen with the needle-end pointing up.
- **Gently tap** the cartridge holder to help any trapped air move to the top.
- **Firmly twist** the cartridge holder into your pen until "**C**" clicks into the notch.
    - Some liquid may appear around the inner needle cover. This is normal.

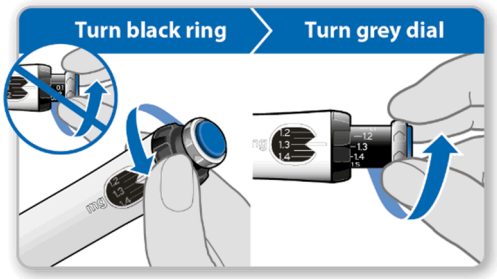
Step 6 Prime Your Pen



Priming removes any remaining air by pushing a small amount of liquid out of your pen. The priming dose is 0.1 mg and is different from the dose your doctor or nurse has prescribed. **Only prime your pen the first time you use it.**

- **Pull** the inner needle cover off and throw it away. **Caution: Do not** touch the needle to avoid a needle stick.
- **Check** that 0.1 mg is set in the memory window.
- **Turn** the **grey dial** in the direction of the arrows until it stops clicking.
- **Hold** your pen with the needle pointing straight up.
- **Push** the blue injection button all the way in.
- **Check** for liquid at the needle tip. If liquid appears, your pen is primed.
    - If liquid does not appear, repeat the priming steps up to two additional times.
    - If liquid still does not appear, do not use your pen. Contact your doctor or nurse for advice.

Step 7 Set and Draw Up Your Dose



The first time you use your pen you will set the dose that your doctor or nurse has prescribed.
You do not need to set the dose again until you start a new pen or your doctor or nurse tells you.

- **Turn** the **black ring counterclockwise** until your dose is lined up with the white pointer in the memory window. **Be careful not to turn the grey dial**.
    - If you turn your dose past the white pointer, turn the black ring back to set your correct dose.

Note: If you cannot turn the black ring, press the blue injection button until it stops clicking. Then try and set your dose again. Note that liquid will come out of the needle.

- **Turn** the **grey dial** in the direction of the arrows until it stops clicking.

Step 8 Check Your Dose

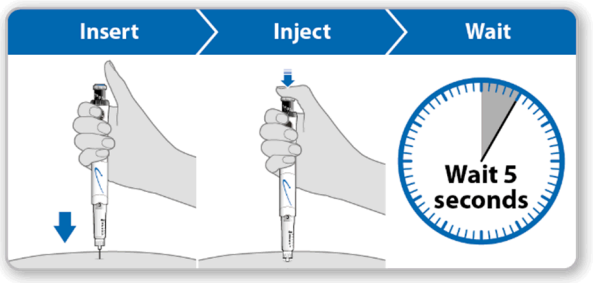


Your dose on the black rod should **line up** with the white pointer.

- **Check** that the dose you drew up on the black rod is the same as the dose you set in the memory window.
    - If the doses match, your pen is ready to give your injection.

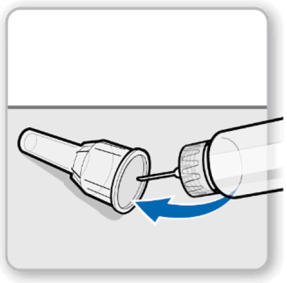
If the doses do not match, make sure you have turned the grey dial in the direction of the arrows until it does not click anymore.

Step 9 Give Your Injection of Genotropin



- **Hold** your pen over the injection site.
- **Insert** the needle straight into the skin.
- **Push** the blue injection button down until it stops clicking.
- **Wait** for a full 5 seconds to ensure that your complete dose is injected. Keep lightly pressing on the blue injection button while you count.
- After 5 seconds, pull the needle straight out of your skin.
  Note: If you see a drop of liquid at the injection site or needle tip, then with your next injection try pressing the blue injection button for longer before pulling the needle out of your skin.

Step 10 Remove Needle



- **Carefully cover** the needle with the outer needle cover.
  Caution: Do not touch the needle to avoid a needle stick.
- Use the needle cover to unscrew the needle.
- **Throw away** (dispose of) the needle in a suitable sharps container.
- **Push** the white cap onto your pen.
- Store your pen in the refrigerator until your next injection.

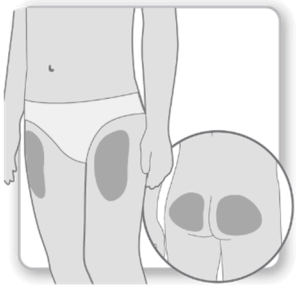
Routine (daily) use of GoQuick Pen

Step 1 Preparation



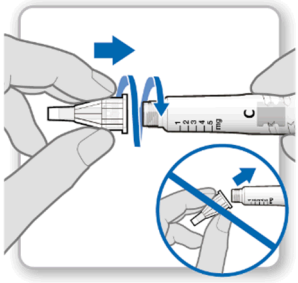
- **Wash and dry** your hands.
- **Gather** the following supplies on a clean flat surface:
  - An already mixed GoQuick Pen
  - A new needle (not included)
  - Suitable sharps container (not included).
- **Check** the expiry date on your pen label. **Do not** use your pen if the pen has passed its expiry date. **Do not** use your pen 28 days after first use.

Step 2 Choose Injection Site



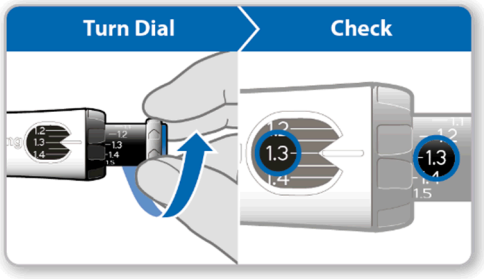
- **Choose and clean** an injection site as recommended by your doctor or nurse. Choose a different site each time you give yourself an injection. Each new injection should be given at least 2 cm from the site you used before.
- Avoid areas that are bony, bruised, red, sore or hard, and areas of the skin that have scars or skin conditions.

Step 3 Attach New Needle



- **Pull** the white cap straight off your pen.
- Take a new needle and peel off the paper seal.
- **Gently push and then screw** the needle onto your pen. **Do not** overtighten.
  Note: Be careful not to attach the needle at an angle. This may cause your pen to leak.
- **Remove** both needle covers.
    - Keep the outer needle cover to remove the needle after your injection.

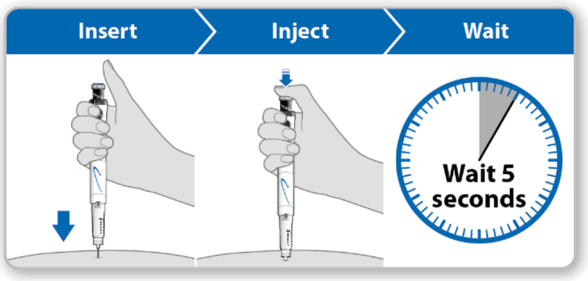
Step 4 Draw Up Your Dose



- **Turn** the **grey dial** in the direction of the arrows until it stops clicking.
- Your dose on the black rod should **line up** with the white pointer.
- **Check** that the dose you drew up on the black rod is the same as the dose you set in the memory window.
    - If the doses match, your pen is ready to give your injection.

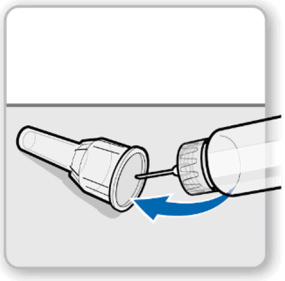
Note: If the dose you drew up is smaller, your pen does not have a full dose of Genotropin.
Follow what your doctor or nurse told you to do when your pen does not have a full dose. Or contact your doctor or nurse for advice.

Step 5 Give Your Injection of Genotropin



- **Hold** your pen over the injection site.
- **Insert** the needle straight into the skin.
- **Push** the blue injection button down until it stops clicking.
- **Wait** for a full 5 seconds to ensure that your complete dose is injected. Keep lightly pressing on the blue injection button while you count.
- After 5 seconds, pull the needle straight out of your skin.
  Note: If you see a drop of liquid at the injection site or needle tip, then with your next injection try pressing the blue injection button for longer before pulling the needle out of your skin.

Step 6 Remove Needle



- **Carefully cover** the needle with the outer needle cover.
  Caution: Do not touch the needle to avoid a needle stick.
- Use the needle cover to unscrew the needle.
- **Throw away** (dispose of) the needle in a suitable sharps container.
- **Push** the white cap onto your pen.
- Store your pen in the refrigerator until your next injection.

Using the Needle Guard (Optional)

The needle guard is an optional feature supplied separately to hide the needle during injection.

Attach the needle guard:

Attach the needle guard after Step 5 (Setting up and using a new GoQuick Pen) to avoid a needle stick.

- Pull the black cap off the needle guard.
    - If the needle shield slides out, push it back into the needle guard until it clicks into place.
- Line up the black logo on the needle guard with the blue logo on your pen. Carefully push the needle guard onto your pen until it snaps into place.
- After Step 6 (Setting up and using a new GoQuick Pen), press the black button to release the shield from the needle guard.
- Follow the instructions as described from Step 7 (Setting up and using a new GoQuick Pen).

To remove the needle with needle guard in place:

- Place the outer needle cover into the end of the needle shield.
- Use the outer needle cover to push in the needle shield until it locks into place.
- Use the needle cover to unscrew the needle and throw away (dispose of) in a suitable sharps container.
- Leave the needle guard on your pen.
- Place the black cap on the needle guard. Store your pen in the refrigerator.

To remove the needle guard:

- Remove the needle first, then gently pull the needle guard off the pen.
- **Do not** throw away the needle guard. It can be used with your next pen.

