Product information

SOMATIN® (Somatropin) is a 191 amino acid protein with molecular weight of 22,000 Daltons. SOMATIN® is a recombinant polypeptide of human growth hormone SOMATIN® is supplied as a sterile solution for subcutaneous injection in ready-to-administer prefilled pens contain 5 and 10 milligram Somatropin with a volume of 1.5 mL.

Pharmacologic Category

Growth hormones, human growth hormones

Mechanism of Action

Somatropin (as well as endogenous GH) binds to a dimeric GH receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamics effects. Some of these pharmacodynamics effects are primarily mediated by IGF-I produced in the liver and also locally (e.g., skeletal growth, protein synthesis), while others are primarily a consequence of the direct effects of Somatropin (e.g., lipolysis)

Pharmacodynamics

Tissue Growth	The primary and most intensively studied action of SOMATIN® is the stimulation of linear growth. This effect is demonstrated in children with GHD.
Skeletal Growth	The measurable increase in bone length after administration of SOMATIN® results from its effect on the cartilaginous growth areas of long bones.
Cell Growth	It has been shown that the total number of skeletal muscle cells is markedly decreased in children with short stature lacking endogenous GH compared with normal children, and that treatment with SOMATIN® results in an increase in both the number and size of muscle cells.
Organ Growth	SOMATIN® influences the size of internal organs, and it also increases red cell mass.
Protein Metabolism	Linear growth is facilitated in part by increased cellular protein synthesis. This synthesis and growth are reflected by nitrogen retention which can be quantitated by observing the decline in urinary nitrogen excretion and blood urea nitrogen following the initiation of SOMATIN® therapy.
Carbohydrate Metabolism	Hypopituitary children sometimes experience fasting hypoglycemia that may be improved by treatment with Somatropin. In healthy subjects, large doses of SOMATIN® may impair glucose tolerance. Insulin levels in serum actually increase as Somatropin levels increase. In addition, mean fasting and postprandial glucose and hemoglobin A_{1c} levels remain in the normal range.

Lipid Metabolism	SOMATIN® stimulates intracellular lipolysis, and administration of SOMATIN® leads to an increase in plasma free fatty acids and triglycerides. Untreated GHD is associated with increased body fat stores, including increased abdominal visceral and subcutaneous adipose tissue.
Mineral Metabolism	Administration of SOMATIN® results in an increase in total body potassium and phosphorus and to a lesser extent sodium. This retention is thought to be the result of cell growth. Serum levels of phosphate increase in children with GHD after SOMATIN® therapy due to metabolic activity associated with bone growth. Serum calcium levels are not altered.
Connective Tissue Metabolism	SOMATIN® stimulates the synthesis of chondroitin sulfate and collagen, and increases the urinary excretion of hydroxyproline.

Clinical Use and recommended dose for pediatric patients

Indication	Definition	dosage
Growth hormone deficiency	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with growth failure due to inadequate secretion of Endogenous growth hormone (GH).	0.025-0.035 mg/kg/dose per day. *Therapy should be discontinued when patient has reached satisfactory height, when epiphyses have fused, or when the patient ceases to respond. Some guidelines recommend discontinuing therapy when growth velocity is <2 to 2.5 cm/year
Noonan syndrome	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature associated with Noonan syndrome.	Up to 0.066 mg/kg/day.
Turner syndrome	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature associated with Turner Syndrome.	Up to 0.067 mg/kg/day.
SGA at birth who fail to catch-up by 2-4 years of age	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature born small for gestational age (SGA) with no catch-up growth by age 2 to 4 years.	Up to 0.067 mg/kg/day or Up to 0.469 mg/kg **weekly** divided into equal doses 7 days/week

Chronic renal insufficiency	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature associated with Chronic renal insufficiency.	0.35 mg/kg weekly divided into daily injections *Continue until the time of renal transplantation
Idiopathic short stature	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature associated with Idiopathic short stature.	0.067 mg/kg/day.
SHOX deficiency	SOMATIN® (Somatropin) injection is indicated for the treatment of pediatric patients with short stature associated with SHOX deficiency.	0.35 mg/kg weekly divided into equal doses 6-7 days per week

Clinical Use and recommended dose for adult patients

Indication	Definition	dosage
Growth hormone deficiency	SOMATIN® (Somatropin) injection is indicated for the replacement of endogenous GH in adults with growth hormone deficiency (GHD) who meet either of the following two criteria: • Adult Onset (AO): Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma. • Childhood Onset (CO): Patients who were GH deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.	Either of two approaches to SOMATIN® dosing may be followed: a non-weight-based regimen or a weight-based regimen: Non-weight based —, a starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day). This dose can be increased gradually every 1 to 2 months by increments of approximately 0.1-0.2 mg/day, according to individual patient requirements based on the clinical response and serum insulin-like growth factor I (IGF-I) concentrations. Weight-based — based on the dosing regimen used in the original adult GHD registration trials, the recommended dosage at the start of treatment is not more than 0.004 mg/kg/day. The dose may be increased to not more than 0.016 mg/kg/day after approximately 6 weeks according to individual patient requirements.
Short-bowel syndrome	SOMATIN® (Somatropin) injection is indicated for the treatment of adult patients with short stature associated with Prader-Willi syndrome	0.1 mg/kg once daily for 4 weeks (maximum: 8 mg/day)

CONTRAINDICATIONS

Acute Critical Illness	Treatment with pharmacologic amounts of SOMATIN® is contraindicated in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental traumas, or those with acute respiratory failure.
Prader-Willi Syndrome in Children	SOMATIN® is contraindicated in patients with Prader-Willi syndrome who are severely obese, have a history of upper airway obstruction or sleep apnea, or have severe respiratory impairment. There have been reports of sudden death when Somatropin was used in such patients.
Active Malignancy	In general, SOMATIN® is contraindicated in the presence of active malignancy. Any preexisting malignancy should be inactive and its treatment complete prior to instituting therapy with SOMATIN®.
Hypersensitivity	SOMATIN® is contraindicated in patients with a known hypersensitivity to Somatropin or any of its excipients.
Diabetic Retinopathy	SOMATIN® is contraindicated in patients with active proliferative or severe non-proliferative diabetic retinopathy.
Closed Epiphyses	SOMATIN® should not be used for growth promotion in pediatric patients with closed epiphyses.

ADVERSE REACTIONS

Peripheral Edema, Edema, Arthralgia, Leg Edema, Myalgia, Infection, Skeletal Pain, Headache, Bronchitis, Flu-like symptoms, Hypertension, Gastroenteritis, Increased sweating, Glucose tolerance abnormal.

Pregnancy

Pregnancy Category C. It is not known whether SOMATIN® can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. SOMATIN® should be given to a pregnant woman only if clearly needed.

Breastfeeding

It is not known whether SOMATIN® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SOMATIN® is administered to a nursing woman.

Geriatric Use

The safety and effectiveness of SOMATIN® in patients aged 65 and over has not been evaluated in clinical studies. Elderly patients may be more sensitive to the action of SOMATIN®, and therefore may be more prone to develop adverse reactions. A lower starting dose and smaller dose increments should be considered for older patients.

Administration

	Steps you should follow for a SOMATIN® injection:
SQ	Step 1. Preparing the SOMATIN® Pen Step 2. Attaching the needle to the SOMATIN® Pen Step 3. Selecting the correct dose of SOMATIN® Step 4. Selecting the injection site and injecting the dose of SOMATIN® Step 5. What to do after the injection is completed.
• SOMATIN® is for use under the skin only (subcutaneous). • Do not share your SOMATIN® Pen and needles with another person. You may give another person an infection or get an infection from them. • Note that the pen is used several times and you can use it until the medicine runs out. • Note that the needle can only be used once	

Storage

- Unused SOMATIN® prefilled pens must be stored at 2°C to 8°C/ refrigerator.
- Do not freeze.
- Avoid direct light.
- After the initial injection, a SOMATIN® prefilled pen may be **EITHER** stored in the refrigerator (2°C to 8ºC) and used within 4 weeks **OR** stored for up to 3 weeks at room temperature not more than 25ºC.
- Discard unused portion.

References

1- *Molitch ME, Clemmons DR, Malozowski S, et al, "Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline," J Clin Endocrinal Metab, 2006, 91(5):1621-34. [PubMed 16636129].*

2- *American Academy of Pediatrics Committee on Drugs. "Inactive" ingredients in pharmaceutical products: update (subject review). Pediatrics. 1997; 99(2):268-278. [PubMed 9024461].*

3- *Gharib H, Cook DM, Saenger PH, et al, "American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Adults and Children - 2003 Update," Endocr Pract, 2003, 9(1):64-76. [PubMed 12917095].*

4- *Molitch ME, Clemmons DR, Malozowski S, et al, "Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline," J Clin Endocrinol Metab, 2006, 91(5):1621-34. [PubMed 16636129]*