Available in 5-mg and 10-mg vials

ZOMACTON™
[somatropin (rDNA origin)] for Injection
5mg and 10mg

5 mg and 10 mg Increases Dosing Flexibility

- 10 mg has a longer shelf-life after reconstitution in comparison to 5 mg
- Premeasured diluent syringe with 10 mg means 1 less step in the dosing process than the 5 mg

Dosage and Administration

The recommended dose is up to 0.1 mg/kg administered subcutaneously 3 times per week (up to 0.3 mg/kg/week).

ZOMACTON™ 5 mg should be reconstituted with 1-5 mL of bacteriostatic 0.9% sodium chloride for injection, USP (benzyl alcohol preserved). Reconstituted ZOMACTON™ 5-mg vials should not be used if the patient has a known sensitivity to benzyl alcohol. Benzyl alcohol as a preservative in bacteriostatic normal saline, USP, has been associated with toxicity in newborns. WHEN ADMINISTERING ZOMACTON™ TO NEWBORNS, RECONSTITUTE WITH STERILE NORMAL SALINE FOR INJECTION, USP.

ZOMACTON™ 10 mg should be reconstituted with 1 mL syringe of bacteriostatic water for injection containing 0.33% metacresol as a preservative. Reconstituted ZOMACTON™ 10-mg vials should not be used if the patient is allergic to metacresol.

The stream of normal saline should be aimed against the side of the vial to prevent foaming. Swirl the vial with a GENTLE rotary motion until the contents are completely dissolved and the solution is clear. DO NOT SHAKE. Since ZOMACTON™ is a protein, shaking or vigorous mixing will cause the solution to be cloudy. If the resulting solution is cloudy or contains particulate matter, the contents MUST NOT be injected.

Occasionally, after refrigeration, some cloudiness may occur. This is not unusual for proteins like ZOMACTON™. Allow the product to warm to room temperature. If cloudiness persists or particulate matter is noted, the contents MUST NOT be used.

Before and after injection, the septum of the vial should be wiped with rubbing alcohol or an alcoholic antiseptic solution to prevent contamination of the contents by repeated needle insertions.

Please see Important Safety Information on next page.

Overdosage

The recommended dosage of up to 0.1 mg/kg of body weight 3 times per week (up to 0.3 mg/kg/week) should not be exceeded. Acute overdose could cause initial hypoglycemia and subsequent hyperglycemia. Repeated use of doses in excess of those recommended could result in signs and symptoms of gigantism and/or acromegaly consistent with the known effects of excess human growth hormone.

Stability and Storage

Before Reconstitution

Vials of ZOMACTON™ (5 and 10 mg) are stable when refrigerated at 36° to 46°F (2°-8°C). Avoid freezing the accompanying diluent. Expiration dates are stated on the labels.

After Reconstitution

ZOMACTON™ 5 mg is stable for up to 14 days when reconstituted with bacteriostatic 0.9% sodium chloride (normal saline), USP, and stored in a refrigerator at 36° to 46°F (2°-8°C). Do not freeze the reconstituted solution.

ZOMACTON™ 10 mg is stable for up to 28 days when reconstituted with 1 mL syringe of bacteriostatic water for injection containing 0.33% metacresol as a preservative, and stored in a refrigerator at 36° to 46°F (2°-8°C). Do not freeze the reconstituted solution.

Indication

ZOMACTON™ [somatropin (rDNA origin)] for injection is indicated for the treatment of children who have growth failure due to an inadequate secretion of normal endogenous growth hormone.

Important Safety Information
Contraindications

- **Hypersensitivity:** Somatropin is contraindicated in patients with a known sensitivity to somatropin or the supplied diluent. Localized reactions are the most common hypersensitivity reactions. Patients with a known sensitivity to either benzyl alcohol or metacresol should not receive somatropin reconstituted with the supplied diluent.
- **Closed Epiphyses:** Somatropin should not be used for growth promotion in pediatric patients with closed epiphyses.
- **Diabetic Retinopathy:** Somatropin is contraindicated in patients with active proliferative or severe non-proliferative diabetic retinopathy.
- **Active Malignancy:** Somatropin is contraindicated in patients with any evidence of active malignancy. Growth hormone deficiency may be an early sign of a pituitary tumor or other intracranial tumor; the presence of such a tumor should be excluded before initiation of somatropin treatment.
- **Acute Critical Illness:** Somatropin should not be used to treat patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure. In adult patients, a significant increase in mortality has been reported in such cases.
- **Prader-Willi Syndrome in Children:** Somatropin is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment. Somatropin is not indicated for the treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Warnings and Precautions

- **Acute Critical Illness:** Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with pharmacologic doses of somatropin.
- **Prader-Willi Syndrome in Children:** There have been reports of fatalities after initiating therapy with somatropin in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway

obstruction or sleep apnea, or unidentified respiratory infection. Male patients with one or more of these factors may be at greater risk than females. Patients with Prader-Willi syndrome should be evaluated for signs of upper airway obstruction and sleep apnea before initiation of treatment with somatropin.

- **Pancreatitis:** Cases of pancreatitis have been reported rarely in children and adults receiving somatropin, with some evidence supporting greater risk in children. Pancreatitis should be considered in any somatropin-treated patient, especially a child, who develops abdominal pain. Girls who have Turner syndrome may be at greater risk than other somatropin-treated children.
- **Benzyl Alcohol:** Benzyl alcohol, a component used to reconstitute the ZOMACTON™ 5-mg vial, has been associated with serious adverse events and death, particularly in pediatric patients. The "gasping syndrome," has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates and low-birth weight neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.
- **Neoplasms:** An increased risk of a second neoplasm has been reported for childhood cancer survivors treated with somatropin for GH deficiency that developed following radiation to the brain/head. Intracranial tumors, in particular meningiomas, were the most common of these. The relationship between somatropin replacement therapy and CNS tumor recurrence in adults is unknown. Monitor for progression or recurrence in patients receiving somatropin therapy who have a history of GH deficiency secondary to an intracranial neoplasm. Thoroughly consider the risks and benefits of starting somatropin in children at increased risk for developing malignancies due to certain rare genetic causes. These patients should be carefully monitored for development of neoplasms. Any pre-existing nevi should be monitored carefully for increased growth or malignant transformation.
- **Glucose Intolerance and Diabetes Mellitus:** Previously undiagnosed impaired glucose tolerance and overt diabetes mellitus may be unmasked during somatropin treatment. New-onset type 2 diabetes mellitus has been reported. As a result, blood glucose concentrations should be monitored periodically in all patients taking somatropin, especially in those with risk factors for diabetes mellitus. Patients with pre-existing type 1 or type 2 diabetes mellitus or impaired glucose tolerance should be monitored closely during somatropin treatment.
- **Hypopituitarism:** In patients with hypopituitarism, standard hormone replacement therapy should be monitored closely when somatropin therapy is administered.
- **Hypothyroidism:** Patients treated with somatropin should have periodic thyroid function tests, and thyroid hormone replacement therapy should be initiated or appropriately adjusted in cases of unmasked or worsening hypothyroidism.
- **Slipped Capital Femoral Epiphysis in Pediatric Patients:** Slipped capital femoral epiphysis may occur more frequently in patients with endocrine disorders and in patients undergoing rapid growth. Any pediatric patient with the onset of a limp or complaints of hip or knee pain during somatropin therapy should be carefully evaluated.
- **Intracranial Hypertension:** Intracranial hypertension with papilledema, visual changes, headache, nausea, and/or vomiting have been reported in a small number of patients treated with somatropin. Funduscopic examination is recommended at the initiation of and periodically during therapy. If papilledema is observed by funduscopy during treatment with somatropin, treatment should be stopped and the patient's condition should be reassessed before treatment is resumed.

Please see Important Safety Information continued on next page.

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Important Safety Information (continued)
Warnings and Precautions (continued)

- **Progression of Scoliosis in Pediatric Patients:** Progression of scoliosis can occur in patients who experience rapid growth. Because somatropin increases growth rate, patients with a history of scoliosis who are treated with somatropin should be monitored for progression of scoliosis.
- **Epiphyseal Maturation:** Bone age should be monitored periodically during somatropin administration, especially in patients who are pubertal and/or receiving concomitant thyroid hormone replacement therapy. Under these circumstances, epiphyseal maturation may progress rapidly.
- **Local and Systemic Reactions:** Injection site should be rotated to avoid tissue atrophy. Patients should be informed that local or systemic allergic reactions may occur and that prompt medical attention should be sought in such cases.
- **Laboratory Tests:** Serum levels of inorganic phosphorus, alkaline phosphatase, parathyroid hormone and IGF-I may increase after somatropin therapy.
- **Potential Drug Interactions:** Somatropin inhibits 11β-hydroxysteroid dehydrogenase type 1 (11βHSD-1) in adipose/hepatic tissue and may significantly impact the metabolism of cortisol and cortisone. As a consequence, in patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked, requiring glucocorticoid replacement therapy. Careful monitoring is advisable when growth hormone is administered in combination with insulin and/or other hypoglycemic agents, other drugs metabolized by CYP450 liver enzymes (e.g., hydrocortisone or other corticosteroids, sex steroids, anticonvulsants, cyclosporine), or other hormone replacement therapy.
- **Pregnancy/Nursing Mothers:** Somatropin should be used during pregnancy only if clearly needed and with caution in nursing mothers because it is not known whether somatropin is excreted in human milk.

Adverse Reactions

The following adverse reactions have been observed during appropriate use of somatropin: headaches (children and adults), gynecomastia (children), and pancreatitis (children and adults). In studies of growth hormone-deficient children, injection-site reactions (e.g., pain, bruise) occurred in 8 of the 164 treated patients. Leukemia and new-onset type 2 diabetes mellitus have been reported.

Please see accompanying Full Prescribing Information for ZOMACTON™.

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FERRING PHARMACEUTICALS