HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OMNITROPE® **safely and effectively. See full prescribing information for** OMNITROPE®**.**

OMNITROPE® [somatropin (rDNA origin) injection], for SUBCUTANEOUS use.
Initial U.S. Approval: 1987

----------RECENT MAJOR CHANGES----------
Indications and Usage (1.1)
Prader-Willi Syndrome
Small for Gestational Age
Dosage and Administration (2.1)
Prader-Willi Syndrome
Small for Gestational Age

----------INDICATIONS AND USAGE----------
OMNITROPE® is a recombinant human growth hormone indicated for:

- ***Pediatric:*** Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age (1.1)
- ***Adult:*** Treatment of adults with either adult onset or childhood onset GHD (1.2)

----------DOSAGE AND ADMINISTRATION----------
OMNITROPE® should be administered subcutaneously (2).

- ***Pediatric GHD:*** 0.16 to 0.24 mg/kg//week, divided into 6 - 7 daily injections, (2.1)
- ***Prader-Willi Syndrome:*** 0.24 mg/kg/week, divided into 6 - 7 daily injections, (2.1)
- ***Small for Gestational Age:*** Up to 0.48 mg/kg/week, divided into 6 - 7 daily injections, (2.1)
- ***Adult GHD:*** not more than 0.04 mg/kg/week (divided into daily injections) to be increased as tolerated to not more than 0.08 mg/kg/week); to be increased gradually every 1 - 2 months (2.2)
- OMNITROPE® Cartridges 5 mg/1.5 mL and 10 mg/1.5 mL must be used with the corresponding OMNITROPE® Pen 5 and Pen 10 delivery system, respectively (2.3)
- Injection sites should always be rotated to avoid lipoatrophy (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

- OMNITROPE® Cartridge 5 mg/1.5 mL (15 IU) is a prefilled sterile solution in a glass cartridge ready to be administered with the Omnitrope® Pen 5. (3.1).
- OMNITROPE® Cartridge 10 mg/1.5 mL (30 IU) is a prefilled sterile solution in a glass cartridge ready to be administered with the Omnitrope® Pen 10. (3.1).
- OMNITROPE® for injection 1.5 mg/vial is supplied with two vials, one containing somatropin as a powder and the other vial containing the diluent (3.2).
- OMNITROPE® for injection 5.8 mg/vial is supplied with two vials, one containing somatropin as a powder and the other vial containing diluent (3.3).

----------CONTRAINDICATIONS----------

- Acute Critical Illness (4.1, 5.1)
- Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment - reports of sudden death (4.2)
- Active Malignancy (4.3)
- Active Proliferative or Severe Non-Proliferative Diabetic Retinopathy (4.4)
- Children with closed epiphyses (4.5)
- Known hypersensitivity to somatropin or excipients (4.6)
- Formulations containing benzyl alcohol (5 mg/1.5 mL Omnitrope Cartridges and the Bacteriostatic Water for Injection diluent for the 5.8 mg/vial Omnitrope) should not be used in premature babies or neonates (4.7)

----------WARNINGS AND PRECAUTIONS----------

- Acute Critical Illness: Potential benefit of treatment continuation should be weighed against the potential risk (5.1)
- Prader-Willi Syndrome in children: Evaluate for signs of upper airway obstruction and sleep apnea before initiation of treatment. Discontinue treatment if these signs occur (5.2).
- Neoplasm: Monitor patients with preexisting tumors for progression or recurrence. Increased risk of a second neoplasm in childhood cancer survivors treated with somatropin - in particular meningiomas in patients treated with radiation to the head for their first neoplasm (5.3).
- Impaired Glucose Tolerance and Diabetes Mellitus: May be unmasked. Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment (5.4).
- Intracranial Hypertension: Exclude preexisting papilledema. May develop and is usually reversible after discontinuation or dose reduction (5.5).
- Fluid Retention (i.e., edema, arthralgia, carpal tunnel syndrome - especially in adults): May occur frequently. Reduce dose as necessary (5.6).
- Hypo pituitarism: Closely monitor other hormone replacement therapies (5.7)
- Hypothyroidism: May first become evident or worsen (5.8)
- Slipped Capital Femoral Epiphysis: May develop. Evaluate children with the onset of a limp or hip/knee pain (5.9)
- Progression of Preexisting Scoliosis: May develop (5.10)

----------ADVERSE REACTIONS----------
Other common somatropin-related adverse reactions include injection site reactions/rashes and lipoatrophy (6.1) and headaches (6.3).

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- Inhibition of 11β-Hydroxysteroid Dehydrogenase Type 1: May require the initiation of glucocorticoid replacement therapy. Patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance doses (7.1, 7.2).
- Glucocorticoid Replacement: Should be carefully adjusted (7.2)
- Cytochrome P450-Metabolized Drugs: Monitor carefully if used with somatropin (7.3)
- Oral Estrogen: Larger doses of somatropin may be required in women (7.4)
- Insulin and/or Oral Hypoglycemic Agents: May require adjustment (7.5)

See 17 **for PATIENT COUNSELING INFORMATION**

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

1.1 Pediatric Patients

Omnitrope® [somatropin (rDNA origin) injection] is indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone (GH).

Omnitrope® [somatropin (rDNA origin) injection] is indicated for the treatment of pediatric patients who have growth failure due to Prader-Willi Syndrome (PWS). The diagnosis of PWS should be confirmed by appropriate genetic testing [see **CONTRAINDICATIONS** (5.2)].

Omnitrope® [somatropin (rDNA origin) injection] is indicated for the treatment of growth failure in children born small for gestational age (SGA) who fail to manifest catch-up growth by age 2 years.

1.2 Adult Patients

Omnitrope® [somatropin (rDNA origin) 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; or
- Childhood Onset (CO): Patients who were GH deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

Patients who were treated with somatropin for growth hormone deficiency in childhood and whose epiphyses are closed should be reevaluated before continuation of somatropin therapy at the reduced dose level recommended for growth hormone deficient adults. Confirmation of the diagnosis of adult growth hormone deficiency in both groups involves an appropriate growth hormone provocative test with two exceptions: (1) patients with multiple other pituitary hormone deficiencies due to organic disease; and (2) patients with congenital/genetic growth hormone deficiency.

2. DOSAGE AND ADMINISTRATION

Therapy with Omnitrope® should be supervised by a physician who is experienced in the diagnosis and management of pediatric patients with short stature associated with GHD, Prader-Willi Syndrome (PWS), those who were born small for gestational age (SGA), and adult patients with either childhood onset or adult onset GHD.

2.1 Dosing of Pediatric Patients

General Pediatric Dosing Information

The Omnitrope® dosage and administration schedule should be individualized based on the growth response of each patient.

Response to somatropin therapy in pediatric patients tends to decrease with time. However, in pediatric patients, the failure to increase growth rate, particularly during the first year of therapy, indicates the need for close assessment of compliance and evaluation for other causes of growth failure, such as hypothyroidism, under nutrition, advanced bone age and antibodies to recombinant human GH (rhGH).

Treatment with Omnitrope® for short stature should be discontinued when the epiphyses are fused.

Pediatric Growth Hormone Deficiency (GHD)

Generally, a dosage of 0.16 - 0.24 mg/kg body weight/week, divided into 6 - 7 daily doses, is recommended.

Prader-Willi Syndrome (PWS)

Generally, a dosage of 0.24 mg/kg body weight/week, divided into 6 - 7 daily doses, is recommended.

Small for Gestational Age (SGA)

Generally, a dosage of up to 0.48 mg/kg body weight/week, divided into 6 - 7 daily doses, is recommended.

2.2 Dosing of Adult Patients

Adult Growth Hormone Deficiency (GHD)

Based on the weight-based dosing utilized in clinical studies with another somatropin product, the recommended dosage at the start of therapy is not more than 0.04 mg/kg/week given as a daily subcutaneous injection. The dose may be increased at 4- to 8-week intervals according to individual patient requirements to not more than 0.08 mg/kg/week. Clinical response, side effects, and determination of age- and gender-adjusted serum IGF-I levels may be used as guidance in dose titration.

Alternatively, taking into account recent literature, a starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight. This dose can be increased gradually every 1-2 months by increments of approximately 0.1-0.2 mg/day, according to individual patient requirements based on the clinical response and serum IGF-I concentrations. During therapy, the dose should be decreased if required by the occurrence of adverse events and/or serum IGF-I levels above the age- and gender-specific normal range. Maintenance dosages vary considerably from person to person.

A lower starting dose and smaller dose increments should be considered for older patients, who are more prone to the adverse effects of somatropin than younger individuals. In addition, obese individuals are more likely to manifest adverse effects when treated with a weight-based regimen. In order to reach the defined treatment goal, estrogen-replete women may need higher doses than men. Oral estrogen administration may increase the dose requirements in women.

2.3 Preparation and Administration

Omnitrope® Cartridge 5 mg/1.5 mL and Cartridge 10 mg/1.5 mL

Each cartridge of Omnitrope® must be inserted into its corresponding Omnitrope® Pen 5 or Omnitrope® Pen 10 delivery system. Instructions for delivering the dosage are provided in the Omnitrope® INSTRUCTIONS FOR USE booklet enclosed with the Omnitrope® drug and the Omnitrope® Pens.

Omnitrope® for injection 1.5 mg/vial and 5.8 mg/vial

Instructions for delivering the dosage are provided in the INSTRUCTIONS FOR USE leaflets enclosed with the Omnitrope® drug.

Once the diluent is added to the lyophilized powder, swirl gently; **do not shake.** Shaking may cause denaturation of the active ingredient.

Parenteral drug products should always be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Omnitrope® MUST NOT BE INJECTED if the solution is cloudy or contains particulate matter. Use it only if it is clear and colorless. Omnitrope must be refrigerated at 2° to 8°C (36° to 46°F).

Patients and caregivers who will administer Omnitrope® in medically unsupervised situations should receive appropriate training and instruction on the proper use of Omnitrope® from the physician or other suitably qualified health professional.

The dosage of Omnitrope® must be adjusted for the individual patient. The dose should be given daily by **subcutaneous** injections (administered preferably in the evening). Omnitrope® may be given in the thigh, buttocks, or abdomen.

Injection sites should always be rotated to avoid lipoatrophy.

3. DOSAGE FORMS AND STRENGTHS

Omnitrope® Cartridges and vials (for injection) are available:

- 5 mg/1.5 mL Cartridge is a prefilled sterile somatropin solution containing benzyl alcohol in a glass cartridge ready to be administered with the Omnitrope® Pen 5.
- 10 mg/1.5 mL Cartridge is a prefilled sterile somatropin solution in a glass cartridge ready to be administered with the Omnitrope® Pen 10.
- 1.5 mg/vial is supplied with two vials, one containing somatropin as a powder and the other vial containing the diluent (Sterile Water for Injection).
- 5.8 mg/vial is supplied with two vials, one containing somatropin as a powder and the other vial containing diluent (Bacteriostatic Water for Injection containing benzyl alcohol as a preservative).

4. CONTRAINDICATIONS

4.1 Acute Critical Illness

Treatment with pharmacologic amounts of somatropin is contraindicated 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. Two placebo-controlled clinical trials in non-growth hormone deficient adult patients (n=522) with these conditions in intensive care units revealed a significant increase in mortality (41.9% vs. 19.3%) among somatropin-treated patients (doses 5.3-8 mg/day) compared to those receiving placebo [see **WARNINGS AND PRECAUTIONS** (5.1)].

4.2 Prader-Willi Syndrome in Children

Somatropin 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 [see **WARNINGS AND PRECAUTIONS** (5.2)].

4.3 Active Malignancy

In general, somatropin is contraindicated in the presence of active malignancy. Any preexisting malignancy should be inactive and its treatment complete prior to instituting therapy with somatropin. Somatropin should be discontinued if there is evidence of recurrent activity. Since GHD may be an early sign of the presence of a pituitary tumor (or, rarely, other brain tumors), the presence of such tumors should be ruled out prior to initiation of treatment. Somatropin should not be used in patients with any evidence of progression or recurrence of an underlying intracranial tumor.

4.4 Diabetic Retinopathy

Somatropin is contraindicated in patients with active proliferative or severe non-proliferative diabetic retinopathy.

4.5 Closed Epiphyses

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

4.6 Hypersensitivity

Omnitrope® is contraindicated in patients with a known hypersensitivity to somatropin or any of its excipients. Localized reactions are the most common hypersensitivity reactions.

4.7 Benzyl Alcohol Sensitivity

Benzyl alcohol, a preservative in Omnitrope Cartridge 5 mg/1.5 mL and in Bacteriostatic Water for Injection, has been associated with toxicity in newborns.

Omnitrope® Cartridge 5 mg/1.5 mL and Omnitrope® for Injection 5.8 mg/vial must not be given to premature babies or neonates.

5. WARNINGS AND PRECAUTIONS

5.1 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 amounts of somatropin [see **CONTRAINDICATIONS** (4.1)]. The safety of continuing somatropin treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with somatropin in patients experiencing acute critical illnesses should be weighed against the potential risk.

5.2 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 (including onset of or increased snoring) and sleep apnea before initiation of treatment with somatropin. If, during treatment with somatropin, patients show signs of upper airway obstruction (including onset of or increased snoring) and/or new onset sleep apnea, treatment should be interrupted. All patients with Prader-Willi Syndrome treated with somatropin should also have effective weight control and be monitored for signs of respiratory infection, which should be diagnosed as early as possible and treated aggressively [see **CONTRAINDICATIONS** (4.2)].

5.3 Neoplasms

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