

PRODUCT INFORMATION

ZOMACTON[®]

somatropin

Name of the Drug

ZOMACTON[®] contains somatropin which is a protein having the structure (191 amino acid residues) of the major component of growth hormone produced by the human pituitary gland. It is produced in E.coli., by a method based on recombinant DNA technology.

Description

ZOMACTON[®] is a sterile white lyophilised powder intended for injection after reconstitution. Each vial of ZOMACTON[®] 1.3 mg contains somatropin 1.3 mg and mannitol 9.7 mg. Each vial of ZOMACTON[®] 4 mg contains somatropin 4 mg and mannitol 25.9 mg. A preserved (benzyl alcohol) diluent is provided with each product. Each vial of diluent contains sodium chloride 45 mg, benzyl alcohol 45 mg and water for injections to 5.0 mL. Vials are intended to be used for a single patient only.

Pharmacology

Pharmacodynamic properties of ZOMACTON[®] are identical to human growth hormone. Human growth hormone stimulates linear growth and increased IGF-1 (Insulin-like growth factor/somatomedin-C) concentrations in children with growth hormone deficiency. The measurable increase in linear growth results from the effect of ZOMACTON[®] on the epiphyseal growth plates of long bone. ZOMACTON[®] is intended to supply the lack of naturally secreted hormone. Somatropin increases skeletal and cell growth in patients with growth hormone deficiency. It increases protein and carbohydrate metabolism.

Clinical trials

A clinical study in 162 children showed an increase during 24 weeks to 24 months of treatment from an annualised growth velocity of 32 mm to 91 mm at 6 months, 83 mm at 12 months and 75 mm at 24 months. Seventy children were studied for 24 months and there are no data for final height. The dose administered was usually 0.1 mg/kg thrice weekly.

Pharmacokinetics following intravenous administration of 0.1 mg/kg ZOMACTON[®] show the elimination half life was about 25 minutes and the mean plasma clearance was 133 mL/min in healthy male volunteers. In the same volunteers, after a subcutaneous injection of 0.1 mg/kg ZOMACTON[®] to the forearm, the mean peak serum concentration was 80 ± 50 ng/mL which occurred approximately 7 hours post injection and the apparent elimination half life was approximately 2.7 hours. Compared to intravenous administration, the extent of systemic availability from subcutaneous administration was approximately 70%.

Indications

For the long-term treatment of children who have growth failure due to inadequate secretion of growth hormone.

Contra-indications

ZOMACTON[®] should not be used in subjects with closed epiphyses.

ZOMACTON[®] should not be used if there is evidence of an active tumor. Intracranial tumours should be inactive and anti-tumor therapy complete before initiating use of ZOMACTON[®].

ZOMACTON[®] should not be used in adults. No studies have been carried out to support its use in adults.

Multi-dose ZOMACTON[®] vials, reconstituted with bacteriostatic saline, should not be used in patients with hypersensitivity to benzyl alcohol.

Precautions

Diabetes Mellitus: Because of the diabetogenic effect of somatropin, ZOMACTON[®] should be used with caution in patients with diabetes mellitus. Regular blood glucose testing and close supervision is imperative in such cases.

Thyroid state: Patients should be euthyroid before ZOMACTON[®] treatment is initiated. Periodic monitoring of thyroid function is recommended to detect hypothyroidism emerging during treatment.

Intracranial lesions: Patients with growth hormone deficiency secondary to intracranial lesions should be closely observed to detect progression or recurrence of the underlying disease.

Steroid therapy: Steroid dosage greater than 15 mg/m² hydrocortisone or its equivalent may inhibit growth. Slipped epiphyses are more likely to occur in children receiving growth hormone, and any child with a limp should be evaluated as this may indicate a slipped epiphysis.

Local reaction at injection site should be avoided by changing the injection site to avoid the risk of lipoatrophy.

ZOMACTON[®] should not be used in pregnancy as its safety has not been established.

Prader-Willi Syndrome: Although Zomacton[®] is not indicated for use in patients who have Prader-Willi syndrome it should be noted that somatropin is contraindicated in patients with Prader-Willi Syndrome who are severely obese or have severe respiratory impairment.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Associations between elevated serum IGF-1 concentrations and risks of certain cancers have been reported in epidemiological studies. Causality has not been demonstrated. The clinical significance of these associations, especially for subjects treated with somatropin who do not have growth hormone deficiency and who are treated for prolonged periods, is not known. Somatropin showed no evidence of mutagenic activity in bacterial or mammalian cells and showed no activity in an assay for DNA damage in rodent hepatic cells.

Studies in animals have not been conducted to assess the effect of ZOMACTON[®] on fertility.

Use in Pregnancy (Category B2)

The use, safety and efficacy of ZOMACTON[®] in pregnant women has not been established. There have been no studies conducted with ZOMACTON[®] in lactating women. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZOMACTON[®] is administered to lactating women.

Adverse reactions

In clinical trials (n = 164) the following side effects were noted: headaches (14%), injection site pain (8%), injection site haematoma (4%), edema (2%), hypothyroidism (6%). The incidence of

side effects is similar to that seen in other growth hormone clinical studies.

Leukemia has been reported in a small number of patients treated with other growth hormone products. It is uncertain whether this risk is related to the pathology of growth hormone deficiency itself, growth hormone therapy, or other associated treatments such as radiation therapy for intracranial tumours.

Dosage and Administration

ZOMACTON[®] dosage must be individualized for each patient. A dosage schedule of up to 0.1 mg/kg body weight administered three times weekly by subcutaneous injection is recommended.

After the dose has been determined, each vial is to be reconstituted with the diluent supplied. The following volumes of diluent are recommended for reconstitution of ZOMACTON[®]:

ZOMACTON[®] 1.3 mg: to achieve a concentration of 1.3 mg/mL use 1.1 mL of diluent.

ZOMACTON[®] 4 mg: to achieve a concentration of 3.3 mg/mL use 1.2 mL of diluent.

To prepare the ZOMACTON[®], inject the diluent into the vial of ZOMACTON[®] aiming the stream of liquid against the vial wall. Then swirl the product vial with a gentle rotary motion until the contents are completely dissolved. Do no shake.

It is recommended that ZOMACTON[®] be administered using sterile disposable syringes and needles. The syringes should be of small enough volume that the prescribed dose can be withdrawn from the vial with reasonable accuracy. After reconstitution, vial contents should be clear, without particulate matter. Occasionally, after refrigeration, some cloudiness may occur. This is not unusual for proteins like ZOMACTON[®]. Allow the product to warm to room temperature. If the cloudiness persists or particulate matter is noted, the contents must not be used.

Before and after injections, the septum of the vial should be wiped with alcohol to prevent contamination of the contents after repeated needle insertions.

Overdosage

Long-term overdosage could result in some clinical features of acromegaly. Short-term overdosage may manifest as disturbances in glucose metabolism.

Presentation

Each vial is intended for use by a single patient only.

ZOMACTON[®] (somatropin) is a sterile white lyophilized powder intended for subcutaneous injection following reconstitution.

ZOMACTON[®] 1.3 mg: each vial contains 1.3 mg somatropin and 9.7 mg mannitol.

ZOMACTON[®] 4 mg: each vial contains 4 mg somatropin and 25.9 mg mannitol.

The diluent contains benzyl alcohol as a preservative. The vials should be used within 14 days following reconstitution. The diluent is added slowly to sterile powder to dissolve while slowly swirling. The solution should not be shaken. The solution should not be used if cloudy or if there is particulate matter.

Storage

ZOMACTON[®], before and after reconstitution with saline, must be stored at 2 – 8°C. Do not freeze.

The reconstituted vials should be used within 14 days.

Name and address of Sponsor

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ZOMACTON[®] 1.3 mg AUST R 79589

ZOMACTON[®] 4 mg AUST R 79590

Initial TGA approval: January 1997

Revised: 8 June 2001

Revised: 16 May 2002 (change of address)

Revised: 16 September 2004 (safety related change)

Revised: 17 September 2007 (new product name)