SCHEDULING STATUS: **S5**

PROPRIETARY NAME (and dosage form):

GENOTROPIN® 16 IU (5,3 mg) (lyophilised powder and solvent for injection)

COMPOSITION:

GENOTROPIN 16 IU (5,3 mg) is a two-compartment cartridge containing the dry lyophilised powder in the front compartment and the solvent in the rear compartment. The powder is reconstituted when inserted into the Genotropin Pen administering device.

After reconstitution the solution contains per ml:

Recombinant somatropin corresponding to:

Somatropin	16 IU (5,3 mg)
M-cresol	0,3 % m/v

PHARMACOLOGICAL CLASSIFICATION:

A 21.10 Tropic hormones

PHARMACOLOGICAL ACTION:

GENOTROPIN (somatropin) is produced by recombinant DNA technology; it is synthesised in bacteria, namely *Escherichia coli*.

Somatropin stimulates linear growth and increases growth rate in children who lack adequate endogenous growth hormone.

Treatment of growth hormone deficient patients with somatropin normalises serum IGF-1 (Insulin-like Growth Factor-1) levels.

In addition, the following actions have been demonstrated for somatropin:

- **Tissue growth**: Stimulation of skeletal muscle growth in patients with growth hormone deficiency (GHD), as well as increase in number and size of muscle cells
- **Protein metabolism**: Nitrogen retention demonstrated by decreased urinary nitrogen excretionand decreased serum urea nitrogen
- **Carbohydrate metabolism**: Children with hypopituitarism sometimes experience fasting hypoglycaemia that is improved by treatment with somatropin. Large doses of human growth hormone may impair glucose tolerance.
- **Lipid metabolism**: In growth hormone deficient patients, administration of somatropin has resulted in lipid mobilisation, reduction in body fat stores and increased plasma fatty acids.
- **Mineral metabolism**: Retention of sodium, potassium and phosphorous is induced by somatropin. Serum concentrations of inorganic phosphate are increased in patients with growth hormone deficiency after treatment with somatropin. Serum calcium is not significantly altered.

Approximately 80 % of GENOTROPIN is absorbed following SC injection and maximum serum concentrations are achieved after 3-4 hours

INDICATIONS:

- Short stature due to decreased or failed secretion of pituitary growth hormone.

Growth hormone deficiency should be verified before the preparation is administered. This requires a thorough investigation of the pituitary function, including proper provocation tests.

- Short stature in gonadal dysgenesis (Turner's Syndrome).
- Growth disturbance in prepubertal children with chronic renal insufficiency

CONTRA-INDICATIONS:

Hypersensitivity to m-cresol.

Pregnancy and breast-feeding.

GENOTROPIN should not be used when there is evidence of activity of a tumour. Intracranial lesions must be inactive and anti-tumour therapy completed prior to starting therapy.

GENOTROPIN should not be used for growth promotion in children with closed epiphyses.

WARNINGS

Hypothyroidism may occur and thyroid function should be monitored during growth hormone treatment.

Hypoglycaemia may occur initially and again after cessation of therapy. Hyperglycaemia may occur during therapy.

In patients with (pan) hypopituitarism standard replacement therapy has to be monitored closely.

In chronic renal insufficiency the renal function should have decreased below 50 % of the norm before institution of therapy. To verify the growth disturbance the growth should have been

followed for a year preceding institution of therapy. Conservative treatment for the renal insufficiency should have been established and should be maintained during treatment.

The GENOTROPIN treatment should be discontinued after renal transplant.

DOSAGE AND DIRECTIONS FOR USE

Short stature due to decreased or failed secretion of pituitary growth hormone:

The dosage is according to individual requirements. Generally, a dose of 0,5 - 0,7 IU/kg body weight per week or approximately 14 - 20 IU/m^2 body surface area per week is recommended.

Turner's Syndrome: Generally, a dose of 1,0 IU/kg body weight per week is recommended, or 28 IU/m^2 body surface area per week.

Chronic renal insufficiency: A dose of 30 IU/m^2 body surface area per week (approximately 1 IU/kg body weight per week) is recommended. Higher doses can be needed if growth velocity is too low. A dose correction can be needed after 6 months of treatment.

The weekly dose should be divided into six to seven subcutaneous injections. The injection site should be varied to prevent lipoatrophy.

Directions for use:

GENOTROPIN 16 IU (5,3 mg) is intended to be used with the Genotropin Pen injection device. The two-compartment cartridge is fitted into the Genotropin Pen causing reconstitution to take place. Instructions for use are enclosed with the Genotropin Pen package.

Missed dose: If a dose is missed one day, continue according to the prescription on the next day. Do not take two prescribed doses on the same day.

Treatment interruption: There are no withdrawal effects described if treatment with GENOTROPIN is stopped from one day to another.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Local skin reactions may occur which may be due to the m-cresol.

Allergic reactions may occur and may necessitate discontinuation of therapy.

Antibodies towards growth hormone are formed in some patients treated with human growth hormone. The frequency of such antibody formation is low. Antibody binding capacity is negligible and without clinical significance.

Hyperlipidaemia, haematuria, hypocalcaemia and albuminuria may occur.

Acute leukaemia has occurred in growth hormone-deficient children treated with somatropin, but no certain association with the growth hormone has been found.

Some rare cases of benign intracranial hypertension have been reported.

In vitro chromosome aberrations have been reported during growth hormone therapy; the clinical significance is unknown.

Precautions:

The diagnosis should be confirmed before treatment starts. Therapy with somatropin should be directed by suitably qualified physicians.

In diabetes mellitus, the dose of insulin might require adjustment when treatment with GENOTROPIN is instituted.

Patients with growth hormone deficiency secondary to an intracranial lesion should be examined frequently for progression or recurrence of the underlying disease process.

In case of severe or recurrent headache, visual problems, nausea and/or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed a diagnosis of benign intracranial hypertension should be considered and if appropriate the growth hormone treatment should be discontinued.

Patients substituted with L-thyroxine should be monitored for thyroid hormone levels including measurement of triiodothyronine (T_3) and thyroxine (T_4).

In patients with endocrine disorders, including growth hormone deficiency, slipped epiphyses of the hip may occur more frequently. Each child limping during treatment with growth hormones should be examined clinically.

Resistance to the therapeutic effect may occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See "SIDE-EFFECTS AND SPECIAL PRECAUTIONS".

Treatment is symptomatic and supportive.

IDENTIFICATION:

GENOTROPIN 16 IU (5,3 mg) is a two-compartment cartridge with a dry, white powder in the front compartment and clear solvent in the rear compartment.

PRESENTATION:

Packs of 1 x 1 ml two-compartment cartridge or 5 x 1 ml two-compartment cartridges

Genotropin Pen administering device.

STORAGE INSTRUCTIONS:

***Lyophilised powder*:** Store between 2 °C and 8 °C (refrigerated). Protect from light.

Stable for 1 month at room temperature (25 °C).

***Reconstituted solution*:** Stable for 28 days at 2 °C to 8 °C protected from light.

Frozen solution should not be used.

The Genotropin Pen needs no maintenance. The exterior can be cleaned by wiping with a damp cloth. The Genotropin Pen is provided in a specially designed pen-case. Keep the Genotropin Pen in the pen-case where it is protected against dirt and damage.

Keep out of reach of children.

REGISTRATION NUMBER:

GENOTROPIN® 16 IU (5,3 mg): X/21.10/214

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

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SOUTH AFRICA

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