Actions that have been demonstrated for Nutropin AQ, somatropin, somatrem, and/or pituitary-derived hGH include:

1) Skeletal Growth: GH stimulates skeletal growth in pediatric patients with growth failure due to a lack of growth hormone (GH) secretion. Linear growth is facilitated in part by GH-stimulated protein synthesis. This is reflected by nitrogen retention as measured by the single indicator of urea nitrogen recovery and is accompanied by skeletal muscle growth as assessed by the measurement of total body nitrogen and concurrent increases in muscle mass.

B. Protein Metabolism

The methods of total body protein mass in response to GH treatment typically result in a significant increase in both muscle and fat mass in children and adults who have GH deficiency. These increases are usually consistent with the changes in measured nitrogen balance and body composition. Elevations in total body protein mass are achieved by GH therapy in both children and adults with GH deficiency and have been used successfully to assist in treatment planning prior to surgical, obstetric, or other high-stress situations.

C. Carbohydrate Metabolism

In studies reporting on the effects of GH therapy on glucose metabolism in GH deficient children, benefits have included a decrease in basal and postprandial insulin levels, more commonly in overweight or obese individuals. In addition, mean fasting and postprandial insulin levels decreased in 15-40% of GH-treated patients with type 2 diabetes mellitus. These results indicate that GH therapy might be beneficial in the treatment of children with impaired glucose tolerance or overt diabetes and in adults with type 2 diabetes mellitus.

Growth Hormone Deficiency in Adults

Two multicenter, double-blind, placebo-controlled clinical trials were conducted using Nutropin® [somatropin (rDNA origin)] subcutaneous injections and Nutropin AQ® [somatropin (rDNA origin) injection]. These trials, called Study 85-023 and Study 85-024, assessed the efficacy and safety of GH therapy in adult patients with GH deficiency of adult onset. GH deficiency of adult onset includes patients with GH deficiency previously diagnosed before age 18 years and patients whose GH abnormality is not apparent until adulthood. The diagnosis of GH deficiency of adult onset is made using standardized pharmacological or biochemical testing or both. GH therapy was administered at doses of 0.3 mg/kg/week, 0.6 mg/kg/week, or 1.2 mg/kg/week in Study 85-023 and 0.3 mg/kg/week or 0.6 mg/kg/week in Study 85-024. Patients continued to receive GH therapy for an average of 25 months in Study 85-023 or 52 months in Study 85-024.

Effects of Nutropin on Growth Failure Due to Chronic Renal Insufficiency (CRI)

Chronic renal insufficiency (CRI) is a progressive disease characterized by impaired renal excretory function that usually begins in childhood and progresses over time. In the absence of dialysis, patients with CRI will reach end-stage renal disease (ESRD) and require dialysis or transplantation. Patients with CRI may have a very short life expectancy and often have multiple co-morbidities, such as cardiovascular disease, diabetes mellitus, and skeletal abnormalities, that require the concomitant use of medications. Nutropin AQ® [somatropin (rDNA origin) injection] is also indicated for the long-term treatment of idiopathic short stature (ISS) in children and adults with growth hormone (GH) deficiency of adult onset.

In a post-marketing surveillance study, the National Cooperative Growth Study, the pattern of adverse events in over 1,000 children and adults who received Nutropin AQ for ISS and GH deficiency of adult onset were similar to that expected in natural populations of the same age and sex. The most common adverse reactions were headache, joint pain, and diarrhea. The most common adverse reactions that lead to withdrawal from the study were headache, joint pain, and depression. In studies of patients with GH deficiency of adult onset, 18% of patients discontinued therapy prior to a maximum 12-month duration of therapy.

In order to optimize therapy for patients who require dialysis, the following guidelines for injection schedule are recommended:

1. Patients who require hemodialysis: Patients should receive their GH injections 3 hours prior to their hemodialysis or 3 hours post-hemodialysis. The following schedule may be considered:
   - Dose: 0.3 mg/kg/week
   - Administration: 0.15 mg/kg/week subcutaneously 4 days/week (Monday, Tuesday, Thursday, and Friday) or 0.075 mg/kg/week subcutaneously 7 days/week (Monday through Sunday)
   - Duration: 12 months

2. Patients who require peritoneal dialysis: Patients should receive their GH injections 4 to 6 hours post-peritoneal dialysis. The following schedule may be considered:
   - Dose: 0.3 mg/kg/week
   - Administration: 0.15 mg/kg/week subcutaneously 4 days/week (Monday, Tuesday, Thursday, and Friday) or 0.075 mg/kg/week subcutaneously 7 days/week (Monday through Sunday)
   - Duration: 12 months

In children and adults with CRI, the use of GH therapy may improve their growth rates and somatic development. However, the long-term effects of GH therapy on the progression of CRI and renal osteodystrophy, the potential for increased mortality risk, and the potential for increased cardiovascular disease risk in this population have not been established. Therefore, GH therapy should be used cautiously in patients with CRI.

Nutropin AQ® [somatropin (rDNA origin) injection] is contraindicated in patients with active uterine carcinoma or precancerous uterine growths and should be used with caution in patients with a history of or risk factors for neoplasia.

The use of GH therapy to treat children with congenital adrenal hyperplasia or children with GH deficiency due to hypopituitarism caused by pituitary disease, hypothalamic disease, surgery, or radiation therapy, is not recommended. The long-term effects of GH therapy on the progression of growth failure secondary to these conditions have not been established.

Nutropin AQ® [somatropin (rDNA origin) injection] is also contraindicated in patients with active growth hormone-secreting tumors (e.g., pituitary adenoma) and in patients with a history of GH-dependent somatic or malignant tumors.

Nutropin AQ® [somatropin (rDNA origin) injection] is not recommended for use in children with Prader-Willi syndrome due to the risk of increased fat mass, which may be detrimental to the patients’ overall health status.

GH therapy in adults with GH deficiency of adult onset was associated with an increase of median fasting insulin from 19.1 mg/dL (interquartile range, 11.9 to 34.0 mg/dL) at baseline to 24.0 mg/dL (interquartile range, 15.5 to 38.2 mg/dL) at 12 months. In addition, a subset of patients who received GH therapy had a decrease in median postprandial insulin from 31.9 mg/dL (interquartile range, 16.9 to 54.5 mg/dL) at baseline to 25.0 mg/dL (interquartile range, 15.0 to 39.0 mg/dL) at 12 months. This decrease was more pronounced in patients who received the higher dose of GH therapy.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.

In a subset of patients with type 2 diabetes mellitus who received GH therapy, the median fasting insulin decreased from 19 mg/dL (interquartile range, 12 to 30 mg/dL) at baseline to 13 mg/dL (interquartile range, 8 to 20 mg/dL) at 12 months. In addition, the median postprandial insulin decreased from 32 mg/dL (interquartile range, 15 to 50 mg/dL) at baseline to 25 mg/dL (interquartile range, 13 to 40 mg/dL) at 12 months.
Nutropin® [somatropin (rDNA origin) for injection]

STABILITY AND STORAGE

After Reconstitution—Vial contents are stable for 14 days when reconstituted with Bacteriostatic Water for Injection, USP (benzyl alcohol preserved)

CONTRAINDICATIONS

Genentech, Inc.

The clinical significance of elevated IGF-I values is unknown. Blunted growth response to exogenous GH in children with severe liver disease has been documented. Nutropin therapy resulted in an increase in mean IGF-I SD score from –0.9±1.0 to –0.2 ±0.9 in Treatment Year 1. During Treatment Year 2, the mean IGF-I SD score was –0.4±1.1, and a similar but smaller increase was noted in the third year of treatment. The clinical significance of this decrease is unknown.

Hepatic Insufficiency—A reduction in rhGH clearance has been noted in patients with severe liver dysfunction. The clinical significance of this decrease is unknown.