Genentech

MATERIAL SAFETY DATA SHEET

Date Issued: September 16, 2009 Version: 4.0
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Section 1 – Product and Company Identification

Product Name:	Nutropin® and Nutropin AQ®
Chemical Name:	Somatropin (rDNA origin) (recombinant human growth hormone)
Chemical Family:	Protein
Company Name:	Genentech, Inc.
Company Address:	1 DNA Way, South San Francisco, CA 94080
Company Phone:	(650) 225-1000
Emergency Phone:	(800) 821-8590

Section 2 – Hazards Identification

Emergency Overview
Nutropin® and Nutropin AQ® derive their therapeutic benefit from human growth hormone (hGH), a protein that is not well absorbed by inhalation or by contact with eyes, skin, or mucous membranes. Adverse health effects have been observed in patients following subcutaneous injection of therapeutic doses for the treatment of various diseases associated with growth hormone deficiency. Although the health effects of occupational exposure to this product are not fully known or characterized, no adverse effects are anticipated as a result of occupational or incidental exposure. Nutropin® is a white, odorless, lyophilized powder. Nutropin AQ® is a clear, colorless, odorless liquid.

For more product information see Section 11 or visit www.gene.com, under “Medicines”.

Routes of Exposure
Direct contact with eyes, skin, or mucous membranes, and inhalation of powder, are the possible primary routes of occupational exposure. No adverse health effects through these routes are expected to occur due to the large size of the protein (22,125 daltons) and its poor potential for absorption.

Section 3 – Composition/Information on Ingredients

Nutropin®

Component(s):	CAS No.:
Somatropin	12629-01-5
Mannitol	69-65-8
Sodium phosphate monobasic	10049-21-5
Sodium phosphate dibasic	75589-79-4

Glycine	139-89-9

Bacterostatic water with 0.9% benzyl alcohol preservative for reconstitution

Nutropin AQ®

Component(s):	CAS No.:
Somatropin	12629-01-5
Sodium chloride	7647-14-5
Phenol	108-95-2
Polysorbate 20	9005-64-5
Sodium citrate	6132-04-3
Water	7732-18-5

Formula (drug substance): Protein composed of 191 amino acid residues
Synonyms (drug substance): rhGH

Section 4 – First Aid Measures

Eye/Skin Contact

Immediately flush eyes thoroughly with water or wash skin for at least 5 minutes as a prudent chemical hygiene practice. Report exposure to supervisor.

Section 5 – Fire Fighting Measures

Flammability/Explosivity

Not flammable or explosive. No special fire fighting measures.

Section 6 – Accidental Release Measures

If material is released or spilled, soak up material with absorbent material and wash spill area thoroughly with soap and water. For the powder, wet down the spilled material and use a soak pillow or other absorbent. Dispose of collected material in accordance with applicable waste disposal regulations.

Section 7 – Handling and Storage

Refrigeration (2-8°C, 36-46°F) is advised to maintain longer pharmacological activity. Protect from sunlight. Avoid agitation.

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Section 8 – Exposure Control and Personal Protective Equipment

Skin Protection

No special protective clothing required. Follow standard chemical hygiene practices, such as wearing a protective outergarment, safety glasses, and washing hands after handling.

Eye Protection

As a prudent chemical hygiene practice, use safety glasses with side shields.

Other

Clean all protective equipment after use.

Section 9 – Physical and Chemical Properties

Molecular Weight	22,125 Daltons
pH:	Not applicable for Nutropin®. Nutropin AQ® has a pH of 6.0.
Boiling Point (°C):	Not applicable for Nutropin®. No data available for Nutropin AQ®.
Melting Point	No data available for Nutropin®. Not applicable for Nutropin AQ®.
Vapor Pressure:	Not applicable for Nutropin®. Nil for Nutropin AQ®.
Solubility in Water:	Soluble
Vapor Pressure:	Not applicable for Nutropin®. No data available for Nutropin AQ®.
Appearance:	White, odorless, lyophilized powder (Nutropin®) Clear, colorless, odorless liquid (Nutropin AQ®).
Specific Gravity:	No data available
Vapor Density:	Not applicable for Nutropin®. No data available for Nutropin AQ®.
Percent Volatile:	Not applicable for Nutropin®. Nil for Nutropin AQ®.

Section 10 – Stability and Reactivity

Stability: Stable
Hazardous Polymerization: Will not occur
Hazardous Decomposition Products: None expected

Section 11 – Toxicological Information

Eye/Skin

No data available

Systemic Toxicity

SIngle-dose

Nutropin Depot was well-tolerated in rabbits administered a single subcutaneous (SC) or intravenous (IV) dose of 300 mg (45 mg recombinant humanized human growth hormone). In monkeys administered a single intramuscular (IM) dose of 50 mg/kg, the only observations were microscopic mild foreign body inflammation and fibrosis.

Repeat-dose

Numerous studies of somatropin in animals have been reported. Rats injected SC with up to 3,125 μg/kg/day of somatropin for 14 days did not exhibit any significant signs of toxicity. In monkeys dosed with 50 mg/kg of Nutropin Depot once monthly for 1-3 months, findings were limited to reversible local tissue reaction. In another study in monkeys, somatropin was administered 3 times a week for 2 to 13 weeks at doses ranging from 125 to 625 μg/kg. There was no evidence of overt toxicity and no significant changes in hematology or serum chemistry. parameters were observed.

Reproductive and Developmental Toxicity

In a study in rats administered 0.3, 1.0, and 3.3 IU (300, 1,000 and 3,300 μg/kg) rhGH daily for 2 weeks before mating, throughout mating, and during the first 7 days of pregnancy, significant prolongation of the estrous cycle was observed at the two highest doses. The number of early resorptions was increased at the highest dose level, and fetal body weights were increased at all doses. In another study in rats, daily SC injections of natural GH during pregnancy of rats (total dose 1.4-2 mg/animal = about 8 mg/kg) yielded no other effects in the offspring than a significant increase of the mean birth weight.

One study of hGH in dogs was found. Male dogs were dosed with 3, 10 or 25 IU/kg/day (= 1, 3.3 or 8.3 μg/kg/day) SC of pituitary derived hGH or rhGH-met. for 20-28 days. The highest dose caused marked reduction of plasma prolactin,LH and testosterone levels associated with reduction of testes and prostate weights, degeneration of germ cells and epithelial atrophy in testes, degenerative changes in epididymis and reduced height of the prostatic epithelium. Similar, although less severe morphological changes were observed after the middle dose. The results indicate that repeated administration of very high doses of hGH interferes with the hormonal regulation of the testis in the dog.

In monkeys, 2.5 μg/kg somatropin administered by SC injection three times weekly over 50 months, no effects on fertility, delivery, nursing, or fetal development were noted.

Carcinogenicity and Genotoxicity

No carcinogenicity studies of Nutropin, somatropin or rhGH have been conducted. In mice dosed at150 mU/animal/day SC (= about 2.5 mg/kg/day based on assumptions: 3 IU = 1 mg; 20 g body weight) for four weeks, significantly increased frequencies of chromosomal aberrations in bone marrow cells as measured by the micronucleus test. *In vitro* treatment of Chinese Hamster

Ovary cells with rhGH (36 or 360 mU/ml = 12 or 120 μg/mL) also induced structural chromosomal aberrations. The monitoring of chromosomal abnormalities in peripheral blood lymphocytes in twelve idiopathic growth hormone deficient patients over 12 months of rhGH therapy did not reveal an increase when compared with age-matched healthy controls.

Medical Conditions Aggravated by Exposure
For the complete description of contraindications and precautions refer to the Genentech web site at www.gene.com, under "Medicines".

Clinical/Human Studies
The most frequent adverse reactions, although infrequent, observed in patients following SC injection of therapeutic doses (0.006-0.025 mg/kg daily for adults or 0.3 or 0.7 mg/kg for pediatric patients) include allergenicity, injection site pain, and leukemia. For the complete description of warnings, precautions, and adverse reactions please refer to the Genentech web site at www.gene.com, under "Medicines".

Occupational Exposure Limit
None currently established by OSHA, NIOSH, ACGIH, or Genentech.

Section 12 – Ecological Information

Persistence and Degradability
The U.S. Food and Drug Administration (FDA) granted for Nutropin a Finding of No Significant Impact (FONSI) on the environment. The conclusion of the European Medicines Agency (EMEA) Ecotoxicity/Environmental Risk Assessment of Nutropin was as follows:

> "Somatropin is identical with the naturally occurring human growth hormone. This peptide hormone is rapidly and completely degraded by enzymatic hydrolysis in the human organism. Thus, the therapeutically administered compound is not released into the eenvironment.
>
> Inadvertent release of wasted material would also not cause any problems in the environment due to its peptide structure which will be rapidly destroyed and mineralised by microbial hydrolytic processes. Therefore, no environmental risk can be expected from the introduction of Nutropin into therapy".

Aquatic Toxicity
No impact on marine life is anticipated since somatropin is a protein that is expected to rapidly denature outside of carefully controlled temperature and pH conditions.

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Section 13 – Disposal Considerations

Dispose of waste residues according to prescribed federal, state, and local guidelines.

Section 14 – Transportation Information

Hazard Class
These are not hazardous materials (dangerous goods) according to the U.S. Department of Transportation (DOT) Hazardous Materials Regulations (HMR, 49 CFR Parts 171-180) or those under the International Air Transport Association (ICAO/IATA), IMDG Code, or other international and national regulations applying the classification criteria appearing in the Dangerous Goods (UN Model Regulations).

Packing Group
Not applicable

UN Number
Not applicable

Section 15 – Regulatory Information

European Union (EU) Risk and Safety Phrases
Not assigned

Other Regulatory
Not listed by IARC, NTP, OSHA or California Proposition 65 as a carcinogen. Not listed by California's Proposition 65 as a reproductive or developmental toxin

Section 16 – Other Information

No additional information.

The above information is offered in good faith and with the belief that it is accurate. While efforts are made to provide useful information relating to handling, in the event of an adverse incident associated with this product, this Material Safety Data Sheet (MSDS) is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.