



NDA 19-640/S-033

Eli Lilly and Company
Attention: Jeffery T. Fayerman, PhD
Senior Regulatory Research Scientist, US Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Fayerman:

Please refer to your new drug application (NDA) dated and received on September 26, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humatrope (somatropin [rDNA origin] for injection) 5, 6, 12, 24 mg vials and cartridges.

We acknowledge receipt of your submissions dated January 6, February 17, March 5, April 2, June 17 and 19, and July 14 and 21, 2003.

This supplemental new drug application provides for the use of Humatrope for the long-term treatment of idiopathic short stature, also called non-growth hormone-deficient short stature, defined by height $SDS_{< -2.25}$, and associated with growth rates unlikely to permit attainment of adult height in the normal range, in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means.

We completed our review of this application, as amended and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert submitted July 21, 2003). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 19-640/S-033.**" Approval of this submission by FDA is not required before the labeling is used.

We encourage the continuation of your ongoing global postmarketing observational research program, entitled "The Genetics and Neuroendocrinology of Short Stature International Study (GeNeSIS-Protocol GDFC). GeNeSIS includes a neoplasia substudy protocol and a growth-predictors substudy protocol as described in your submissions dated September 26, 2002 and March 25 and June 19, 2003. The goal of GeNeSIS is to evaluate further the long-term efficacy and safety of Humatrope treatment

in pediatric patients receiving the drug for short stature, including idiopathic short stature. This program gathers information on adverse event frequencies by documenting, at each visit, the presence or absence of protocol-identified adverse events that have been associated with growth hormone use. Additionally, the program collects auxological data and laboratory data on carbohydrate metabolism, thyroid function, as well as IGF-1 and IGF binding protein-3 (IGFBP-3) levels, whenever these tests are obtained by the patient's physician. Updated GeNeSIS information will be reported to the FDA on a regular basis. Submit the protocols related to GeNeSIS to your IND for this product.

We also remind you of the risk management plan related to the use of Humatrope for idiopathic short stature that you plan to implement as outlined in your submissions dated September 26, 2002 and March 25 and June 19, 2003. Elements of that plan include:

- Restrictive Humatrope labeling for idiopathic short stature
- Physician education
- Limited marketing to (pediatric) endocrinologists
- Limited sales force
- No direct-to-consumer advertising
- Controlled distribution process

We request that you provide FDA with information about any changes to this plan at the time the changes are made and periodically report to FDA data on the extent of use of Humatrope for idiopathic short stature.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Monika Johnson, Regulatory Project Manager, at (301) 827-9087.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug
Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation Research

Enclosure: Draft package insert

A4.0 NL1641 AMP

HUMATROPE[®]
SOMATROPIN (rDNA ORIGIN) FOR INJECTION
VIALS
and
CARTRIDGES FOR USE WITH THE

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

David Orloff

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