NDA 21-148

Novo Nordisk Pharmaceuticals, Inc.
Attention: Barry Reit, Ph.D.
Vice President, Regulatory Affairs
100 Overlook Center, Suite 200
Princeton, NJ 08540-7810

Dear Dr. Reit:

Please refer to your new drug application (NDA) dated June 30, 1999, received July 1, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norditropin (somatropin [rDNA origin] injection) Cartridges, 5mg/1.5mL, 10mg/1.5mL, and 15mg/1.5mL.

We acknowledge receipt of your submissions dated September 29, 1999, and February 24 and 25, March 8, 16, and 23, April 3 (2), 5, 6, 7, 11, 13, and 17, and May 25, 2000.

This new drug application provides for a ready-to-inject solution of Norditropin (somatropin [rDNA origin] injection) Cartridges (5 mg/1.5mL, 10mg/1.5mL, and 15mg/1.5mL) and for the new NordiPen 5, NordiPen 10, and NordiPen 15 (Dial-A-Dose Somatropin Delivery Devices), reuseable injection devices. Norditropin Cartidges are to be used for the long-term treatment of children who have growth failure due to inadequate secretion of endogenous growth hormone.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert, pen device instructional manual, immediate container, and carton labels submitted May 25, 2000). 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 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-148." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated April 7, 2000. These commitments, along with any completion dates agreed upon, are listed below.

> You will conduct a study to compare Norditropin Cartridges to Norditropin for Injection, 4 mg or 8 mg, in terms of adverse experiences reported. Each treatment group will have at least 50 patients who will be followed for at least one year, with quarterly clinical study visits. The study will be initiated by October 1, 2000, and completed by October 1, 2002. Final reports will be available by April 1, 2003.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have fulfilled the pediatric study requirement at this time.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

> Division of Drug Marketing, Advertising, and Communications, HFD-40
> Food and Drug Administration
> 5600 Fishers Lane
> Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Crystal King, P.D., M.G.A., Regulatory Project Manager, at 301-827-6423.

Sincerely yours,

John K. Jenkins, M.D.
Acting Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research