DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-148/S-006

Novo Nordisk Pharmaceuticals, Inc.
Attention, Lorraine Lucas, PhD
Associate Director, Regulatory Affairs
100 College Road West
Princeton, NJ 08540

Dear Dr. Lucas:

Please refer to your supplemental new drug application dated October 31, 2003, received November 3, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norditropin NordiFlex (somatropin [rDNA origin] injection).

We acknowledge receipt of your submissions dated May 21, August 26, and September 20, 2004.

Your submission of May 21, 2004 constituted a complete response to our March 3, 2004 action letter.

This supplemental new drug application provides for a new, pre-filled, multiple dose, and disposable Norditropin NordiFlex Pen device for use with Norditropin cartridges, 5 mg/mL, 10 mg/mL, and 15 mg/mL.

We completed our review of this application, as amended. This application 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 submitted labeling (package insert, patient information, Instructions for use, immediate container (pen) and carton labels) submitted August 26, 2004, revised as follow:

Package insert
-Revise the HOW SUPPLIED section to state that the pens are individually cartoned.

Instructions for use
-In the first sentence, "Norditropin NordiFlex… is a disposable dial-a-dose growth hormone delivery system…0.025mg to 1.50 mg.", revise "1.50 mg" to read "1.5 mg".
-In instruction 1.A, reference is made to wiping the threaded cap. Please label the threaded cap on the diagram of the device.
-In the last sentences in instruction F (regarding the need to use a second pen when the last dose in a pen is not sufficient), revise the text to provide instructions to assist the patient is remembering the dose already received with the first pen.

Container (pen) Label
-Revise the text to read as follows:

> "Store non-injected/unused pen refrigerated ($2^{o}C$-$8^{o}C$/$36^{o}F$-$46^{o}F$). After initial injection, keep pen refrigerated. Do not freeze. Use within 4 weeks. Discard unused portion. Avoid direct light."

-Revise established and proprietary names to read:

> "Norditropin® NordiFlex®
> Somatropin (rDNA origin) injection
> 5 mg/1.5 mL (or 10 mg/1.5 mL)(or 15 mg/1.5mL) Prefilled Pen"

Cartons
-Add "Do not store with needles"
-Add "For subcutaneous administration only"
-Revise the text to read as follows:

> "Store non-injected/unused pen refrigerated ($2^{o}C$-$8^{o}C$/$36^{o}F$-$46^{o}F$). After initial injection, keep pen refrigerated. Do not freeze. Use within 4 weeks. Discard unused portion. Avoid direct light."

-Revise established and proprietary names to read:

> "Norditropin® NordiFlex®
> Somatropin (rDNA origin) injection
> 5 mg/1.5 mL (or 10 mg/1.5 mL)(or 15 mg/1.5mL) Prefilled Pen"

These revisions are terms of the approval of this application.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-148/S-006." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send 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-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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

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) 301-827-9087.

Sincerely,

{See appended electronic signature page}

David G. Orloff, MD
Director
Division of Metabolic & Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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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