



NDA 21-536

Novo Nordisk Inc.
Attention: Mary Ann McElligott, Ph.D.
Associate Vice President, Regulatory Affairs
100 College Road West
Princeton, NJ 08540

Dear Dr. McElligott:

Please refer to your new drug application (NDA) dated December 5, 2002, received December 5, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Levemir (insulin detemir [rDNA origin] injection).

We acknowledge receipt of your submissions dated October 22, and November 21, 2003, May 21, June 22, and December 20, 2004, and January 21 and 24, March 10 and 21, April 4, 7, 8, and 26, May 11, and June 1, 10, 14 (2), 15, and 16 (2), 2005.

The December 20, 2004, submission constituted a complete response to our October 2, 2003, action letter.

This new drug application provides for the use of Levemir (insulin detemir [rDNA origin] injection) for once or twice-daily subcutaneous administration in the treatment of adult patients with Type 1 or Type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and the editorial revision listed below:

The "Sample Not For Resale" statement should be displayed prominently on all of the panels of the sample carton labeling for the vial, 3 mL PenFill cartridge, 3 mL FlexPen, and 3 mL InnoLet.

We remind you that the color used on the labels and labeling for Levemir, "Green C," should not be used for any other insulin product in the International Diabetes Foundation color coding scheme.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package insert and text for the patient package inserts submitted June 16, 2005; immediate container and carton labels submitted June 10, 2005) as edited above. Marketing the product with FPL that is

not identical to the approved labeling text as edited 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 - NDAs*. 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 21-536.**” Approval of this submission by FDA is not required before the labeling is used.

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. We note that you have fulfilled the pediatric study requirement for this application for ages 6 and above.

Additionally, we are deferring submission of your pediatric studies for ages birth through 5 years old until June 30, 2009.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of diabetes in pediatric patients ages birth through 5 years old.

Final Report Submission: June 30, 2009

Submit the final study report to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment should be clearly designated “**Required Pediatric Study Commitments**”.

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 the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Julie Rhee, Regulatory Project Manager, at (301) 827-6424.

Sincerely,

{See appended electronic signature page}

Robert J. Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Labeling pieces enclosed:

1. Physician Insert
2. Information For The Patient for 10 mL Vial and 3 mL PenFill Cartridge
3. Information For The Patient for 3 mL FlexPen
4. Information For The Patient for 3 mL InnoLet
5. Levemir FlexPen (3 mL) sample carton
6. Levemir FlexPen (3 mL) sample container
7. Levemir FlexPen (3 mL) trade carton
8. Levemir InnoLet (3 mL) sample carton
9. Levemir InnoLet (3 mL) sample container
10. Levemir InnoLet (3 mL) trade carton
11. Levemir PenFill (3 mL) sample carton
12. Levemir PenFill (3 mL) sample container
13. Levemir PenFill (3 mL) trade carton
14. Levemir vial (10 mL) sample carton
15. Levemir vial (10 mL) sample container
16. Levemir vial (10 mL) trade container

Labeling pieces not enclosed:

1. Levemir FlexPen (3 mL) trade container
2. Levemir InnoLet (3 mL) trade container
3. Levemir PenFill (3 mL) trade container
4. Levemir vial (10 mL) trade carton

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

/s/

Robert Meyer

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