

NDA 20-164/S-034

Aventis Pharmaceuticals Products Inc.
Attention: Edmond Roland, M.D.
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19426-0107

Dear Dr. Roland:

Please refer to your supplemental new drug application dated November 3, 1999, received November 4, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lovenox® (enoxaparin sodium) Injection.

This supplemental new drug application provides for the following change: in the PRECAUTIONS section of the package insert, the addition of a "Geriatric use" subsection, in response to the final rule entitled "Specific Requirements on Content and Format of Labeling for Human Prescription Drugs' Addition of "Geriatric Use" Subsection in the Labeling, published in August 27, 1997 Federal Register (62 FR 45313-45326).

We have completed the review of this supplemental 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 and with the minor editorial revisions listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

Revise the text to read (red-line/strikeout edit) as follows:

Geriatric Use: Over ~~5469~~ 2800 patients, 65 years and older, have been enrolled received enoxaparin sodium in pivotal clinical trials. studies with enoxaparin sodium, of whom approximately half were 65 years or older. The efficacy of Lovenox Injection in the elderly (≥65 years) was similar to that seen in younger patients (<65 years). The incidence of bleeding complications was similar between elderly and younger patients when 30 mg every 12 hours or 40 mg once a day doses of Lovenox Injection were employed. The incidence of bleeding complications was higher in elderly patients as compared to younger patients when Lovenox Injection was

administered at doses of 1.5 mg/kg once a day or 1 mg/kg every 12 hours.
The risk of Lovenox Injection-associated bleeding ~~appeared to increase-~~
increased

with age. ~~as experienced with other anticoagulants.~~ Serious adverse events
increased with age for patients receiving Lovenox Injections. Other clinical
experience (including postmarketing surveillance and literature reports) has not
revealed additional differences in the safety of Lovenox Injection between
elderly and younger patients. Careful attention to dosing intervals and
concomitant medications (especially antiplatelet medications) is advised.
Monitoring of geriatric patients with low body weight (<45 kg) and those
predisposed to decreased renal function should be considered. (See
CLINICAL PHARMACOLOGY and **General** and **Laboratory Tests** subsections
of **PRECAUTIONS**).

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (package insert submitted November 3, 1999).

These revisions are terms of the approval of this application.

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.

The submission should include the appropriate number of copies of the package insert from both the Maison-Alfort and the Dagenham printing sites. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-164/S-034". Approval of this submission by FDA is not required before the labeling is used.

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

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Karen Oliver, Regulatory Health Project Manager, at (301) 827-7457.

Sincerely,

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

