



Aventis Pharmaceuticals Products Inc.
Attention: Joseph A. Carrado, M.Sc., R.Ph.
Global Drug Regulatory Affairs
Global Therapeutic Area Head
Route 202-206
PO Box 6800
Bridgewater, NJ 08807-0800

Dear Mr. Carrado:

Please refer to your supplemental new drug applications dated August 23, 2000, received August 24, 2000 [S-040], and August 14, 2001, received August 15, 2001 [S-045 and S-046], submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lovenox[®] (enoxaparin sodium) Injection.

We acknowledge receipt of your submissions dated October 27, and December 1 and 29, 2000, and July 11, August 14, November 12 and 28, 2001, to S-040.

These supplemental new drug applications provide for the following:

Supplement 040, submitted as a "Supplement - Changes Being Effected" (CBE) supplement, provides for the following changes: (1) in the WARNINGS section, the addition of a new subsection, titled "Prosthetic Heart Valves"; and (2) in the PRECAUTIONS section, the "Pregnancy" subsection, the "*Non-teratogenic Effects*" sub-subsection, the addition of a third paragraph in the sub-subsection describing a clinical study of pregnant women with prosthetic heart valves given enoxaparin (1 mg/kg bid) to prevent thromboembolism.

Supplement 045, submitted as a prior approval supplement, provides for revisions to the ADVERSE REACTIONS section, the "Ongoing Safety Surveillance" subsection of the package insert, specifically updating the number of spinal epidural hematomas.

Supplement 046, submitted as a prior approval supplement, provides for the revisions to the PRECAUTIONS section, the "Pregnancy" subsection of the package insert.

We have completed the review of these supplemental applications, 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 final printed labeling (FPL) submitted August 14, 2001. Accordingly, these supplemental applications are approved effective on the date of this letter.

However, at the next printing, we request that you revise the Maison-Alfort PI as follows: in the ADVERSE REACTIONS section, the "Major bleeding Episodes Following Hip or Knee Replacement Surgery" table, information pertinent to that table should be the same column to facilitate continuity and ease of readability. As submitted, the table is located at the bottom of column 4 and at the top of column 5.

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-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We request that the letter (draft submitted November 28, 2001) 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 within 30 days of receipt of this letter. Further, please 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 Project Manager, at (301) 827-7457.

Sincerely,

Victor F. C. Raczkowski, M.D., M.Sc.
Acting Director
Division of Gastrointestinal and Coagulation Drug
Products
Office of Drug Evaluation III
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/

Joyce Korvick
1/9/02 10:51:18 AM
For Dr. Victor Raczkowski