

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-164/S-041

Name: Lovenox® (Enoxaparin Sodium) Injection

Sponsor: Aventis Pharmaceutical Products, Inc.

Approval Date: December 14, 2000

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APPLICATION NUMBER:
NDA 20-164/S-041

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APPROVAL LETTER



NDA 20-164/S-041

Aventis Pharmaceuticals Products Inc.
Attention: Dhiren N. Shah, Ph.D.
10236 Marion Park Drive
Kansas City MO 64134-0627

Dear Dr. Shah:

Please refer to your supplemental new drug application dated August 31, 2000, received September 1, 2000, 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 September 29, 2000.

This "Changes Being Effected in 30 days" supplemental new drug application provides for an additional manufacturing site, Aventis Pharma Industrial Operations Pte Ltd. (61 Gul Circle, Jurong, Singapore 629585), for enoxaparin sodium, the drug substance for Lovenox Injection.

We have completed the review of this supplemental application, and it is approved.

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,

Liang Zhou, Ph.D.
Chemistry Team Leader for the
Division of Gastrointestinal and Coagulation Drug
Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/

Liang Zhou

12/14/00 02:06:17 PM

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APPLICATION NUMBER:
NDA 20-164/S-041

CHEMISTRY REVIEW

CHEMIST'S REVIEW #1		1. Organization: FDA	2. NDA Number: 20-164
3. Name and Address of Applicant (City & State): Aventis Pharmaceuticals 10236 Marion Park Drive Kansas City MO 64134-0627		4. AF Number:	
6. Name of Drug: lovenox Injection	7. Nonproprietary name enoxaparin sodium	Numbers: SCM-041 BC	Dates: 31-Aug-2000 29-Sep-2000
8. Supplement Provides for: the manufacture and testing of enoxaparin sodium, by the previously approved method of synthesis and of analytical testing, at an additional Aventis Pharma manufacturing facility, Aventis Pharma Industrial Operations Pte Ltd, 61 Gul Circle Jurong, Singapore 629585.		9. Amendments and Other (Reports, etc.) Dates: FDA CDER EES 15/Sep/00; Aventis Pharma, Jurong, SN	
10. Pharmacological Category: anticoagulant	11. How Dispensed: RX xxx__ OTC	12. Related IND/NDA/DMF(s):	
13. Dosage Form: Injection (SVS)			
14. Potency: 10 mg/0.1mL			
15. Chemical Name and Structure: See page 51 of this supplement.		16. Records and Reports:	
17. Comments: CBE-30; Dhiren Shah, US FDA Liaison/Contact. See Review Notes cc: NDA /20-164 HFD-180/Div File HFD-181/CSO/OliverK HFD-180/TalaricoL HFD-180/SieczkowskiJ R/D init by: ZhouL typist: /JS F/T Word 20164041.1JS.doc			
18. Conclusions and Recommendations: The submitted CMC for the manufacture of enoxaparin sodium batches and the subsequent formulation of drug product with the Singapore drug substance batches, including specification and stability testing, support the use of the Singapore site for enoxaparin manufacture. The supplement should be approved and the CSO should prepare an approval letter for Dr Zhou's signature.			
19. Reviewer			
Name: Joseph Sieczkowski		Signature	Date Completed: 13-Dec-2000

REVIEW NOTES

The following is a review of the supplemental submission according to the supplement headings.

4. Chemistry, Manufacturing and Controls Section (CMC)

Note: Page numbers in the supplement are in the upper right hand corner.

4.1 Introduction

Comment: This section provides an adequate explanation concerning what Aventis intends to do in the manufacture and testing of enoxaparin sodium at the new manufacturing site. A comparison of batch sizes at the original and proposed new site is provide in Figure 1, page 4.

ADEQUATE

4.2 Drug Substance

4.2.1 Manufacturer

Current manufacturing site:
Aventis Pharma
Villeneuve-La-Garenne Plant
35, Avenue Jean Jaures
92390 Villeneuve-La-Garenne, France

Proposed manufacturing site (CFN 9612059):
Aventis Pharma Industrial Operations Pte Ltd
61 Gul Circle
Jurong, Singapore 629585

Heparin suppliers: []

ADEQUATE

4.2.2 Method of Manufacture

Comment: The method of manufacture is essentially unchanged. Three improvements by Aventis to the manufacturing process are noted:

1. []
2. []
3. []

ADEQUATE

4.1.1.1 Manufacturing Process Summary, Complimentary Physico-Chemical Data, and Comparative Analytical Results
SUBMITTED INFORMATION:

A manufacturing process summary was provided with flow diagrams for each stage of manufacture:

STAGE

FLOW DIAGRAM

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW # 1

/s/

Joe Sieczkowski
12/14/00 06:59:09 AM
CHEMIST

Liang Zhou
12/14/00 09:47:30 AM
CHEMIST

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ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

NDA 20-164/S-041

Aventis Pharmaceuticals Products Inc.
c/o Quintiles Inc.
Attention: Ms. Michelle Kliewer
Mail Stop F3-3026
P.O. Box 9708
Kansas City, MO 64134-0708

Dear Ms. Kliewer:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Lovenox[®] (enoxaparin sodium) Injection

Supplement number: S-041

Date of supplement: August 31, 2000

Date of receipt: September 1, 2000

This supplemental application, submitted as "Supplement – Changes Being Effected in 30 days," proposes the following change: an additional manufacturing site, Aventis Pharma Industrial Operations Pte Ltd. (61 Gul Circle, Singapore 629585), for enoxaparin sodium, the drug substance for Lovenox Injection.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on October 31, 2000, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be March 1, 2001.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastrointestinal and
Coagulation Drug Products, HFD-180
Attention: Division Document Room, 6B-24
5600 Fishers Lane
Rockville, Maryland 20857

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If you have any questions, call me at (301) 827-7457.

Sincerely yours,

Karen Oliver, RN, MSN
Regulatory Health Project Manager
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:

Archival NDA 20-164
HFD-180/Division file
HFD-180/K. Oliver
HFD-180/Team Leaders and reviewers
DISTRICT OFFICE

Drafted by: hw/9/14/00

Initialed by: ko/9/18/00

Final: hw/9/18/00

Filename: C:\DATA\CSO\N\20164.S041.ACK.0KO

SUPPLEMENT ACKNOWLEDGEMENT (AC)