CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-164/S-042

Name: Lovenox® (Enoxaparin Sodium) Injection

Sponsor: Aventis Pharmaceutical Products, Inc.

Approval Date: July 5, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-164/S-042

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-164/S-042

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-164/S-042

Aventis Pharmaceuticals Products Inc.
Attention: Dhiren N. Shah, Ph.D.
Director – CMC, US Drug Regulatory Affairs
Somerset Corporate Center
300 Somerset Corporate Boulevard
Bridgewater, NJ 08807-2854

Dear Dr. Shah:

Please refer to your supplemental new drug application dated January 8, 2001, received January 9, 2001, 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 January 18 and 27, 2001.

This supplemental application, submitted as a "Supplement – Changes Being Effected in 30 days" supplement, provides for the following change: an additional manufacturing site, Laboratories Fisons SA, Le Trait, France, to manufacture the 60 mg/0.6 mL, 80 mg/0.8 mL, and 100 mg/1.0 mL graduated, prefilled syringes.

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

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

/s/

Ali Al-Hakim
7/5/01 01:19:10 PM
Ali Al-Hakim, Acting Team Leader

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-164/S-042

CHEMISTRY REVIEW

CHEMIST'S REVIEW # 1	1. Organization: HFD-180	2. NDA number: 20-164	
3. Name and Address of Applicant (City & State): Aventis Pharmaceuticals Products Inc. 10236 Marion Park Drive, PO Box 9720 Kansa City, MO 64134		4. AF Number:	
		5.Supplement(s)	
6. Name of Drug: Lovenox Injection	7. Nonproprietary Name: enoxaparin sodium injection	Numbers SCM-042 BC BC	Dates 08-Jan-2001 18-Jan-2001 27-Jun-2001
8. Supplement Provides for: an additional manufacturing site for Lovenox (enoxaparin sodium) Injection (60mg/0.6mL,80mg/0.8mL,100mg/1.0mL) in 1.0mL graduated pre-filled syringes [redacted] at Laboratoires Fisons SA, 76 580 Le Trait, France.		9. Amendments and Other (Reports, etc.) Dates: EES: Acceptable/ 22-May-2001	
10. Pharmacological Category: Anti-thrombotic	11.How Dispensed: RX-xxx OTC	12. Related IND/NDA/DMF(s): SCM-032/ Approved 27-Jan-2000 For Laboratoires Fisons, SA;DMF [redacted] DMF [redacted]	
13.Dosage Form: Injection (SVS)	14. Potency: 100mg/1.0mL		
15. Chemical Name and Structure: See USP Dictionary(2001)		16. Records and Reports:	
		Current Yes X No	
		Reviewed Yes X No	
17. Comments: See Review Notes (CBE-30; Previously approved manufacturing site for Lovenox 30&40 mg pre-filled syringes) cc: NDA 20-164 HFD-180/Div File HFD-181/CSO/KOliver HFD-180/L.Talarico HFD-180/JSieczkowski			
18. Conclusions and Recommendations: The supplement should be approved from the Review Chemist's viewpoint, however the microbiologist's consult review is pending. Based on the Microbiologist's review recommendation, the CSO should prepare a letter, for the Chemistry Team Leader's signature, to be sent to Aventis Pharmaceuticals.			
19.Reviewer			
Name: Joseph Sieczkowski,PhD	Signature	Date Completed: July 3,2001	

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information from

CHEMISTRY REVIEW #1

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/s/

Joe Sieczkowski
7/3/01 09:51:04 AM
CHEMIST
Ali Al-Hakim is the Acting Team Leader for Liang Zhou, July 2-13, 2001
.

Ali Al-Hakim
7/3/01 09:55:44 AM
CHEMIST
Ali Al-Hakim, Acting Team Leader

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-164/S-042

MICROBIOLOGY REVIEW

REVIEW FOR HFD-180
MICROBIOLOGIST'S REVIEW #1 OF SUPPLEMENT
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY REVIEW STAFF

July 03, 2001

NDA/Supplement Numbers **21-164/SCM-042**

Document Date: January 8, 2001

Date Assigned for Review: January 23, 2001

Amendments and Others: (none)

Name and Address of Applicant: Aventis Pharmaceutical Products, Inc.
399 Interpace Parkway
Parsippany, NJ 07504

Name of Drug: LOVENOX (enoxaprin sodium)

Supplement Provides For: the addition of Laboratories Fisons SA, in Le Trait, France, as a manufacturing site for 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/1.0 mL strengths. These strengths are currently manufactured at Aventis ProPharm, in Maisons-Alfort Cedex, France. The facility in Le Trait already manufactures this product at strengths of 20 mg, 30 mg, 40 mg and 150 mg.

Pharmacological Category: anti-coagulant

Dosage Form: Pre-filled syringes

Related Documents: none

Comments: This has been a very active NDA. The Le Trait site was added (SCM-032) for the manufacture of this product (30 and 40 mg strengths) in September 1999. The current supplement proposes to add Le Trait, France, as a manufacturing site for 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/1.0 mL strengths. There were five volumes in this supplement even though there was very little new information contained in them.

Conclusions and Recommendations: The supplement is recommended for APPROVAL.

David Hussong, Ph.D.

cc:

Original NDA 20-164/SCM-042
HFD 160/Consult File
HFD 180/Division File
HFD 180/CSO/Oliver
HFD 180/Chemist/Sieczkowski
HFD 805/D. Hussong

Drafted by: D. Hussong, 07/03/2001
R/D initialed by: P. Cooney

Filename, d:\nda\s\20-164S042rv1.doc

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MICROBIOLOGY REVIEW #1

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/s/

David Hussong
7/3/01 02:21:03 PM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-164/S-042

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-164/S-042

CBE-30 SUPPLEMENT

Aventis Pharmaceuticals Products Inc.
Attention: Dhiren N. Shah, Ph.D.
Director - CMC, US Drug Regulatory Affairs
10236 Marion Park Drive, PO Box 9720
Kansas City, MO 64134-9720

Dear Dr. Shah:

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

NDA Number: 20-164

Supplement Number: S-042

Date of Supplement: January 8, 2001

Date of Receipt: January 9, 2001

This supplemental application, submitted as a "Supplement - Changes Being Effected in 30 days" supplement, proposes the following change: an additional manufacturing site, Laboratories Fisons SA, Le Trait, France, to manufacture the 60mg/0.6 mL, 80 mg/0.8 mL, and 100 mg/1.0 mL graduated, prefilled syringes.

Unless we notify you within 60 days of our 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 March 10, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 9, 2001.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/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, Rm. 6B-24
5600 Fishers Lane
Rockville, Maryland 20857

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

Sincerely,

{See appended electronic signature page}

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

/s/

Karen Oliver
1/23/01 09:05:56 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

DO *(Division/Office)*: Microbiology, HFD-160
ATTENTION: Dr. Peter Cooney, Team Leader

FROM: HFD-180 (Division of Gastrointestinal and Coagulation Drug Products) Phone # 827-7457

DATE:	IND NO.:	NDA NO.:	TYPE OF DOCUMENT :	DATE OF DOCUMENT
01/16/01		20-164	SCM-042	01-08-01

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Lovenox® (enoxaparin sodium) Injection	Standard		User fee Due Date: 6 mo: July 9, 2001

NAME OF FIRM: Aventis Pharmaceuticals Products

REASON FOR REQUEST

I. GENERAL

☐ NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY

☐ PRE--NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT

☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

☐ DISSOLUTION
BIOAVAILABILITY STUDIES
☐ PHASE IV STUDIES

☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RICK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: SCM-042 provides for the addition of an NDA-approved manufacturing site, Laboratories Fisons SA, Le Trait, France, for NDA-approved strengths of the drug product, specifically the Lovenox pre-filled syringes for the following strengths: 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1.0 mL. Six volumes (the complete submission) are being consulted. The chemistry reviewer is Dr. Joseph Sieczkowski. Thanks, Karen Oliver, Project Manager ; cc: Orig NDA 20-164/S-042; HFD-180/Div. Files; HFD-180/K.Oliver; J.Sieczkowski

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one): ☐ MAIL ☒ HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

/s/

Karen Oliver
1/16/01 01:35:27 PM