CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-261/S021

Trade Name: Lescol Capsules

Generic Name: flusvastatin sodium

Sponsor: Novartis Pharmaceutical Corporation

Approval Date: May 14, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-261/021

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Approvable Letter	
Labeling	
Medical Review(s)	
Chemistry Review(s)	X
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S021

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-021

Novartis Pharmaceuticals Corporation
Attention: Donna Kapples
CMC Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080

MAY 14 1999

Dear Ms. Kapples:

Please refer to your supplemental new drug application dated January 21, 1999, received January 25, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) capsules.

We acknowledge receipt of your submission dated April 14, 1999.

This supplemental new drug application provides for an alternate method of manufacture of the _____ to be implemented at the approved bulk drug facility in Ringaskiddy, Ireland only.

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, contact Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

Stephen K. Moore 5/14/99

Stephen K. Moore, Ph.D.
Chemistry Team Leader I for
Division of Metabolic and
Endocrine Drug Products, (HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-261
HFD-510/Div. Files
HFD-510/M. Simoneau
HFD-510/Reviewers and Team Leaders
HFD-95/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: Mas/May 12, 1999
Initialed by:WBerlin5.12.99/SMoore5.13.99/EGalliers5.13.99
final:Mas5.14.99
filename: 20261.21

APPROVAL (AP)

FOI: Please redact

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S021

CHEMISTRY REVIEW(S)

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP II, HFD-510	20-261
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
		SCS-021 21-JAN-1999
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Lescol	Fluvastatin Sodium	14-APR-1999
8. SUPPLEMENT PROVIDES FOR An alternate method of manufacture of the [redacted], to be implemented at the approved bulk drug facility in Ringaskiddy Ireland only.		
9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
Antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
Capsules, oral	10, 20, 40 mg	
14. CHEMICAL NAME AND STRUCTURE		
See Chemistry Review #1		
15. COMMENTS		

The primary concern with this type of change is a loss in purity if the [redacted]. In support of this change the applicant has provided extensive analytical characterization of the [redacted] Fluvastatin sodium by both methods of manufacture. Of primary interest, the qualitative nature of the [redacted] although there is a slight increase in the "Total Unknown substances" in the final bulk, the increase is modest [redacted] and well below the approved limit of NMT [redacted]. In addition, the applicant has provided updated control procedures and tests methods, which may have been filed in an annual report, but are being implemented with the change in the method of manufacture, and so were included with this supplement. Lastly, the 'residual solvents' test has been validated to detect the new process solvent, [redacted] that replaces [redacted] the [redacted] Lastly, the applicant has committed to stability testing of [redacted] lot each of the current and proposed [redacted] batches of drug substance.

16. CONCLUSION AND RECOMMENDATION

The proposed alternate method of synthesis has been shown not to result in a product of decreased quality or purity in comparison to that produced according to the current process. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		19-APR-1999

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

AP

Stephen K. Moore
5/11/99

3 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry-20-269
S021

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S021

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-021

Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, NJ 07936

FEB 3 1999

Attention: Donna Kapples,
CMC Project Manager
Drug Regulatory Affairs

Dear Ms. Kapples:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Lescol® Capsules (Fluvastatin Sodium)
NDA Number:	20-261
Supplement Number:	S-021
Date of Supplement:	January 21, 1999
Date of Receipt:	January 25, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on March 26, 1999, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-261/S-021
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\DATA\WPFILES\20261ACK.

SUPPLEMENT ACKNOWLEDGEMENT / PA

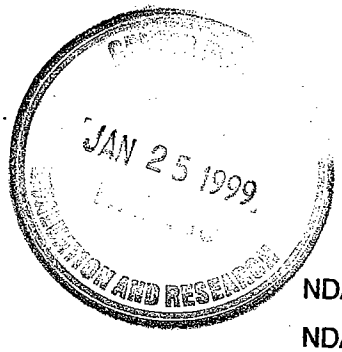
ORIGINAL

Novartis Pharmaceuticals Corporation
Drug Regulatory Affairs
59 Route 10
East Hanover, NJ 07936-1080

Tel 973 781 7500
Fax 973 781 6325

NOVARTIS

21-Jan-99



NDA 20-261
Lescol® Capsules
(fluvastatin sodium)

NDA NO. 20-261 REF NO. 021
NDA SUPPL FOR SCS

Supplement for Approval - Chemistry, Manufacturing and Controls

REVIEWS COMPLETED
AP LTR 5-14-99
CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
Mas 5-14-99
CSO INITIALS DATE

FDA Center for Drug Evaluation and Research
Office of Drug Evaluation II
Document Control Room 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

Attention: Solomon Sobel, MD, Director
Division of Metabolic and Endocrine Drug Products/HFD-510

Dear Dr. Sobel:

In accordance with 21 CFR 314.70(b), Novartis Pharmaceuticals Corporation herewith submits a supplemental new drug application for Lescol® (fluvastatin sodium) Capsules. This supplement provides for an alternate method of manufacture of [redacted] drug substance, fluvastatin sodium. The overall synthetic route for the drug substance has not changed.

The currently approved sites to manufacture [redacted] are Novartis Pharma AG, Basel, Switzerland and Novartis Ringaskiddy Ltd., Ireland. Novartis Ringaskiddy proposes to prepare [redacted] This "[redacted]" proposed as an alternate synthesis, and will only be performed at Novartis Ringaskiddy. For optimization reasons, the solvent used in the [redacted] Details are provided in the Summary of Changes module.

The quality of fluvastatin sodium prepared by either the currently approved process or via the [redacted] remains the same. Comparative analytical data are provided for [redacted] Also, comparative analytical data and spectra are provided for fluvastatin sodium. A stability commitment is also included.

Should you have any comments or questions regarding this submission or any other Chemistry, Manufacturing and Controls issues, please contact me directly at (973) 781-6929. If there are any general or Clinical related issues, please contact Mr. Jerry Klimek, DRA Therapeutic Area representative at (973) 781-8145.

Sincerely,

Donna Kapples

Donna Kapples
Chemistry, Manufacturing and Controls
Drug Regulatory Affairs

Attachments
Submitted in Duplicate

cc: Ms. Regina Brown
New Jersey District Office, North Brunswick Resident Post - Certified Field Copy