CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-261/S016

Trade Name: Lescol Tablets

Generic Name: fluvastatin sodium

Sponsor: Novartis Pharmaceutical Corporation

Approval Date: April 23, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-261/S016

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Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

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APPLICATION NUMBER:

NDA 20-261/S016

APPROVAL LETTER

NDA 20-261/S-016

APR 23 1998

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

Dear Ms. Kapples:

Please refer to your supplemental new drug application dated December 19, 1997, received December 29, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) capsules.

The User Fee goal date for this application is June 29, 1998.

The supplemental application provides for an alternate source for the drug substance ——

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

Sincerely yours,

Stephen K. Moore 4/23/98

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

cc:
Original NDA 20-261
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau
HFD-510/W.Berlin/S.Moore/E.Barbehenn/R.Steigerwalt/E.Galliers
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: Mas/April 20, 1998/20261.16
Initialed by:WBerlin4.21.98/S.Moore4.20.98/EBarbehenn4.21.98/RSteigerwalt4.20.98
EGalliers4.22.98
Final:Mas4.23.98

APPROVAL (AP)

FOI: Please redact the word ——

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S016

CHEMISTRY REVIEW(S)

ORIGINAL

APR - 7 1998

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP II, HFD-510	20-261
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Novartis Pharmaceuticals Corp. 59 Route 10 East Hanover, NJ 07936		SCS-016 12-19-97
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Lescol®	fluvastatin sodium	
8. SUPPLEMENT PROVIDES FOR		
An alternate source for the drug substance starting material [redacted]		
9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
Capsules, oral	20, 40 mg	
14. CHEMICAL NAME AND STRUCTURE		
See Chemistry Review #1		
15. COMMENTS		

The sponsor has provided data to support the purchase of [redacted] (currently manufactured [redacted], the drug substance [redacted] commercial suppliers. Included in the supplement are complete descriptions of the drug substance manufacturing process including in-process controls and tests and specifications. Analytical comparison for t [redacted] ("different suppliers were used") batches of [redacted] were provided (no raw data), and included appearance, LOD, as well as assay and impurities by HPLC (vol. 2, p. 495). No significant differences are apparent from the data. Additionally, data for [redacted] batches of [redacted] in the synthesis were provided (vol. 2, p. 496). Results were provided for appearance, ID (TLC and IR), LOD, as well as assay and impurities by HPLC. Again, no significant differences are apparent from the data provided. Finally, results of the tests and specifications for the final drug substance, fluvastatin sodium, for t [redacted] batches are provided.

(continued next page)

16. CONCLUSION AND RECOMMENDATION

The sponsor has adequately demonstrated that manufacture using commercially-supplied starting material, [redacted] results in no decrease in drug substance quality. The stability commitment provided is acceptable. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN	[signature]	3-7-98

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

AP

Stephen K. Moore 4/7/98

1 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-261
5016

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APPLICATION NUMBER:

NDA 20-261/S016

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-016

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

JAN 6 1998

Attention: Donna Kapples

Dear Ms. Kapples:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	LESCOL® (fluvastatin sodium) Capsules
NDA Number:	20-261
Supplement Number:	S-016
Date of Supplement:	December 19, 1997
Date of Receipt:	December 29, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 27, 1998, 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 20-261/016
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\DATA\WPFILES\20261ACK

SUPPLEMENT ACKNOWLEDGEMENT

NDA SUPPLEMENT

NDA NO. 20261 REF. NO. 016

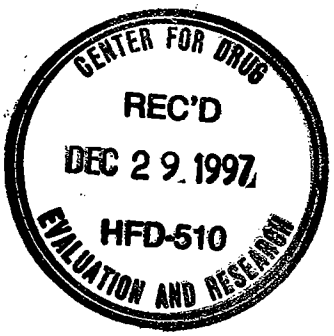
NDA SUPPL FOR SE5

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

Tel 201 503 7500
Fax 201 503 6325

NOVARTIS

ORIGINAL



December 19, 1997

Solomon Sobel, MD
Director
Division of Metabolic and
Endocrine Drug Products/HFD-510
Office of Drug Evaluation II
Attn: Document Control Room 14B-04
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA No. 20-261
LESCOL®
(fluvastatin sodium) Capsules

SUPPLEMENTAL NEW DRUG APPLICATION

EXPEDITED REVIEW REQUESTED

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 the purchase ——— , the ——————— in the synthesis of the drug substance, Fluvastatin Sodium.

The currently approved sites for the synthesis of ——— Novartis Basel, Switzerland and Novartis Ringaskiddy, Ireland. —— , is now commercially available. As a result, Novartis Pharmaceuticals Corporation is providing the documentation to qualify the supply ——— from external sources. The quality of Fluvastatin Sodium synthesized using purchased —— is equivalent to the quality of Fluvastatin Sodium synthesized by the currently approved process. This equivalence is demonstrated by the analytical comparisons of ——————— Fluvastatin Sodium. The intermediates and drug substance made by the currently approved process were compared analytically to the intermediates and drug substance made using two external sources of ——— Summaries of the analytical data comparisons are included in the supplement as well as the ——— for the Fluvastatin Sodium batches

The control of purchased —— will be in accordance with the currently approved procedures and specifications established for ——————— Additionally, the vendor certificate of analysis for ——— will also be reviewed against the internally generated data.

The synthesis and quality of Fluvastatin Sodium remains essentially unchanged. The purchased [redacted] currently approved process. In addition to the analytical comparisons provided, the supplement includes updated control documents, as well as an [redacted] procedure for the chemical [redacted] Also, during a telephone conversation held on December 17, 1997 between Dr. William Berlin (reviewing chemist, Division of Metabolic and Endocrine Drug Products) and Donna Kapples (Novartis Pharmaceuticals Corporation), an agreement was made that stability would be reported on [redacted] batches of drug substance derived from purchased [redacted] Three month stability data on these batches will be provided as an amendment to this supplement early in 1998. It was also agreed that drug product stability would not be specifically required at this time due to the nature of the proposed change.

Due to the high demand of Lescol Capsules, the availability of Fluvastatin Sodium in the United States, using the currently approved synthesis, is [redacted] We look forward to working with the Agency to respond to any questions in an expeditious manner.

A certified copy of this NDA supplement is being provided to our local office in compliance with the preapproval inspection requirements.

If you have any questions or comments, please contact me at (973) 503-6929.

Sincerely,

Donna Kapples

Donna Kapples
Chemistry, Manufacturing and Controls
Drug Regulatory Affairs

/ajm-cw
Attachments
Submitted in duplicate
Desk copy: Regina Brown, New Jersey District Office, North Brunswick Resident Post

REVIEWS COMPLETED

CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
Mas AP 4/23/98
CSO INITIALS DATE