CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-261/S029

Trade Name: Lescol Capsules

Generic Name: fluvastatin sodium

Sponsor: Novartis Pharmaceuticals Corporation

Approval Date: May 23, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S029

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S029

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-029

Novartis Pharmaceuticals Corporation
Attention: Robert J. Clark
Drug Regulatory Affairs, Chemistry, Manufacturing and Controls
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Mr. Clark:

Please refer to your supplemental new drug application dated January 29, 2001, received January 31, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) capsules.

We acknowledge receipt of your amendments dated March 9, and May 4, 2001.

This supplemental new drug application provides for the elimination of microbiological testing of the drug product.

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 Margaret Simoneau, R.Ph., Regulatory Project Manager, at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

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

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/s/

Stephen Moore
5/23/01 04:36:28 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S029

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

1. ORGANIZATION CDER/HFD-510
Division of Metabolism and Endocrine Drug Products

2. NDA # 20-261
Original NDA approved:

3. NAME AND ADDRESS OF APPLICANT
Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, NJ 07936-1080

4. SUPPLEMENT SCM-029 (29-JAN-2001 Rec. 31-JAN-2001)

5. Name of the Drug Lescol Capsules™

6. Nonproprietary Name
Fluvastatin sodium

7. SUPPLEMENT PROVIDES for the elimination of microbiological testing of the solid dosage form. Amendments contain data requested by the Agency.

8. AMENDMENT -- SCM-029 (09-MAR-2001 Rec. 12-MAR-2001) AND SCM-029 (04-MAY-2001 Rec. 07-MAY-2001)

9. PHARMACOLOGICAL CATEGORY
Hypercholesterolemia

10. HOW DISPENSED
Oral

11. RELATED
-N. A. -

12. DOSAGE FORM Capsule

13. POTENCY 20 mg and 40 mg

14. CHEMICAL NAME AND STRUCTURE
7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid, monosodium salt, Mol wt = 433.46, C24H25FNO4.Na Salt/Base Ratio 1.053

15. COMMENTS Amendment March 9 contains the approved release and stability specifications, including the microbial limits. Amendment May 4 contains data for each of the products from 1998 forward in support of the proposal to eliminate the microbiological testing. Data for Lescol Capsules, 20 mg and 40 mg, showed no significant microorganisms were recovered.

16. CONCLUSIONS AND RECOMMENDATIONS Microbiological testing on the solid oral drug product can be eliminated. From the Chemistry point of view, this supplement can be approved. Issue Approval letter.

17. REVIEWER NAME (AND SIGNATURE) **DATE**
COMPLETED 21-MAY-2001
Sharon Kelly, PhD
R/D INITIATED BY

filename: 20261#29A NDA

DISTRIBUTION: Original: NDA 20261 cc: HFD-510 Division File CSO Reviewer

AP

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/s/

Sharon Kelly
5/22/01 02:41:44 PM
CHEMIST

Paper copy signed May 22, 2001

Stephen Moore
5/22/01 02:47:44 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S029

MICROBIOLOGY REVIEW(S)

REVIEW FOR
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF BUNDLED SUPPLEMENT
16 May 2001

A. 1. APPLICATIONS

HFD-580
NDA 06-035/SCS-065
NDA 17-962/SCS-060

HFD-550
NDA 17-534/SCS-054
NDA 19-429/SCS-017
NDA 20-232/SCS-013

HFD-110
NDA 19-546/SCS-024

HFD-510
NDA 20-261/SCS-029

HFD-120
NDA 18-706/SCS-025
NDA 19-758/SCS-043
NDA 20-234/SCS-019

HFD-600
ANDA 88-616/S

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

2. PRODUCT NAMES:

NDA 06-035:	Methergine® Tablets, USP
NDA 17-534:	Fiorinal® Capsules, USP
	Fiorital® Capsules, USP
NDA 17-962:	Parodel® Tablets/Capsules, USP
	Bromocriptine Mesylate Tablets/Capsules, USP
NDA 18-706:	Hydergine® Liquid Capsules
NDA 19-429:	Fiorinal/Codeine® Capsules, USP
	Fiorital/ Codeine® Capsules, USP
NDA 19-546:	Dynacirc® Capsules
NDA 19-758:	Clozaril® Tablets
NDA 20-232:	Fioricet/Codeine® Capsules
NDA 20-234:	Tegretol®-XR Extended Release Tablets
NDA 20-261:	Lescol® Capsules
ANDA 88-616:	Fioricet® Capsules

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The products are a variety of capsules or tablets for oral administration.

4. METHODS OF STERILIZATION:

1 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Microbiology- 20-261
5029

Paul Stinavage, Ph.D.

cc: HFD-120/D. Klein/T. Oliver/M. Guzewska
HFD-550/S.-C. Lin
HFD-580/J. Mercier
HFD-640/A. High
HFD-800/S. Lange
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 16 May 2001
R/D initialed by P. Cooney

E. REVIEW NOTES

These supplements provide for the elimination of microbiological testing of the specified drug products. These products are solid oral dosage forms. The applicant states that microbiological testing of the products had been instituted several years ago as a result of an internal company policy. The company states that they have not experienced any failures in 5 years of testing. Data generated during the last three years were provided and reviewed for several of the tablets/capsules. These data and the fact that the products are solid oral dosage forms that are unlikely to sustain microbial replication support the applicant's desire to eliminate testing. The applicant also correctly points out that it is not "industry practice" to routinely perform microbiological testing on solid oral drug products.

Satisfactory

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/s/

Paul Stinavage
5/16/01 02:08:46 PM
MICROBIOLOGIST
Bundled supplements to eliminate microbiological testing of solid oral dosage forms.

Peter Cooney
5/16/01 02:28:53 PM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-261/S029 `

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

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

Tel 973 781 7500
Fax 973 781 6325

NOVARTIS ORIGINAL

NDA NO. 20-261 REF NO. 24
NDA SUPPL FOR SCM

January 29, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JAN 31 2001
HFD-510

1/31/01 Note: See e-mail dated 1/31/01 from Steve Moore to Susan Fang et al to bundle micro testing + lead reminder. MAS

NDA 20-261
Lescol® Capsules
(fluvastatin sodium)

Supplemental New Drug Application - Chemistry, Manufacturing and Controls
Bundled Submission

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

REVIEWS COMPLETED		
APlt 5/23/01		
CSO ACTION:		
☑ LETTER	☐ N.A.I.	☐ MEMO
CSO INITIALS		DATE

Dear Dr. Orloff:

Novartis Pharmaceuticals Corporation is submitting a supplemental New Drug Application for the above cited drug product. This supplement provides for the elimination of microbiological testing of the dosage form.

Novartis is proposing this change following the review of data generated over the past 5 years. That review indicated that there were no failures for the above cited dosage form (as well as the others cited on the list below). Please therefore note that Novartis is proposing to eliminate the reporting of microbilogical test results at release and on stability due to these findings.

Please note that the microbiological testing for this drug product had been instituted several years ago as a result of an internal company policy. Since this material (a solid oral dosage form) has not experienced any failures, Novartis feels that it would be prudent at this time to eliminate that testing. In addition it is not "industry practice" to routinely perform microbiological testing on solid oral drug products.

This submission is being made to several NDAs simultaneously since many Novartis products are affected. Please see the table below for a complete list of all the products/NDAs to which this change is being submitted.

If you have questions and/or comments regarding this submission, please do not hesitate to contact me at (973) 781-7005.

Sincerely,

Robert J. Clark
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

NDA/ ANDA	Product Name	FDA Division
		Anti-Inflammatory, Analgesic & Ophthalmologic (HFD-550)
20-232	Fioricet/Codeine® Capsules	
19-429	Fiorinal/Codeine® Capsules, USP Fiorital/Codeine® Capsules, USP	
17-534	Fiorinal® Capsules, USP Fiorital® Capsules, USP	
		Cardio-Renal (HFD-110)
19-546	Dynacirc® Capsules	
		Reproductive and Urologic (HFD-580)
06-035	Methergine® Tablets, USP	
		Special Pathogen and Immunologic (HFD-590)
		Neuropharmacological (HFD-120)
19-758	Clozaril® Tablets	
17-962	Parlodel® Tablets/Capsules, USP Bromocriptine Mesylate Tablets/Capsules, USP	
18-706	Hydergine® Liquid Capsules	
20-234	Tegretol®-XR Extended-Release Tablets	
		Metabolic and Endocrine (HFD-510)
20-261	Lescol® Capsules	
		Generic Division (HFD-600)
88-616	Fioricet® Tablets	

Dr. Susan Lange at the Office of New Drug Chemistry has been forwarded a copy of an example submission to a typical drug product. She will be coordinating a bundled review of these supplements.

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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Competing This Form

1. APPLICANT'S NAME AND ADDRESS

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

2. TELEPHONE NUMBER (*Include Area Code*)
(973) 781-7005

3. PRODUCT NAME
Lescol® Capsules

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. No

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:
- ☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.
- ☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO (APPLICATION NO. CONTAINING THE DATA)

5. USER FEE I.D. NUMBER.

6. LICENSE NUMBER / NDA NUMBER
20-261

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

- ☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (*Self Explanatory*)
- ☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (*See item 7, reverse side before checking box.*)
- ☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (*See item 7, reverse side before checking box.*)
- ☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (*See item 7, reverse side before checking box.*)
- ☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT ISTRIBUTEDCOMMERCIALLY(*Self Explanatory*)

FOR BIOLOGICAL PRODUCTS ONLY

- ☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION
- ☐ A CRUDE ALLERGENIC EXTRACT PRODUCT
- ☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY
- ☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
- ☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☐ NO

(See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	Robert J. Clark Director Drug Regulatory Affairs	29-Jan-01