CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-261/S020

Trade Name: Lescol Capsules

Generic Name: flusvastatin sodium

Sponsor: Novartis Pharmaceutical Corporation

Approval Date: April 21, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-261/020

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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/S020

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-020

APR 21 1999

Novartis Pharmaceuticals Corporation
Attention: Joan A. Materna
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Ms. Materna:

Please refer to your supplemental new drug application dated December 23, 1998, received December 24, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lescol (fluvastatin sodium) Capsules.

We acknowledge receipt of your submissions dated March 18 and April 9, 1999.

This supplemental new drug application provides for a packaging equivalency protocol for alternate container/closure systems for Lescol capsules, together with supporting analytical data.

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 4/21/99

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/April 21, 1999
Initialed by:WBerlin4.21.99/EGalliers4.21.99
final:Mas4.21.99
filename: 20261.20

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S020

CHEMISTRY REVIEW(S)

ORIGINAL

APR 20 1999

20-261/S-020

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 Corporation 59 Route 10 East Hanover, NJ 07936		SCP-020 23-DEC-1998
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Lescol	Fluvastatin Sodium	18-MAR-1999 9-APR-1999

8. SUPPLEMENT PROVIDES FOR

A packaging equivalency protocol for alternate container/closure systems for Lescol capsules, together with supporting analytical data.

9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
antihypercholesteremic	RX	
12. DOSAGE FORM	13. POTENCY	
capsules	20, 40 mg	

14. CHEMICAL NAME AND STRUCTURE

See Chemistry Review #1

15. COMMENTS

These supplements were "bundled" by the agency, and lead review was performed by Don Klein of HFD-120, and signed off by Robert Severs, HFD-120 chemistry Team Leader (see review of NDA 10-187/S-055 dated 16-MAR-1999 and memorandum dated 12-APR-1999). The applicant's purpose of these submissions was to reduce the number of HPDE bottle and closure suppliers approved for use under what were originally Ciba and Sandoz applications. This resulted in new container/closures for most of the products. The changes in the bottle suppliers would have required an annual report. The proposed 'harmonized' container/closure systems were described in pages 4 and 5 of the original supplements. They consist of [redacted] manufactured by [redacted] and closures of [redacted] both child-resistant and non resistant) supplied by [redacted] and [redacted] non-child resistant (no change in supplier). The applicant has complied with USP<671> for comparability testing of the current and proposed packaging systems. Lastly, the applicant has committed to testing [redacted] lot of the two drug products in the new container/closure system (for Lescol this includes [redacted] bottle sizes of 20 and 40 mg strengths, each for a total of [redacted] stability lots). The stability commitments are acceptable. This reviewer wishes to re-iterate that the proposed changes would have qualified as "annual reportable", and recommends approval for the two supplements which are the subject of this review. The amendments contained further LOAs for DMFs and additional data relevant to the results of the USP<671> which were omitted from the original application, and are acceptable.

Lastly, according to the internal memo, dated 12-APR-1999, the proposed stability protocols for both products covered under this review is adequate, as there are [redacted] and there is an extensive history of stability data for Lescol capsules.

16. CONCLUSION AND RECOMMENDATION

The proposed equivalency protocol is acceptable, as are the stability commitments provided by the applicant. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		29-MAR-1999

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

AP

Stephen K. Moore
4/20/99

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-261/S-020

Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, NJ 07936

DEC 30 1998

Attention: Joan A. Materna,
Associate Director
Drug Regulatory Affairs

Dear Ms. Materna:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Lescol® (Fluvastatin Sodium)
NDA Number:	20-261
Supplement Number:	S-020
Date of Supplement:	December 23, 1998
Date of Receipt:	December 24, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 22, 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-020
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

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

SUPPLEMENT ACKNOWLEDGEMENT

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-261/S020

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ORIGINAL

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

Tel 973 781 7500
Fax 973 781 6325

NOVARTIS

December 23, 1998

NDA NO. 20-261 REF NO. 020
NDA SUPPL FOR SCP

NDA 20-261
Lescol® Capsules
(fluvastatin sodium)

Container Harmonization
Supplement for Approval - Chemistry Manufacturing and Controls

REVIEWS COMPLETED
AP Ltr 4/21/99
CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
MAS 4-22-99
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 an agreement reached with the Office of New Drug Chemistry at a 19-October-98 meeting, Novartis Pharmaceuticals Corporation is submitting NDA Supplements for alternate container/closure configurations for solid oral dosage forms packaged in the US, for the marketed products currently packaged in approved Ciba and Sandoz configurations.

These harmonized configurations represent Novartis' efforts to standardize the future packaging of marketed tablets and capsules having established stability histories, based on:

- an approved package equivalency protocol
- data according to the package equivalency protocol demonstrating equivalence of the currently approved and proposed harmonized container/closure systems when available
- a review of individual product stability history to identify products with potential issues
- commitments for stability study of product packaged in the harmonized containers, once implemented.

A fundamental component of this program is the understanding that a solid oral dosage form known to be stable, with an established stability history in a particular container/closure configuration, will continue to be stable when packaged in an equivalent container/closure system. The container harmonization program will result in reduction in the total number of container sizes and configurations, and a consolidation of the approved resin, bottle and closure supplier base.

As discussed with the Agency, this container harmonization program will affect numerous approved NDAs for commercially marketed tablets and capsules packaged in US facilities and will be phased in over time. It is Novartis' understanding that review of these SNDAs will be bundled, with submission to the various NDAs over two weeks time to allow adequate administrative and log in activities at the Agency. Dr. Susan Lange at the Office of New Drug Chemistry will be forwarded a copy of an example of a submission to a typical drug product, as she will be coordinating the bundled review of the Supplements.

Further, it is Novartis' understanding from the 19-October-98 meeting that SNDA review will be addressed by the FDA in two parts:

- review of the package equivalency protocol and data supporting the equivalency of the harmonized container/closure configurations to those currently approved will be bundled and approved by one reviewer; and
- review of the stability protocols provided for each product will be addressed by the CMC reviewers responsible for each product in accordance with the Novartis marketed product stability program, within the following general parameters:
    - each product strength will be tested each year of manufacture
    - each container size will be tested
    - each container/closure configuration [redacted] will be tested
    - each dosage form count will not be tested as long as a representative container/closure configuration has been tested
    - results of the ongoing stability studies will be reported to each NDA/ANDA in future Annual Reports.

In support of this container harmonization program, Novartis is providing the following information:

Attachment I - a list of affected NDAs, presented by FDA Division

Attachment II - a summary of package equivalency protocols and data, including supplier information

Attachment III - the stability protocols/commitments applicable for the particular product NDA

During prior Agency communications, Novartis indicated that rapid review and approval of this container harmonization proposal is desired, as consolidation of configurations is of benefit from operational and compliance perspectives. It is our understanding that the bundling process will provide Novartis and the FDA the most efficient route to achieve our stated goal of rapid review, approval and implementation.

As of 1/1/97, the former Ciba Pharmaceuticals Division and Sandoz Pharmaceuticals Corporation became Novartis Pharmaceuticals Corporation. Consequently, some of the documents included in this submission may include the former names.

Should you have any comments or questions regarding this submission, please do not hesitate to contact the undersigned at 973-781-3379. If you have a question regarding any other Chemistry, Manufacturing and Controls issue please contact Donna Kapples directly at (973) 781-6929.

If there are any general or Clinical related issues please contact Jerry Klimek, DRA Therapeutic Area at (973) 781-8145.

Joan A. Materna,

Joan A. Materna
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

Desk copies:
Ms. Susan Lange, Office of New Drug Chemistry bundling coordinator (cover letter only)