CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-702/S013

Trade Name: Lipitor

Generic Name: Atorvastatin calcium

Sponsor: Parke-Davis Research and Development

Approval Date: June 25, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S-013

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Reviews / Information Included in this NDA Review.

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Approvable Letter	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S013

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-702/S-013

JUN 25 1998

Parke-Davis
Attention: Philip G. Simonson, Ph.D.
Senior Manager, CMC, Worldwide Reg. Affairs
2800 Plymouth Road, P.O. Box 1047
Ann Arbor, Michigan 48106-1047

Dear Dr. Simonson:

Please refer to your supplemental new drug application dated April 1, 1998, received April 2, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lipitor (atorvastatin calcium) Tablets.

The user fee goal date for this application is October 2, 1998.

This supplemental new drug application provides for the addition an [redacted] procedure for atorvastatin calcium 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, contact Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

Stephen K Moore 6/25/98

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 20-702
HFD-510/Div. Files
HFD-510/M. Simoneau
HFD-95/DDMS
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: Mas/June 22, 1998
Initialed by: X.Ysern6.22.98/S.Moore6.22.98/E.Galliers6.24.98
final:Mas6.25.98
filename: 70201.13

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S013

CHEMISTRY REVIEW(S)

ORIGINAL

MAY 20 1998

CHEMIST'S REVIEW

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

2. NDA # 20-702
Approved: 17-DEC-1996

3. NAME AND ADDRESS OF APPLICANT
Parke-Davis Pharmaceutical Research

Division of Warner-Lambert Company
2800 Plymouth Road
P.O. Box 1047
Ann Arbor, MI 48106-1047 (313) 966-5000

4. SUPPLEMENT SCS-013
Doc 01-APR-1998 Rec 02-APR-1998

5. Name of the Drug Lipitor Tablets

6. Nonproprietary Name
Atorvastatin Calcium

7. SUPPLEMENT PROVIDES for an additional [redacted] procedure for Atorvastatin Calcium drug substance.

8. AMENDMENT --

9. PHARMACOLOGICAL CATEGORY Lipid Modifier.
HMG-CoA reductase inhibitor/ Antihyperlipoproteinemic agent.

10. HOW DISPENSED

11. RELATED
-N. A.-

12. DOSAGE FORM Tablet

13. POTENCY 10, 20 and 40 mg

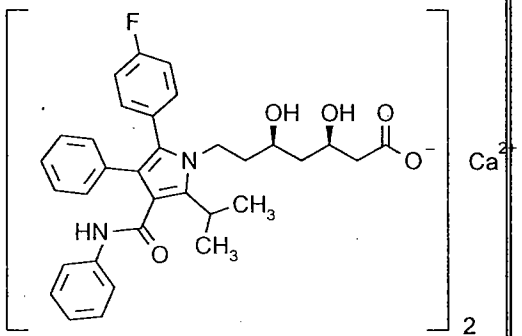
14. CHEMICAL NAME AND STRUCTURE

Atorvastatin Calcium

$(C_{33}H_{34}FN_2O_5)_2Ca$

CAS 134523-03-8
CAS 134523-00-5 (atorvastatin)

FW 2 x 557.7 + 40.0 = 1155.38
FW calcium salt trihydrate $(C_{33}H_{34}FN_2O_5)_2Ca.3H_2O$ = 1209.42
FW free acid $C_{33}H_{35}FN_2O_5$ = 558.66



1*H*-Pyrrole-1-heptanoic acid, 2-(4-flourophenyl)-β,–δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-,calcium salt (2:1), [*R*-(*R**,*R**)]-

15. COMMENTS The supplement (SCS-013, ref. # 13) provides for an additional [redacted] procedure for Atorvastatin Calcium drug substance. In the approved NDA procedure, Atorvastatin that does not meet specifications is [redacted] Atorvastatin. The new procedure, adequately described in attachment I, does not [redacted] The analytical results for [redacted] lots of Atorvastatin calcium [redacted] manufactured in Holland, Michigan, and [redacted] manufactured in Warner-Lambert Export, Cork, Ireland) reworked using the procedure are provided in attachment 2. All lots meet the approved NDA analytical specifications.

16. CONCLUSIONS AND RECOMMENDATIONS Adequate information has been provided to support the new [redacted] procedure for the manufacture of Atorvastatin Calcium drug substance.
Issue Approval Letter.

17. REVIEWER NAME (AND SIGNATURE) Xavier Ysern **DATE COMPLETED** 12-MAY-1998
Xavier Ysern, PhD

R/D INITIATED BY

filename: /nda/20702s13.doc

DISTRIBUTION: Original: NDA 20-702 cc: HFD-510 Division File / CSO / MooreS/ YsernX

AP

Stephen K. Moore
5/20/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S013

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Pharmaceutical Research
2800 Plymouth Road Phone: (734) 622-7000
Ann Arbor, MI
48105

PARKE-DAVIS

NDA NO. 20702 REF. NO. 013
NDA SUPPL FOR SCS

April 1, 1998

NDA 20-702
Ref. No. 62
Lipitor® (atorvastatin calcium) Tablets

ORIGINAL

Re: **Supplement** -

Solomon Sobel, M.D.
Director
Division of Metabolic and Endocrine
Drug Products (HFD-510)
Document Control Room 14B-19
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

REVIEWS COMPLETED
CSO ACTION: AP 6/25/98
LETTER FINAL MEMO
DATE

CENTER FOR DRUG
REC'D
APR 0 2 1998
HFD-510

Dear Dr. Sobel:

Reference is made to NDA 20-702 for Lipitor® (atorvastatin calcium) Tablets. The NDA is being supplemented to add an procedure for atorvastatin drug substance.

The new procedure is intended for atorvastatin calcium The procedure is described, for a suitable scale of operation, in Attachment 1.

In the approved NDA procedure, atorvastatin which does not meet specifications is approved synthesis to produce atorvastatin. The new procedure does not atorvastatin calcium.

The suitability of this new rework procedure has been demonstrated on production scale. The analytical results for lots of atorvastatin calcium manufactured in Holland and manufactured in Warner-Lambert Export) reworked using the new procedure are provided in Attachment 2. All lots meet the approved NDA analytical specifications.

Should you have any questions or require additional information, please contact me at 734/622-5781 or FAX 734/622-7890.

Sincerely,

Philip G. Simonson, Ph.D.
Senior Manager
Chemistry, Manufacturing and Control
Worldwide Regulatory Affairs

SB\rp\rm
t:\nda\20-702\040198-62

Attachments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ORIGINAL

NDA 20-702/S-013

APR 22 1998

PARKE -DAVIS RESEARCH AND DEVELOPMENT
WARNER-LAMBERT COMPANY
2800 Plymouth Road
Ann Arbor, MI 48105

Attention: Philip G. Simonson, Ph.D.
Senior Manager, CMC Worldwide Regulatory Affairs

Dear Dr. Simonson:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: LIPITOR (atorvastatin calcium) Tablets

NDA Number: 20-702

Supplement Number: S-013

Date of Supplement: April 01, 1998

Date of Receipt: April 02, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on June 01, 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 20-702/S-013
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\DATA\WPFILES\20702ACK

SUPPLEMENT ACKNOWLEDGEMENT

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

Form Approved: OMB No. 0910-0297
Expiration Date: November 30, 1996

USER FEE COVER SHEET

See Instructions on Reverse Before Completing This Form

1. APPLICANTS NAME AND ADDRESS

Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company
2800 Plymouth Rd.
Ann Arbor, MI 48105

2. USER FEE BILLING NAME, ADDRESS, AND CONTACT

William Rosen
Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105

3. TELEPHONE NUMBER *(INCLUDE AREA CODE)* (734)622-5168

4. PRODUCT NAME

Lipitor ® Tablets

5. DOES THIS APPLICATION CONTAIN CLINICAL DATA? ☐ YES ☒ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM

6. USER FEE I.D. NUMBER

7. LICENSE NUMBER

8. 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 BEFORE 9/1/92

☐ AN INSULIN PRODUCT SUBMITTED UNDER 506

☐ THE APPLICATION IS SUBMITTED UNDER 505(b)(2) *(See reverse before checking box.)*

☐ Other: Orphan Drug - See attached.

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

☐ A CRUDE ALLERGIC EXTRACT PRODUCT

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGIC PRODUCT LICENSED UNDER 351 OF THE PHS ACT

9. a. HAS THIS APPLICATION QUALIFIED FOR A SMALL BUSINESS EXCEPTION? ☐ YES *(See reverse if answered YES)* ☐ NO

b. HAS A WAIVER OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES *(See reverse if answered YES)* ☐ NO

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Sean Brennan	Senior Manager Worldwide Regulatory Affairs	April 1, 1998