CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-702/S021

Trade Name: Lipitor

Generic Name: Atorvastatin calcium

Sponsor: Parke-Davis Research and Development

Approval Date: December 1, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S-021

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S021

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-702/S-021

Parke-Davis Pharmaceutical Research, agent for
Warner-Lambert Export, Limited
Attention: Philip G. Simonson, Ph.D.
Director, CMC, Worldwide Regulatory Affairs
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Dr. Simonson:

Please refer to your supplemental new drug application dated September 22, 1999, received September 23, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lipitor (atorvastatin calcium) Tablets.

We acknowledge receipt of your submission dated October 4, 1999.

This supplemental new drug application provides for the removal [redacted] from the 90-count [redacted] bottles of Lipitor (Atorvastatin Calcium) Tablets.

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 12/1/99

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 20-702
HFD-510/Div. Files
HFD-510/M. Simoneau
HFD-510/XYsern/SMoore
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: Mas/November 24, 1999
Initialed by:XYsern11.24.99/SMoore11.24.99/EGalliers11.30.99
final:Mas12.1.99
filename: 20702.21

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S021

CHEMISTRY REVIEW(S)

NOV 14 1999

CHEMIST'S REVIEW

1. Organization CDE/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 SCP-021
Doc. 22-SEP-1999 Rec. 23-SEP-1999

5. Name of the Drug
Lipitor Tablets

6. Nonproprietary Name
Atorvastatin Calcium

7. Supplement provides for the removal of [redacted] from the 90-count [redacted] bottles of Lipitor (Atorvastatin Calcium) Tablets.

8. Amendment
Doc. 04-OCT-1999 Rec.05-OCT-1999

9. Pharmacological Category Lipid Modifier.
HMG-CoA reductase inhibitor/ Antihyperlipoproteinemic agent.

10. How Dispensed
Rx

11. Related
-N. A.-

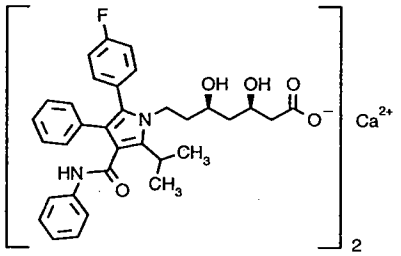
12. Dosage Form Tablet

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 current container/closure system for the 90-count bottles contain [redacted] This supplement (originally submitted as Special Supplement Changes Being Effected, Parke-Davis ref. # 95), SCP-021, proposes the removal of [redacted] the 90-count [redacted] bottles of Lipitor (Atorvastatin Calcium) Tablets [redacted] The October 4, 1999, amendment (ref. # 96), request that the supplement be converted to one requiring prior approval and clarifies the post-approval stability commitment associated with this change. **In support of this application the applicant provides stability data** (samples from [redacted] lot of each strength 10-, 20- and 40-mg tablets) **from drug product packaged in the proposed container/closure and in the approved container/closure** (control). The results of the stability study, six months at accelerated conditions [redacted] and nine months at room temperature [redacted], are similar for both container/closure systems. Stability studies will be continued through the current expiration period of these products. The information provided supports that **the [redacted] from the container closure does not have any detriment in the quality of the drug product.**

16. Conclusions and Recommendations The information provided in this supplement shows that the tablets can be adequately packaged with [redacted] **Issue Approval Letter.**

17. Reviewer Name (and Signature) Xavier Ysern **Date Completed** 14-OCT-1999

Xavier Ysern, PhD

R/D INITIATED BY

filename: /nda/20702s21.doc

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

AP

Stephen K. Moore 10/14/99

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-702/S021

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

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

PARKE-DAVIS

September 22, 1999

ORIGINAL

NDA 20-702
Ref. No. 095
NDA NO. 20-702 REF NO. 021
Lipitor® (atorvastatin calcium) Tablets
NDA SUPPL FOR SCP

Re: **Special Supplement**
Changes Being Effected:

see amendment dated 04-OCT-1999 requesting change from CBE to one requiring prior approval
X. Tsai
10/5/99

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

Dear Dr. Sobel:

AP
see cover
X. Tsai
10/5/99

On behalf of, and as agent for Warner Lambert Export, reference is made to approved NDA 20-702 for Lipitor® (atorvastatin calcium) Tablets. The purpose of this supplement is to provide for the [redacted] the 90-count [redacted] bottles of Lipitor 10-mg, 20-mg and 40-mg Tablets. This change will be implemented in November 1999.

Our current container/closure system for the 90-count bottles [redacted] described in the approved NDA. In the proposed container/closure system, [redacted] The remaining components of the container/closure system are unchanged from the original NDA.

Stability studies have been conducted according to the approved stability protocol on [redacted] lot of each tablet strength packaged in the proposed container closure system. Tablets from each of these lots were also packaged in the approved container/closure system and placed on stability as control samples. Six months accelerated [redacted] and 9 months room temperature [redacted] stability results for tablets packaged in the proposed container and the approved container are provided in the attachment. The stability results are similar for both container/closure systems and demonstrate that the tablets can be packaged [redacted]

Should you have any questions regarding this submission, please contact me at 734/622-5781 or via FAX at 734/622-7890 or Dr. Sean Brennan at 734/622-7596.

Sincerely,

Philip G. Simonson, Ph.D.
Director, CMC
Worldwide Regulatory Affairs

Desk Copy: Ms. Regina Brown, North Brunswick FDA District Office
Dr. Xavier Ysern, Division of Metabolism and Endocrine Drug Products

PS:kb
09-22-1999\RN-095\20-702\CI-0981\Letter

Attachment

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS
DATE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-702/S-021

Warner-Lambert Export
2800 Plymouth Road, P.O. Box 1047,
Ann Arbor, MI 48106-1047

SEP 28 1999

Attention: Philip G. Simonson, Ph.D.
Director, 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-021

Date of Supplement: September 22, 1999

Date of Receipt: September 23, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on November 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 20-702/S-021
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\WPFILES\20702.WPD

SUPPLEMENT ACKNOWLEDGEMENT