CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-702/S024

Trade Name: Lipitor Tablets

Generic Name: atorvastatin calcium

Sponsor: Parke Davis Pharmaceutical

Approval Date: November 11, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-702/S024

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APPLICATION NUMBER:

NDA 20-702/S024

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-702/S-024

Parke-Davis
Attention: Philip Simonson, Ph.D.
Director, CMC Worldwide Regulatory Affairs
2800 Plymouth Road
P.O. Box 1047
Ann Arbor, MI 48106-1047

Dear Dr. Simonson:

Please refer to your supplemental new drug application dated July 13, 2000, received July 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lipitor (atorvastatin calcium) tablets.

We acknowledge receipt of your submissions dated August 1 and September 29, 2000.

This supplemental new drug application provides for the use of the firm's facility located in Ringaskiddy, Ireland, as an additional manufacturing and testing facility for Lipitor 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, call Margaret Simoneau, R.Ph., Regulatory Project Manager, at (301) 827-6418.

Sincerely,

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

/s/

Steve Moore
11/14/00 10:29:28 AM

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APPLICATION NUMBER:

NDA 20-702/S024

CHEMISTRY REVIEW(S)

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 SCM-024
Doc. 13-JUL-2000 Rec. 14-JUL-2000

5. Name of the Drug
Lipitor Tablets

6. Nonproprietary Name
Atorvastatin Calcium

7. Supplement provides for the use of the Sponsor facility located in Ringaskiddy, Ireland, as an additional manufacturing and testing facility for Lipitor (Atorvastatin Calcium) Tablets.

8. Amendment
Doc. 29-SEP-2000 Rec. 02-OCT-2000

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

10. How Dispensed
Rx

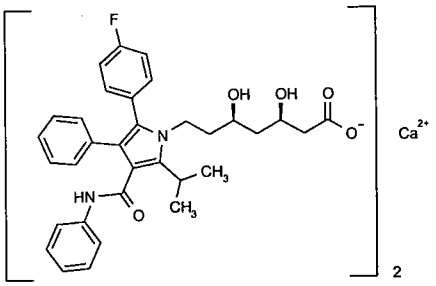
11. Related
-N. A.-

12. Dosage Form Tablet

13. Potency 10-, 20-, 40- and 80-mg

14. Chemical Name and Structure

Atorvastatin Calcium
$(C_{33}H_{34}FN_2O_5)_2Ca$
FW = 2 x 557.7 + 40.0 = 1155.38 (anhydrous calcium salt)
CAS 134523-03-8
CAS 134523-00-5 (atorvastatin)
FW free acid $C_{33}H_{34}FN_2O_5$ = 558.66
FW calcium salt trihydrate $(C_{33}H_{34}FN_2O_5)_2Ca\ H_2O$ = 1209.42



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

15. Comments: This supplement, SCM-024 (ref. # 112), provides for the use of the Sponsor facility located in Ringaskiddy, Ireland, as an additional manufacturing and testing facility for Lipitor (Atorvastatin Calcium) Tablets. Information pertaining the manufacture of the drug product is provided in the original supplemental submission. The original supplement lacked information regarding stability. Drug product stability information was requested and it was adequately provided in the 29-SEP-2000 amendment (ref. # 118). The stability data provided in the amendment includes batch of each strength, stored in the commercial packaging for three months at (accelerated conditions) and at (controlled room temperature). After inspection, some deficiencies were found and a form 483 was issued. A facsimile copy of the firm responses to the 483 was provided on 13-NOV-2000. After evaluation of the firm responses to the deficiencies, the District Office issued an acceptable recommendation (EER summary report dated 13-NOV-2000 attached). *All regulatory requirements have been satisfied.*

16. Conclusions and Recommendations: Adequate CMC information has been provided to assure the quality of the drug product manufactured at the sponsor facility located in Ringaskiddy, Ireland. **Issue Approval Letter.**

17. Reviewer Name (and Signature) **Date Completed** 13-NOV-2000

Xavier Ysern, PhD

R/D INITIATED BY

filename:

/nda/20702s24.doc

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

AP

6 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-702 S02

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 20702/024**
Priority: **1P**
Org Code: **510**
Stamp: **14-JUL-2000** Regulatory Due: **14-NOV-2000**
Action Goal:
District Goal: **10-OCT-2000**
Applicant: **WARNER LAMBERT EXPOR**
C/O PARKE DAVIS PHARMACEUTIC.
2800 PLYMOUTH RD
ANN ARBOR, MI 481061047
Brand Name: **LIPITOR (ATORVASTATIN CALCIUM)10/20/40MG**
Established Name:
Generic Name: **ATORVASTATIN CALCIUM**
Dosage Form: **TAB (TABLET)**
Strength: **10, 20, 40 AND 80 MG**

FDA Contacts:			
M. SIMONEAU	**(HFD-510)**	**301-827-6418**	**, Project Manager**
X. YSERN	**(HFD-510)**	**301-827-6420**	**, Review Chemist**
S. MOORE	**(HFD-510)**	**301-827-6430**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 13-NOV-2000 by M. GARCIA (HFD-322) 301-594-0095
WITHHOLD on 13-NOV-2000 by M. GARCIA (HFD-322) 301-594-0095

Establishment: **9612161**
DMF No:
PFIZER IRELAND PHARMACEUTICA
AADA No:

RINGASKIDDY, COUNTY CORK, EI

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **13-NOV-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
FIRM RESPONSE TO DEFIC. ADEQU

Responsibilities: **FINISHED DOSAGE MANUFACTURER**
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

/s/

Xavier Ysern
11/13/00 05:42:42 PM
CHEMIST

AP

Steve Moore
11/13/00 05:46:33 PM
CHEMIST