CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-699/S-013

Name:	Effexor XR Extended-Release Capsules
Generic Name:	venlafaxine hydrochloride
Sponsor:	Wyeth Pharmaceuticals Inc.
Approval Date:	7/20/00
Indications:	For the treatment of depression and generalized anxiety disorder.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-699/S-013

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-699/SCM-013

JUL 20 2000

Wyeth-Ayerst
Attention: Patricia Foti Mann
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Mann :

Please refer to your supplemental new drug application dated April 18, 2000, received April 19, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor.

The user fee goal date for this application is August 19, 2000

This supplemental new drug application provides for an alternate site for the manufacture of the drug substance, venlafaxine hydrochloride.

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 Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

7/20/00

Robert H. Seevers, Ph.D.
Chemistry Team Leader, Psychiatric Drugs for the
Division of Neuropharmacological Drug Products,
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-699
HFD-120/Div. Files
HFD-120/P.David
HFD-120/R.Seevers
HFD-120/S.McLamore
HFD-095/DDMS-IMT
HFD-810/DNDC Division Director
DISTRICT OFFICE

Drafted by: SDM/July 18, 2000
Initialed by:
final:
filename: 20699LET

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-699/S-013

CHEMISTRY REVIEW(S)

JUL 20 2000

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION**:	HFD-120
2. **NDA**	20-699
3. **SUPPLEMENT NUMBER AND DATES**:	SCM-013
LETTER DATE:	04-18-00
STAMP DATE:	04-19-00
4. **AMENDMENT/REPORTS/DATES**	02-11-00
5. **RECEIVED BY CHEMIST**:	04-25-00

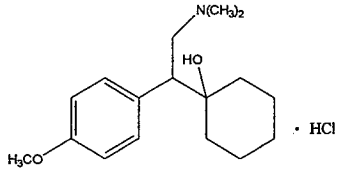
6. **APPLICANT NAME & ADDRESS**: Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

7. **NAME OF DRUG**: Effexor ® XR Extended Release Capsules

8. **NONPROPRIETARY NAME**: Venlanfaxine hydrochloride

9. **CHEMICAL NAME and STRUCTURE**:

(*R,S*)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol hydrochloride



10. **DOSAGE FORMS**:	Extended Release Capsules
11. **POTENCY**:	37.5 mg; 75 mg, 100 mg, 150 mg
12. **PHARMACOLOGICAL CATEGORY**:	anti-depressant/ general anti-anxiety disorder
13. **HOW DISPENSED**:	X (Rx) _____(OTC)
14. **RECORD and REPORTS CURRENT**:	X Yes _____No
15. **RELATED IND/NDA/DMF**:	DMF [ ] and NDA 20-151

16. **SUPPLEMENT PROVIDES FOR:** This supplement provides for the following:

- a change the site of manufacture for the drug substance, venlafaxine hydrochloride
- [redacted]

17. **ADDITIONAL COMMENTS**: The applicant references DMF [ ] for the manufacturing, controls and packaging of the drug substance. The applicant also indicates that there were no changes in the synthesis, drug substance specification or in the drug substances physical properties. The sponsor also indicates that the new manufacturer, [ ], produces drug substance that exhibits an equivalent impurity profile to the approved manufacturer. The site was submitted to EES for a recommendation and was acceptable on May 9, 2000 based on the district recommendation (see attached report).

The site change qualifies as a Level 3 Change as defined by SUPAC-MR Guidance, Section V.C. Accordingly, the applicant has included dissolution and stability documentation. The stability documentation includes 3 months of stability data for 2 batches of each dosage form (37.5 mg, 75 mg and 150 mg) made from drug substance manufactured at the new site.

There were no changes reported in the drug product.

18. **CONCLUSIONS & RECOMMENDATIONS**: The sponsor has submitted adequate information to support the changes requested in this application. It is the recommendation of the CMC reviewer that this supplement be **APPROVED**.

Sherita D. McLamore, Ph.D. (Review Chemist)

7-20-00
Date

Robert Seevers, Ph.D. (Chemistry Team Leader)

7-20-00
Date

cc:
Division File NDA 20-699
HFD-120/SMcLamore
HFD-120/RSeevers
HFD-120/PDavid
HFD-800/SLange

Redacted 6 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-699/S-013

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-699/S-013

APR 25 2000

Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Attention: Patricia Foti Mann
Associate Director Worldwide Regulatory Affairs

Dear Ms. Mann:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Effexor XR (venlafaxine hydrochloride) Extended Release Capsules

NDA Number: 20-699

Supplement Number: 013

Date of Supplement: 18-Apr-00

Date of Receipt: 19-Apr-00

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on 18-Jun-2000 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 Neuropharmacological Drug Products, HFD-120
Office of Drug Evaluation I
Attention: Document Control Room 4008
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

4/25/00

John S. Purvis
Chief, Project Management Staff
Division of Neuropharmacological Drug Products, HFD-120
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 20-699/013
HFD-120/Div. Files
HFD-120/CSO/David

filename:

SUPPLEMENT ACKNOWLEDGEMENT

WYETH-AYERST *RESEARCH*

P.O. BOX 8299 • PHILADELPHIA, PA 19101-8299 • (610) 902-3710
FAX: (610) 964-5973

Division of American Home Products Corporation

U.S. REGULATORY AFFAIRS

NDA SUPPLEMENT

NDA NO. 20-699 REF NO. SCM-013
NDA SUPPL FOR Manufacturing Change

April 18, 2000

ORIGINAL

NDA No. 20-699
Effexor® XR (venlafaxine hydrochloride) Extended Release Capsules

CENTER FOR DRUG EVALUATION AND RESEARCH

APR 19 2000

RECEIVED HFD-120

Russell G. Katz, M.D., Director
Division of Neuropharmacological Drug Products, HFD-120
Center for Drug Evaluation and Research
Food and Drug Administration
Attn: Document Control Room 4008, 4th floor
1451 Rockville Pike
Rockville, MD 20852

PRIOR APPROVAL SUPPLEMENT

Dear Dr. Katz:

Reference is made to Wyeth-Ayerst Laboratories New Drug Application No. 20-699 for Effexor® XR (venlafaxine hydrochloride) Extended Release Capsules, 37.5 mg, 75 mg, 100 mg, and 150 mg.

In accordance with the November 1999 Guidance *Changes to an Approved NDA or ANDA*, we hereby are submitting, in duplicate, this supplement to provide for the following:

- An alternate site for the manufacture of the active pharmaceutical ingredient, venlafaxine hydrochloride.
- [redacted]

The currently approved source of venlafaxine hydrochloride is [redacted]
We have qualified an alternate source, listed below:

[redacted]

Reference is made to the [ ] Drug Master File No. [ ] for the manufacture, controls and packaging information for venlafaxine hydrochloride. [ ] has had a successful FDA inspection, [ ], for the appropriate profile class, (CSN, Nonsterile bulk by chemical synthesis), and there are no outstanding issues.

In support of this alternate source, we are providing information regarding the drug substance and its use to make the drug product. Laboratory data on the chemical and physical characterization of venlafaxine hydrochloride manufactured by [ ] are provided in this supplemental application. An assessment of the changes on the identity, strength, quality, purity and potency of the drug product has been conducted and is included herein. Additionally, it should be noted:

- There is no change in the [ ]
- There are no changes in drug substance specifications.
- There are no changes to [ ] specifications or physical properties of the drug substance.
- The [ ] venlafaxine hydrochloride exhibits an equivalent impurity profile to the approved source of venlafaxine hydrochloride.

We have manufactured three venlafaxine hydrochloride spheroid batches from three separate lots of [ ] [ ] drug substance. These spheroid batches were subsequently encapsulated as six Effexor XR capsule production scale batches, two batches each of the 37.5 mg, 75 mg and 150 mg strengths and placed on stability study under ICH accelerated and room temperature storage conditions. Test results and stability data are provided herein. This information demonstrates that the changes outlined above have no adverse effects on the identity, strength, quality, purity and potency of either the drug substance or the Effexor XR drug product.

Please note Wyeth-Ayerst Laboratories has a [ ] contractual agreement with [ ] to supply venlafaxine hydrochloride and maintains rigorous control over any changes to the manufacture of the drug substance.

Wyeth-Ayerst Laboratories hereby certifies that a complete copy of this amendment has been forwarded as a Field Copy to the FDA District Office at the address below:

Mr. John Podsadowski
Program Coordinator for Field Copy Submissions
Buffalo District
Food and Drug administration
599 Delaware Avenue
Buffalo, New York 14202

To assist the Agency's administrative coordination of this supplement, we also have provided a copy of the amendment's cover letter to the FDA Home District Office for Wyeth-Ayerst Laboratories located in Philadelphia, PA.

We trust that you will find this amended supplement satisfactory and that it will be approved at your earliest convenience. If you have any questions, please contact the undersigned at (610) 902-3727 or Mr. Louis Antinori at (610) 902-3716.

Sincerely,

WYETH-AYERST LABORATORIES

Patricia Foti Mann

Patricia Foti Mann
Associate Director
Worldwide Regulatory Affairs

Cover letter w/o attachments
cc Ms. Debra Pagano
Program Coordinator for Field Copy Submissions
Department of Health and Human Services
Food and Drug Administration
2nd and Chestnut Streets
Philadelphia, PA 19101-2973

EffexorXR[ ].doc