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.
## Reviews / Information Included in this NDA Review.

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APPLICATION NUMBER:
NDA 20-699/S-013

APPROVAL LETTER
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,

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.Seevres
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)
APPLICATION NUMBER:
NDA 20-699/S-013

CHEMISTRY REVIEW(S)
CHEMIST REVIEW
OF SUPPLEMENT

1. ORGANIZATION: HFD-120
2. NDA: 20-699
3. SUPPLEMENT NUMBER AND DATES:
   LETTER DATE: SCM-013
   STAMP DATE: 04-18-00
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
   Venlafaxine hydrochloride

8. NONPROPRIETARY NAME:
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/INDA/DMF:
   DMF C ___ 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

17. ADDITIONAL COMMENTS: The applicant references DMF C 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, C 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.
cc:
Division File NDA 20-699
HFD-120/SMcLamore
HFD-120/RSeevers
HFD-120/PDavid
HFD-800/SLange
Redacted ___ page(s)
of trade secret and/or
confidential commercial
information from
Chemistry Review
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,

[Signature]

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

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.

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

□ □
Reference is made to the drug master file number 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
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