

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-699/S-038

Name: Effexor XR Extended-Release Capsules

Generic Name: venlafaxine hydrochloride

Sponsor: Wyeth Pharmaceuticals Inc.

Approval Date: 09/02/03

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APPLICATION NUMBER:
NDA 20-699/S-038

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APPLICATION NUMBER:
NDA 20-699/S-038

APPROVAL LETTER



NDA 20-699/S-038/S-043

Wyeth Pharmaceuticals
Attention: Tracy D. Rockney, JD
Director, Global Brand Management
Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-1245

Dear Ms. Rockney:

Please refer to the your supplemental new drug applications dated March 7, 2003 (S-043), and April 16, 2003 (S-038), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor XR (venlafaxine hydrochloride) Extended Release 37.5 mg, 75 mg, and 150 mg Capsules.

The above submissions, submitted as "Changes Being Effected" supplemental applications, provide for the following revisions to labeling:

S-043

- This supplement provides for revisions to the Effexor XR Patient Brief Summary to add the new indication of social anxiety disorder which was approved in an Agency letter dated February 11, 2003 under S-022 as well as the addition of the term "palpitation" under the list of most common side effects.

S-038

- This supplement provides for revisions to the Effexor XR Patient Brief Summary to add the term "seizures" to the list of discontinuation symptoms.

We have completed the review of these supplemental applications, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling. Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

NDA 20-699/S-038/S-043

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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 regarding this letter, call Mr. Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Russell Katz
9/2/03 04:48:00 PM

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APPLICATION NUMBER:
NDA 20-699/S-038

MEDICAL REVIEW(S)

**Review and Evaluation of Clinical Data
NDA #20-699**

Sponsor: Wyeth
Drug: Effexor XR (venlafaxine HCl extended-release capsules)
Indications: MDD, GAD, SAD
Material Submitted: Special Supplement - CBE
SLR-038
Correspondence Date: April 16, 2003
Date Received: April 17, 2003

I. Background

Wyeth has submitted this CBE labeling supplement to amend the Effexor XR Patient Brief Summary which was approved on 2-26-03 (under NDA 20-699/S-032). Changes are reviewed below.

II. Changes to the Effexor XR Patient Brief Summary

The sponsor indicates that the adverse event term "seizures" has been added to the list of possible adverse experiences associated with the sudden discontinuation of Effexor XR. Information supporting the addition of this term to the corresponding section of Effexor XR product labeling was submitted simultaneously with this submission under SLR-039 to this NDA. The 8-6-03 clinical review of that supplement found this labeling change to be generally acceptable.

My comparison of the annotated Effexor XR Patient Brief Summary provided in this submission (see Tab A) with that approved under S-032 revealed other changes as well:

- under the heading **What is Effexor XR?**, the sponsor has added the recently approved indication of Social Anxiety Disorder (approved 2-11-03 under NDA 20-699/S-022).
- a new section describing the nature of Social Anxiety Disorder has been added to follow the analogous descriptions of depression and generalized anxiety disorder.

• under the heading **What are the possible side effects of Effexor XR?**, the adverse event term "palpitation" has been added. Although this event was not considered a common, drug-related event in short-term, placebo-controlled study pools for any of the approved indications (i.e., reported in at least 5% of Effexor XR patients at an incidence at least twice that in the placebo group), it is listed in the 2% AE Table for Social Anxiety Disorder (reported in 3% of Effexor XR and 1% of placebo patients) in Effexor XR approved labeling.

III. Conclusions and Recommendations

I have no objection to any of the changes implemented in the Effexor XR Patient Brief Summary. It is recommended that this supplement be approved.

Gregory M. Dubitsky, M.D.
August 7, 2003

cc: NDA #20-699
HFD-120 (Div. File)
HFD-120/GDubitsky
/TLaughren
/PAndreason
/PDavid

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/s/

Greg Dubitsky
8/7/03 11:24:02 AM
MEDICAL OFFICER

Thomas Laughren
8/7/03 12:41:32 PM
MEDICAL OFFICER

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APPLICATION NUMBER:

NDA 20-699/S-038

ADMINISTRATIVE and
CORRESPONDENCE DOCUMENTS

**REGULATORY PROJECT MANAGER
LABELING REVIEW**

Drug: Effexor XR (venlafaxine hydrochloride) Extended Release 37.5 mg, 75 mg, and 150 mg Capsules
 NDA: 20-699
 Sponsor: Wyeth
 Indication: Major Depressive Disorder (MDD)/Generalized Anxiety Disorder (GAD)/Social Anxiety Disorder (SAD)
 Supplements:

NDA	Supplement	Dated	Action
Effexor XR (venlafaxine hydrochloride) Extended Release 37.5 mg, 75 mg, and 150 mg Capsules			
20-699	SLR-032	11-21-02, and amended on 1-23-03	AP letter dated 2-26-03
20-699	SLR-043	3-7-03	Open
20-699	SLR-038	4-16-03	Open

Notes of Interest

- The Agency approved an Effexor XR Patient Brief Summary in an action letter dated 2-11-03 (SLR-032).

Review

20-699/SLR-043

Dated: 3-7-03

CBE: Yes

Label Code: N/A

Reviewed by Medical Officer: Yes, Acceptable

- This supplement provides for revisions to the Effexor XR Patient Brief Summary to add the new indication of social anxiety disorder which was approved in an Agency letter dated 2-11-03 under SE1-022 as well as the addition of the term "palpitation" under the list of most common side effects.

20-699/SLR-038

Dated: 4-16-03

CBE: Yes

Label Code: N/A

Reviewed by Medical Officer: Yes, Acceptable

- This supplement provides for revisions to the Effexor XR Patient Brief Summary to add the term "seizures" to the list of discontinuation symptoms.

Conclusions

1. I compared the last approved Effexor XR Patient Brief Summary (approval letter dated 2-26-03) to the revisions proposed by the sponsor, and there were no other changes than those noted above.
2. The medical officer finds the revisions to the Patient Brief Summary acceptable.
3. I recommend that an approval letter issue.

{See appended electronic signature page}

Paul David, R.Ph., Senior Regulatory Health Project Manager

{See appended electronic signature page}

Robbin Nighswander, R.Ph., Supervisory Regulatory Health Project Manager

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/s/

Paul David
8/27/03 11:49:55 AM
CSO

Robbin Nighswander
8/27/03 12:01:24 PM
CSO