DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

SUPPLEMENT APPROVAL

NDA 20151 / S-056 / S-057
NDA 20699 / S-090

Wyeth Pharmaceuticals, Inc.
Attention: Dr. Kimberly A. McCormick
Senior Manager, Global Regulatory Affairs
PO Box 8299
Philadelphia, PA 19101-8299

Dear Dr. McCormick:

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Effexor (venlafaxine HCl) Tablets and Effexor XR (venlafaxine HCl) Extended-Release Capsules as follows:

- NDA 20151/S-056, Effexor (venlafaxine HCl) Tablets, dated and received July 1, 2009.

  This "Changes Being Effected" labeling supplement adds the term "angioedema" to the **ADVERSE REACTIONS, Postmarketing Reports,** *Adverse Events* subsection of the labeling. The **HOW SUPPLIED** section is also revised to reflect the discontinuation of several product presentations.

- NDA 20699/S-090, Effexor XR (venlafaxine HCl) Extended-Release Capsules, dated June 23, 2009 and received June 24, 2009.

  This "Changes Being Effected" labeling supplement adds the term "angioedema" to the **ADVERSE REACTIONS, Postmarketing Reports,** *Adverse Events* subsection of the labeling.

- NDA 20151 / S-057, Effexor (venlafaxine HCl) Tablets, dated and received September 23, 2009.

  This "Prior Approval" labeling supplement updates the information under the **CONTRAINDICATIONS** and **WARNINGS.** The **CONTRAINDICATIONS** section of the labeling has been revised to include a description of the anticipated consequences of the contraindicated use, in accordance with the draft FDA Guidance for Industry: Warnings and Precautions, Contraindications, and Box Warning Sections of Labeling for Human Prescription Drug and Biological Products — Content and Format, (2006, pages 6-8). The

information added to the **CONTRAINDICATIONS** section is a revised version of the information previously found in **WARNINGS**. The **WARNINGS** section of the label has been revised to remove this information. The changes are as follows (additions underlined, deletions strikethrough):

CONTRAINDICATIONS
Hypersensitivity to venlafaxine hydrochloride or to any excipients in the formulation.

~~Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated (see **WARNINGS**).~~Effexor must not be used concomitantly in patients taking MAOIs or in patients who have taken MAOIs within the preceding 14 days due to the risk of serious, sometimes fatal, drug interactions with SNRI or SSRI treatment or with other serotonergic drugs. These interactions have been associated with symptoms that include tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia with features resembling neuroleptic malignant syndrome, seizures, rigidity, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. Based on the half-life of venlafaxine, at least 7 days should be allowed after stopping Effexor before starting an MAOI (see **DOSAGE AND ADMINISTRATION**).

WARNINGS
~~**Potential for Interaction with Monoamine Oxidase Inhibitors**~~
~~Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on Effexor, or who have recently had Effexor therapy discontinued prior to initiation of an MAOI. These reactions have included tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia with features resembling neuroleptic malignant syndrome, seizures, and death. In patients receiving antidepressants with pharmacological properties similar to venlafaxine in combination with a monoamine oxidase inhibitor, there have also been reports of serious, sometimes fatal, reactions. For a selective serotonin reuptake inhibitor, these reactions have included hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. Some cases presented with features resembling neuroleptic malignant syndrome. Severe hyperthermia and seizures, sometimes fatal, have been reported in association with the combined use of tricyclic antidepressants and MAOIs. These reactions have also been reported in patients who have recently discontinued these drugs and have been started on an MAOI. Therefore, it is recommended that Effexor not be used in combination with an MAOI, or within at least 14 days of discontinuing treatment with an MAOI. Based on the half-life~~

~~of Effexor, at least 7 days should be allowed after stopping Effexor before starting an MAOI.~~

We have completed our review of these applications and they are approved, effective on the date of this letter, for use as recommended in the enclosed labeling.

Please resubmit the enclosed content of labeling in SPL format as soon as possible, but no later than 14 days from the date of this letter. For administrative purposes, please designate this submission, "**SPL for approved NDA 20151 / S-056 / S-057 and NDA 20699 / S-090.**"

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, email CAPT Steven D. Hardeman, R.Ph., Chief, Project Management Staff, at Steven.Hardeman@FDA.HHS.GOV.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20151	SUPPL-56	WYETH PHARMACEUTICALS INC	EFFEXOR (VENLAFAXINE HCL) TABLETS
NDA-20151	SUPPL-57	WYETH PHARMACEUTICALS INC	EFFEXOR (VENLAFAXINE HCL) TABLETS
NDA-20699	SUPPL-90	WYETH PHARMACEUTICALS INC	EFFEXOR XR E-R CAPS.(VENLAFAXINE HCL)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

THOMAS P LAUGHREN
01/06/2010