**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-699 / S-067
NDA 20-151 / S-041

Wyeth Pharmaceuticals, Inc.
Attention: Kenneth R. Bonk
Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Bonk:

Please refer to your supplemental new drug applications dated October 25, 2005, received October 26, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor XR (venlafaxine HCl) Extended Release Capsules and Effexor (venlafaxine HCl) Immediate Release.

We acknowledge receipt of your submissions of November 3, 2006, constituting a complete response to our action letter of April 28, 2006.

These "Changes Being Effected" supplemental new drug applications provide for revisions to the package inserts to add the results of a pharmacokinetic study with ketoconazole to the **PRECAUTIONS/Drug Interactions**/*Drugs that Inhibit Cytochrome P450 Isoenzymes* section.

We have completed our review of these applications, as amended, and they are approved effective on the date of this letter for use as recommended in the agreed-upon labeling text (email of November 19, 2007) as follows:

> Ketoconazole: A pharmacokinetic study with ketoconazole 100 mg b.i.d. with a single dose of venlafaxine 50 mg in extensive metabolizers (EM; n = 14) and 25 mg in poor metabolizers (PM; n = 6) of CYP2D6 resulted in higher plasma concentrations of both venlafaxine and O-desmethylvenlafaxine (ODV) in most subjects following administration of ketoconazole. Venlafaxine $C_{max}$ increased by 26% in EM subjects and 48% in PM subjects. $C_{max}$ values for ODV increased by 14% and 29% in EM and PM subjects, respectively.
>
> Venlafaxine AUC increased by 21% in EM subjects and 70% in PM subjects (range in PMs - 2% to 206%), and AUC values for ODV increased by 23% and 33% in EM and PM (range in PMs - 38% to 105%) subjects, respectively. Combined AUCs of venlafaxine and ODV increased on average by approximately 23% in EMs and 53% in PMs, (range in PMs 4% - 134%).
>
> Concomitant use of CYP3A4 inhibitors and venlafaxine may increase levels of venlafaxine and ODV. Therefore, caution is advised if a patient's therapy includes a CYP3A4 inhibitor and venlafaxine concomitantly.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved supplements NDA 20-699 / S-067 and NDA 20-151 / S-041."

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

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 New Drug Evaluation I
Center for Drug Evaluation and Research

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

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/s/
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Thomas Laughren
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