DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-151/S-028/S-030/S-032
NDA 20-699/S-041/S-048/S-052

Wyeth Pharmaceuticals, Inc.
Attention: Kenneth R. Bonk
Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-1245

Dear Mr. Bonk:

We acknowledge receipt of your supplemental new drug applications dated April 30, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor (venlafaxine hydrochloride) Immediate Release Tablets (NDA 20-151/S-032) and Effexor XR (venlafaxine hydrochloride) Extended Release Capsules (NDA 20-699/S-052).

Your April 30, 2004, submission also constituted a complete response to our action letter dated March 19, 2004 for supplemental applications 20-151/S-028/S-030 and 20-699/S-041/S-048.

Reference is also made to a conference call dated April 28, 2004 between representatives of the Agency and yourself to discuss the Agency's class labeling initiatives.

The above supplemental applications provide for the following changes to product labeling:

NDAs 20-151/S-028 & 20-699/S-041

1. Revisions to the **PRECAUTIONS-Usage in Children** section to denote hostility and suicide related adverse events in pediatric clinical trials.
2. The addition of the term "tinnitus" to the **DOSAGE AND ADMINISTRATION-Discontinuing Effexor** or **Effexor XR** sections.
3. Revisions to the Patient Brief Summary.

We note your agreement to our request to remove your proposed addition of hostility and suicide related adverse events from the **PRECAUTIONS-Usage in Children** section. As discussed during that April 28, 2004 meeting, we continue to feel that it would not be helpful to include the language regarding reports of hostility and suicidality that you have proposed for the **Pediatric Use** section. As currently written, the language is uninterpretable, since it notes that there were increased reports, but without noting with reference to what data. If a reference to placebo data were added, this would suggest a causal association, however, this suggestion would be contradicted by the new language that follows. The difficulty, of course, is that it remains unclear at this point exactly what has been captured under the crude terms used to capture events. The currently proposed language for **WARNINGS** is intended to comprehensively address this complex issue and our current understanding of the available data, and we feel it would be confusing and potentially misleading to maintain your proposed language for the **Pediatric Use** section.

NDAs 20-151/S-030 & 20-699/S-048

These applications provide for revisions to the **DOSAGE and ADMINISTRATION/Discontinuing Effexor** or **Effexor XR** sections of product labeling.

Again, we note your agreement to revise product labeling to incorporate the class labeling initiative for all of the selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), to change labeling in regards to discontinuation symptoms and to adverse events occurring in neonates exposed to any of the SSRIs or SNRIs late in the third trimester.

NDAs 20-151/S-032 & 20-699/S-052
These applications provide for antidepressant class labeling revisions to incorporate the following changes to product labeling:

1. The addition of a new subsection under **WARNINGS** entitled **Clinical Worsening and Suicide Risk**.
2. Revisions to the **PRECAUTIONS-Information for Patients** section.
3. Delete the section in **PRECAUTIONS-General** entitled “Suicide”.
4. Add a reference to the **WARNINGS** section at the end of the **PRECAUTIONS- Pediatric Use** section, i.e., (see **WARNINGS-Clinical Worsening and Suicide Risk**).

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 your labeling submitted on April 30, 2004 and as attached to this letter. 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

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 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

Attachment

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

/s/

Thomas Laughren
5/13/04 01:49:01 PM
Signed for Russell Katz, M.D.