



NDA 20-151/S-027
NDA 20-699/S-039/S-050

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

Dear Mr. Bonk:

Please refer to your supplemental new drug applications dated April 16, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor (venlafaxine hydrochloride) Immediate Release Tablets (NDA 20-151) and Effexor XR (venlafaxine hydrochloride) Extended Release Capsules.

We acknowledge receipt of your submissions dated December 9, and December 3, 2003, to the Effexor and Effexor XR applications, 20-151/S-027 and 20-699/S-039, respectively.

These submissions constituted a complete response to our September 16, 2003 action letter.

We additionally acknowledge receipt of your supplemental new drug application dated February 13, 2004 (S-050), submitted for Effexor XR (venlafaxine hydrochloride) Extended Release Capsules.

Supplemental applications 20-151/S-027 and 20-699/S-039 submitted as "Changes Being Effected" supplemental applications, provide for the following revisions to product labeling:

1. The revision of the **PRECAUTIONS-Drug Interactions-Lithium** section to add a cross reference to the section on **CNS-Active Drugs**.
2. The revision of the **PRECAUTIONS-Drug Interactions-CNS-Active Drugs** section to add new language on the potential for serotonin syndrome.
3. The revision of the **ADVERSE REACTIONS-Postmarketing Reports** section to add the terms dyskinesia and rhabdomyolysis.
4. The revision of the **DOSAGE AND ADMINISTRATION-Discontinuing Effexor** section to add the term "seizure" to the list of discontinuation symptoms.

We note that you have incorporated revisions to the **PRECAUTIONS-Drug Interactions-CNS-Active Drugs** and **OVERDOSAGE-Human Experience** sections of labeling as requested in our September 16, 2003 action letter.

Additionally, we note your commitment to provide the Agency with more information for the terms rhabdomyolysis, extrapyramidal symptoms, and tardive dyskinesia as requested in our September 16, 2003 action letter. The other request, contained in our September 16, 2003 letter, pertaining to seizures in the **DOSAGE AND ADMINISTRATION-Discontinuing Effexor** section of labeling was submitted as a separate supplement (20-151/S-030 and 20-699/S-048). These submissions will be addressed in a separate letter.

Supplemental application 20-699/S-050 provides for corrections to vital sign and weight information contained in Effexor XR labeling regarding placebo-controlled studies in Social Anxiety Disorder (SAD).

We have completed the review of your submissions, 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 December 9, 2003, and February 13, 2004, labelings. Accordingly, these applications are approved effective on the date of this letter.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDAs 20-151/S-027 and 20-699/S-039/S-050." Approval of this submission by FDA is not required before the labeling is used.

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., 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

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

/s/

Russell Katz
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