



NDA 20699/S-104

SUPPLEMENT APPROVAL

Pfizer Pharmaceuticals, Inc.
Attention: Mary A. Pias, Regulatory Strategist
445 Eastern Point Road
Groton, CT 06340

Dear Ms. Pias:

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 13, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Effexor XR (venlafaxine hydrochloride) Extended-Release 37.5mg, 75mg, and 150mg Capsules.

We acknowledge receipt of your amendment dated August 29, 2014.

Your August 29, 2014, amendment constituted a complete response to our action letter dated July 16, 2014.

This “Changes Being Effected” supplemental new drug application [REDACTED] (b) (4)
[REDACTED] as requested in our letter dated July 16, 2014.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text. We note that your August 29, 2014, submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the patient package insert, Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

POSTMARKETING REQUIREMENTS UNDER 505(o)

We remind you of the following postmarketing requirement as conveyed in our Agency letter dated July 16, 2014:

2175-1 A single-center, randomized, placebo-controlled and active-controlled thorough QT (TQT) trial of Effexor Extended-Release (venlafaxine hydrochloride) in normal (or healthy) subjects. Please refer to ICH E14 guidance to design the trial and submit the protocol to the agency for comments. The doses studied should ensure the clinical concentration-response relationship for QTc prolongation is characterized, including exploration of higher concentrations than those achieved following the anticipated therapeutic dose. Include the highest tolerable dose in the trial. Because O-desmethylvenlafaxine, the primary metabolite of venlafaxine hydrochloride, has a much longer elimination half-life (11 hours) compared to the parent drug (5 hours), conduct the TQT study at steady state.

The following timetable proposes the schedule by which you will conduct this trial:

Final Protocol Submission: 12/2014

Trial Completion: 06/2015

Final Report Submission: 12/2015

Submit the protocol to your IND 41412, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **“Required Postmarketing Protocol Under 505(o)”**, **“Required Postmarketing Final Report Under 505(o)”**, **“Required Postmarketing Correspondence Under 505(o)”**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

REPORTING REQUIREMENTS

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, call CDR Kofi Ansah, Pharm.D., Senior Regulatory Project Manager, at (301) 796-4158 or email at Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, M.D.
CAPT, USPHS
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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

/s/

MITCHELL V Mathis
10/21/2014