DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 020699/S-110/S-111

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT

Pfizer Inc.
Attention: Beatrice A. Curran, MS
Director, Pfizer Essential Health Global Regulatory Affairs R&D
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Curran:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received June 30, 2017 (NDA 020699/S-110), and December 1, 2017 (NDA 020699/S-111), and your amendment, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Effexor XR (venlafaxine hydrochloride) 37.5 mg, 75mg, and 150 mg extended-release capsules.

We also refer to our letter dated October 12, 2017, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for serotonin and norepinephrine reuptake inhibitor (SNRI) products. This information pertains to the risk of Takotsubo cardiomyopathy.

These supplemental new drug applications provide for the following changes to product labeling:

sNDA 020699/S-110

This Prior Approval supplemental new drug application proposes revisions to the Pharmacodynamics section (12.2) based upon your postmarketing study report.

sNDA 020699/S-111

This "Changes Being Effected" supplemental new drug application provides for revisions to the labeling for Effexor XR consistent with our October 12, 2017 letter.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

We note that your December 8, 2017, 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.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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 package insert, and 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 include 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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated June 30, 2017, containing the final report for the following postmarketing requirement listed in the July 16, 2014, postapproval postmarketing requirement letter.

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 Odesmethylvenlafaxine, 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.

We have reviewed your submission and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our July 16, 2014, letter.

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 Ermias Zerislassie, Safety Regulatory Project Manager, at (301) 796-2770.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, MD
Division Director
Division of Psychiatry
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
12/19/2017