



NDA 021992/S-033/S-036

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING  
REQUIREMENT**

Wyeth Pharmaceuticals, Inc., a subsidiary of Pfizer  
Attention: Maria A. Pias  
Associate Director  
Worldwide Regulatory Strategy, Pfizer  
PO Box 8299  
Philadelphia, PA 19101-8299

Dear Ms. Pias:

Please refer to the following Supplemental New Drug Applications (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pristiq (desvenlafaxine) 50 mg, 100 mg Extended-Release Tablets:

- **S-033**, dated April 16, 2012, received April 17, 2012, a “Prior Approval” supplemental new drug application that proposes to add data in support of a new indication in adults for desvenlafaxine SR for the maintenance treatment of Major Depressive Disorder (MDD) and
- **S-036**, dated November 12, 2012 and received November 13, 2012, a “Changes Being Affected” supplemental new drug application that provides safety data updates to *Section 6 Adverse Reactions*.

We acknowledge receipt of your amendments dated:

May 31, 2012	October 16, 2012	January 25, 2013
June 22, 2012	November 5, 2012	February 8, 2013
July 12, 2012	November 21, 2012	February 14, 2013
September 7, 2012	December 18, 2012	

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 April 17, 2012 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 (package insert and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (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).

## **FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)**

We have received your submission dated April 16, 2012, containing the final report for the following postmarketing requirement listed in the February 29, 2008 approval letter.

**1229-3** Although your NDA for desvenlafaxine succinate demonstrates effectiveness of recommended doses (50-100 mg/day) as a treatment for Major Depressive Disorder over an interval of 8 weeks, it does not provide information about the duration and conditions of treatment with desvenlafaxine that are necessary to sustain its antidepressant effects over the full duration (likely 6 months to a year or longer) of an acute major depressive episode at these same recommended doses. While it is widely assumed that continued treatment of symptomatically remitted patients reduces their risk of relapse, [...] we have no evidence that desvenlafaxine at these lower doses has efficacy after 8 weeks. Once you have established the lower end of the dose-response curve for efficacy, you have agreed to conduct and submit the results of a randomized withdrawal study to address longer-term efficacy for your drug at appropriate doses. If the lower dose study establishes that 50 mg/day is the lowest effective dose, this study will evaluate doses of 50 and 100 mg/day. You have agreed to submit the results of

this trial no later than 3 years after the date of initiation, or approximately 5.5 years from the date of approval for this NDA.

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

We remind you that there are postmarketing commitments listed in the February 29, 2008 approval letter that are still open.

### **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.

We acknowledge your submission, dated January 24, 2013, proposing to waive the pediatric study requirement for ages 0 to 6 years and defer the studies for the 7 to 17 years.

We are waiving the pediatric study requirement for ages 0 to 6 years because necessary studies are impossible or highly impracticable. MDD cannot be reliably diagnosed in this age group.

We are deferring submission of your pediatric studies for the maintenance treatment of MDD for ages 7-17 years (children and adolescents) until the data for PMC 1229-1 is received and reviewed. Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of this/these postmarketing studies must be reported annually according to 21 CFR 314.81(FOR NDAs)/21 CFR 601.70(FOR BLAs) and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. Until PMC 1229-1 is fulfilled, the deferred pediatric study will need to meet the following deadlines:

- Deferred pediatric study under PREA for the maintenance treatment of Major Depressive Disorder (MDD) in subjects age 7 to 17 years

Protocol Submission Date: June 30, 2018

Study Completion Date: December 31, 2024

Final Report Submission: June 25, 2025

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated “**Required Pediatric Study Commitments**”.

## **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **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, email Juliette Touré, PharmD, Senior Regulatory Project Manager, at [Juliette.Toure@fda.hhs.gov](mailto:Juliette.Toure@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

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

ENCLOSURE:  
Content of Labeling

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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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MITCHELL V Mathis  
02/14/2013