



NDA 21520/S-039/S-037
NDA 18936/S-101/S-100
NDA 20592/S-063
NDA 21086/S-041
NDA 21235/S-021

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Ashraff Rampersaud, M.S. PMP
Manager, Global Regulatory Affairs – US
Lilly Corporate Center
Drop Code 2543
Indianapolis, IN 46285

Dear Mr Rampersaud:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received September 28, 2012 (NDA 21520/S-039, NDA 18936/S-101, NDA 20592/S-063), dated and received October 9, 2012 (NDA 21086 S-041), and dated and received April 25, 2012 (NDA 21520/S037, NDA 18936/S-100, NDA 21235/S-021), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Symbyax (olanzapine and fluoxetine hydrochloride) (NDA 21520) 3mg/25mg, 6mg/25mg, 6mg/50mg, 12mg/25mg, 12mg/50mg Capsules, Prozac (fluoxetine hydrochloride) (NDA 18936) 10mg, 20mg, 40mg Pulvules, Prozac (fluoxetine hydrochloride) (NDA 21253) 90mg Delayed Release Capsules, Zyprexa (olanzapine) (NDA 20592) 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg Tablets, Zyprexa Zydys (olanzapine) (NDA 21086) 5mg, 10mg, 15mg, 20mg Orally Disintegrating Tablets.

These “Prior Approval” supplemental new drug applications provide for

NDA 21520/S-039, NDA 18936/S-101, NDA 20592/S-063, NDA 21086/S-041 –

When using olanzapine and fluoxetine in combination, the indication of treatment of depressive episodes associated with bipolar I disorder in patients 10-17 years of age.

NDA 21520/S-037, NDA 18936/S-100, NDA 21235/S-021 –

Additions to the Warnings and Precautions and Overdosage sections to include information on QT prolongation.

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

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, 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).

FULFILLMENT OF POSTMARKETING COMMITMENT

Your submission of September 28, 2012 (NDA 21520/S-039) contained the final report for the following postmarketing commitment listed in the April 9, 2007 approval letter.

320-1 Pediatric safety and efficacy study under PREA for the treatment of major depressive episodes associated with bipolar disorder in pediatric patients ages 10 to 17.

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

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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, call Keith Kiedrow, Pharm.D., RAC, Senior Regulatory Project Manager, at (301) 796-1924.

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

ENCLOSURES: Content of Labeling, Medication Guide

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
07/26/2013