



NDA 21520/S-041
NDA 18936/S-102

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
COMMITMENT**

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 December 13, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Symbyax (olanzapine and fluoxetine) (NDA 21520) 3mg/25mg, 6mg/25mg, 6mg/50mg, 12mg/25mg, 12mg/50mg Capsules and Prozac (fluoxetine) (NDA 18936) 10mg, 20mg, 40mg Pulvules.

We acknowledge receipt of your amendments dated February 7, 2014, February 10, 2014, March 12, 2014, August 1, 2014, and October 3, 2014.

These “Prior Approval” supplemental new drug applications provide for additions to labeling describing results from study H6P-MC-HDAY, which was undertaken in response to a postmarketing commitment issued in the approval letter of March 19, 2009 (NDA 21520/S-012).

66-1 Since TRD is a chronic illness, you are required to assess the longer-term effectiveness and safety of Symbyax in TRD. You have agreed to submit the results of this trial during the first quarter of 2015.

**APPROVAL, LABELING, & FULFILLMENT OF POSTMARKETING
COMMITMENT**

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 have also concluded that the above commitment was fulfilled. This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our March 19, 2009, letter.

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, text for the 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).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 21520/S-041.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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.

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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. 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).

NDA 21520/S-041

NDA 18936/S-102

Page 4

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

Division of Psychiatry Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling

Carton and Container 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
10/10/2014