



NDA 21427/S-040/S-041

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Isabelle Murray, M.Sc.
Manager, Global Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms. Murray:

Please refer to your Supplemental New Drug Applications (sNDAs) dated April 3, 2012 (S-040) and April 19, 2012 (S-041), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Cymbalta (duloxetine hydrochloride) 20 mg, 30 mg, and 60 mg Capsules.

We acknowledge receipt of your amendments to S-040 dated:

- (1) August 2, 2012 (3) September 20, 2012
- (2) August 31, 2012

We also acknowledge receipt of your amendments to S-041 dated:

- (1) May 9, 2012 (5) August 30, 2012
- (2) May 10, 2012 (6) September 12, 2012
- (3) June 12, 2012 (7) September 27, 2012
- (4) August 13, 2012 (8) October 10, 2012

The “Prior Approval” supplemental new drug application, S-040, provides for class labeling language regarding the risk of serotonin syndrome associated with the use of linezolid and methylene blue. The “Prior Approval” supplemental new drug application, S-041, provides a response to the pediatric Written Request issued on June 23, 2006, and subsequently amended on September 22, 2009 and November 2, 2009. Additionally, S-041 provides a response to the Agency’s required study, under the Pediatric Research Equity Act, in pediatric patients to assess the safety and effectiveness of Cymbalta as a treatment for Major Depressive Disorder in patients ages 7 to 17.

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.

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 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 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)

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 note that you have fulfilled the following pediatric study requirement listed in the August 3, 2004 approval letter:

- | | |
|--------|---|
| 1454-1 | You are required to assess the safety and effectiveness of Cymbalta as a treatment for Major Depressive Disorder in pediatric patients ages 7 to 17 (children and adolescents). |
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We remind you that there are postmarketing requirements that are still open.

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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Hiren Patel, Regulatory Project Manager, at (301) 796-2087.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
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/

THOMAS P LAUGHREN
10/18/2012