



NDA 022173 S-023

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 Application (sNDA) dated and received February 25, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zyprexa Relprevv (olanzapine) For Extended Release Injectable Suspension, 210 mg, 300 mg, and 405 mg vials.

We acknowledge receipt of your amendments dated March 14, 2014, April 3, 2014, August 25, 2014, and September 19, 2014.

This “Prior Approval” supplemental new drug application provides for modifications to the Zyprexa Relprevv (olanzapine) risk evaluation and mitigation strategy (REMS), to update various appended REMS materials.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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, REMS), 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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Zyprexa Relprevv (olanzapine) was originally approved on December 11, 2009, and the last REMS modification was approved on March 27, 2013. The REMS consists of a Medication Guide, communication plan, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of:

1. Revisions to the Instructions to Reconstitute and Administer Zyprexa Relprevv Poster to include updates to name and patent, latex-free statements, graphics, address combinations, the removal of the term “non-pyrogenic”, and the addition of a cautionary statement on single use medical devices.
2. Changes in hours of operation for Patient Care Program Call Center
3. Removal of references/links on the Zyprexa Relprevv REMS website to Spanish Translations of the United States Prescribing Information (USPI) and Medication Guide
4. Addition of language to the Zyprexa Relprevv Patient Care Program Instructions Brochure, Pharmacy Registration Form, and Buy & Bill Pharmacy Service Provider Registration Form to reinforce the requirement that dispensers report the date Zyprexa Relprevv is dispensed prior to the Convenience Kit leaving the premises.
5. Revisions to the Zyprexa Relprevv Patient Care Program Instructions Brochure, Pharmacy Registration Form and Buy & Bill Pharmacy Service Provider Registration Form, changing the term “vial kit” to “Convenience Kit” to provide consistency in terminology throughout the REMS and REMS appended materials.

The timetable for submission of assessments of the REMS will remain the same as that approved on July 8, 2010. There are no changes to the REMS assessment plan described in our March 25, 2014 letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 022173 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT
METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**NDA 022173 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022173
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022173
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling
Medication Guide
REMS
REMS Program Materials

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
10/30/2014