DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20592/S-067
NDA 21086/S-043
NDA 21253/S-056
NDA 22173/S-025
NDA 21520/S-046

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Anindita Sen, Ph.D.
Director, Global Regulatory Affairs - US
Lilly Corporate Center
Drop Code 2543
Indianapolis, IN 46285

Dear Dr. Sen:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received June 9, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zyprexa (olanzapine) (NDA 20592) 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg Tablets, Zyprexa Zydis (olanzapine) (NDA 21086) 5mg, 10mg, 15mg, 20mg Orally Disintegrating Tablets, Zyprexa Intramuscular (olanzapine) (NDA 21253) 10mg Vials, Zyprexa Relprevv (olanzapine) (NDA 22173) For Extended Release Injectable Suspension 210mg, 300mg, 305mg Vials, Symbyax (olanzapine and fluoxetine hydrochloride) (NDA 21520) 3mg/25mg, 6mg/25mg, 6mg/50mg, 12mg/25mg, 12mg/50mg Capsules.

We also refer to our letter dated May 10, 2016, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Zyprexa, Zyprexa Zydis, Zyprexa Intramuscular, Zyprexa Relprevv, and Symbyax. This information pertains to an association between olanzapine and drug reactions with eosinophilia and systemic symptoms (DRESS).

These supplemental new drug applications provide for revisions to the labeling for Zyprexa, Zyprexa Zydis, Zyprexa Intramuscular, Zyprexa Relprevv, and Symbyax, consistent with our May 10, 2016 letter.

APPROVAL & LABELING

We have completed our review of this supplemental application. 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), 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 include 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).

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, PharmD, MS, RAC, Senior Regulatory Project Manager, at (301) 796-1924.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
Content of Labeling
REMS (for NDA 22173)

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
10/06/2016