DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020592/S-068/S-069
NDA 021086/S-044/S-045
NDA 021253/S-057/S-058
NDA 022173/S-026/S-028

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 (sNDA) dated October 31, 2016 (NDAs 020592/S-068, 021086/S-044, 021253/S-057, 022173/S-026), and January 20, 2017, (NDAs 020592/S-069, 021086/S-045, 021253/S-058, 022173/S-026), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zyprexa (olanzapine) 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg Tablets (NDA 020592), Zyprexa Zydis (olanzapine) 5mg, 10mg, 15mg, 20mg Orally Disintegrating Tablets (NDA 021086), Zyprexa Intramuscular (olanzapine) 10mg Vials, Powder, for Solution for Intramuscular use (NDA 021253), Zyprexa Relprevv (olanzapine) for Extended Release Injectable Suspension 210mg, 300mg, 405mg Vials (NDA 022173).

We also refer to our letter dated November 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 conventional and atypical antipsychotics. This information pertains to the risk of falls especially for patients with diseases, conditions, or medications that could exacerbate these effects.

These supplemental new drug applications provide for the following revisions to labeling:

- sNDA 020592/S-068, 021086/S-044, 021253/S-057, 022173/S-026: the addition of restless leg syndrome to the Adverse Reactions-Postmarketing Experience section (6.4).
- sNDA 020592/S-069, 021086/S-045, 021253/S-058, 022173/S-028: revisions to the labeling for Zyprexa, Zyprexa Zydis, Zyprexa Intramuscular, and Zyprexa Relprevv consistent with our November 10, 2016 safety labeling change notification letter.

APPROVAL & LABELING

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.

We note that your January 20, 2017, submission includes final printed labeling (FPL) for your package insert. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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 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).

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.

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, Team Leader, Senior Regulatory Project Manager, at 301-796-1924 or Keith.kiedrow@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE:
Contents 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/

MITCHELL V Mathis
02/23/2017