DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-592 / S-051
NDA 21-086 / S-030
NDA 21-253 / S-036

Eli Lilly and Company
Attention: Gregory T. Brophy, Ph.D.
Director, US Regulatory Affairs
Lilly Corporate Center
Indianapolis, Indiana 46285

Dear Dr. Brophy:

Please refer to your supplemental new drug applications dated and received on August 3, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ZYPREXA (olanzapine) Tablets, 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, and 20 mg, ZYPREXA ZYDIS (olanzapine) Orally Disintegrating Tablets 5 mg, 10 mg, 15 mg, and 20 mg, and ZYPREXA (olanzapine) IM Injection, 10 mg/vial.

Reference is also made to our letter dated April 5, 2009, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for the entire class of antipsychotic drugs. This information pertains to the risk of leukopenia, neutropenia, and agranulocytosis. The decision to require safety labeling changes was based on new safety information about this risk identified since these products were approved. You were directed to submit a prior approval supplement proposing changes to the approved labeling in accordance with the above direction, or notify FDA that you do not believe a labeling change is warranted, and submit a statement detailing the reasons why such a change is not warranted.

On May 5, 2009, FDA received your notification detailing the reasons why you believe a labeling change to address the risk of agranulocytosis is not warranted and your proposed labeling changes to address the risk of leukopenia and neutropenia. Our review of this and subsequent submissions found that your proposed labeling changes did not adequately address the new safety information regarding the risk of leukopenia, neutropenia, and agranulocytosis with the use of antipsychotic drugs, including Zyprexa (olanzapine). On July 19, 2009, we issued a letter ordering you, under the authority of Section 505(o)(4)(E) of the FDCA, to make specific changes in the HIGHLIGHTS OF PRESCRIBING INFORMATION and the WARNINGS AND PRECAUTIONS sections of labeling, pertaining to the risk of leukopenia, neutropenia, and agranulocytosis.

Your supplemental new drug applications provide for revisions to the HIGHLIGHTS OF PRESCRIBING INFORMATION and the WARNINGS AND PRECAUTIONS sections of labeling, to add information pertaining to the risks of leukopenia, neutropenia, and agranulocytosis, consistent with our July 19, 2009 Safety Label Change Order letter.

We have completed our review of these supplemental applications. These applications are approved, effective on the date of this letter, and the package insert has been revised accordingly (see enclosed package insert).

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, **"SPL for approved supplement NDA 20-592 / S-051, NDA 21-086 / S-030, and NDA 21-253 / S-036."**

In addition, within 21 days of the date of this letter, amend any pending applications for these NDAs with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Failure to make these changes within the specified period of time could make your products misbranded under 21 USC 321(n) and 352(a).

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

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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, please contact Doris J. Bates, Ph.D., Safety Regulatory Project Manager, at (301)796-2260.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert 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
08/31/2009