DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-592 / S-029
NDA 21-086 / S-011
NDA 21-253 / S-006

Eli Lilly and Company
Attention: Robin Wojcieszek, R.Ph.
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms. Wojcieszek:

Please refer to your supplemental new drug applications dated September 7, 2004, received September 8, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the Zyprexa (olanzapine) products [Zyprexa Tablets, Zyprexa Zydis Tablets, Zyprexa IntraMuscular Injection].

We acknowledge receipt of your submissions dated September 10, 2004 and August 18, 2005.

These "Changes Being Effected" supplemental new drug applications provide for labeling changes under **PRECAUTIONS**, **General**, Hemodynamic Effects as follows (additions/deletions highlighted):

> For intramuscular olanzapine for injection therapy, patients should remain recumbent if drowsy or dizzy after injection until examination has indicated that they are not experiencing postural hypotension, ~~and/or~~ bradycardia, and/or hypoventilation.
>
> Olanzapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) where the occurrence of syncope, or hypotension and/or bradycardia might put the patient at increased medical risk.
>
> Caution is necessary in patients who receive treatment with other drugs having effects that can induce hypotension, bradycardia, respiratory or central nervous system depression (*see* Drug Interactions). Concomitant administration of intramuscular olanzapine and parenteral benzodiazepine has not been studied and is therefore not recommended. If use of intramuscular olanzapine in combination with parenteral benzodiazepines is considered, careful evaluation of clinical status for excessive sedation and cardiorespiratory depression is recommended.

We have completed our review of these supplemental new drug applications and they are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on September 7, 2004 (attached).

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, email LCDR Keith Kiedrow, Pharm.D., Regulatory Project Manager, at Keith.Kiedrow@HHS.FDA.GOV.

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren
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