

**OLANZAPINE  
LY170053**

- CLASS:**
  - Antipsychotic
- MODE OF ACTION:**
  - 5HT<sub>2</sub> and D<sub>2</sub>/D<sub>1</sub> receptor antagonist
- INDICATION:**
  - Treatment of schizophrenia and other psychosis where delusions, hallucinations, and thought disorders are prominent symptoms.
- ROUTE OF ADMINISTRATION:**
  - Oral and parenteral
- DOSAGE:**
  - Once daily
- PRODUCT FEATURES:**
  - Low potential for acute extrapyramidal side effects (EPS) and tardive dyskinesia in animal models
  - Produces transient elevations of liver enzymes in some patients
  - Open-label data demonstrates improvements in positive, negative, and general psychopathological symptoms, without emergence of extrapyramidal symptoms or other serious adverse events
- PATENT STATUS:**
  - In December 1992, a new patent was approved in the U.S., extending patent life to 2010. New patents are pending in 25 countries, including major Europe and Japan. Expectations for approval are high in Europe and moderate in Japan.
- CLINICAL STATUS:**
  - Phase II studies:
    - compared to haloperidol
    - U.S. (>260 patients randomized) enrollment underway
    - Europe (>380 patients randomized) enrollment underway
    - Japanese open-label early Phase II completed (79 patients)
  - Phase III to begin June 1, 1993
    - U.S./Europe

GRH:bw  
5/3/93

**OLANZAPINE**  
LY170053 (Cont'd)

**CRITICAL SUCCESS  
FACTORS FOR  
PRODUCT DECISION:**

- Efficacy with respect to positive symptoms
  - decrease in BPRS > placebo
  - percent responders  $\geq$  haloperidol
- Efficacy with respect to negative symptoms
  - decrease in PANS subscale and SANS statistically significant relative to baseline and > haloperidol
- Safety
  - incidence of tardive dyskinesia < haloperidol
  - No hematological monitoring requirements
  - elevations of liver enzymes transient and non-progressive
  - no "black box" hepatic monitoring requirement

**ISSUES:**

- Numerous competitors in development so speed to market is critical.
- Formulations needed: oral solid, reconstitutable powder (to use as liquid), and granules for Japan. Depot formulation as line extension.

**TIMING:**

- IND filing: July 24, 1986
- Product decision: 5/6/93
- NDA submission: 4Q95
- NDA approval: 1Q97 (U.S. & Europe)  
2Q98 (Japan)

GRH:bw  
5/3/93



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

~~FBI~~ OCT 03 1995

NDA 20-592

Food and Drug Administration  
Rockville MD 20857

JR

SEP 29 1995

Lilly Research Laboratories  
Attention: Timothy R. Franson, M.D.  
Lilly Corporate Center  
Indianapolis, Indiana 46285

Dear Dr. Franson:

We have received your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Zyprex™ (olanzapine) 2.5 mg, 5.0 mg, 7.5 mg and 10 mg Tablets
Therapeutic Classification:	Standard
Date of Application:	September 21, 1995
Date of Receipt:	September 22, 1995
Our Reference Number:	20-592

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on November 21, 1995, in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations and in accordance with the policy described in the Center for Drug Evaluation and Research Staff Manual Guide CDER 4820.6, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Please request the meeting at least 15 days in advance. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact Steve Hardeman, R.Ph., Regulatory Management Officer, at (301) 594-2777.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

*For*

John S. Purvis  
Chief, Project Management Staff  
Division of Neuropharmacological  
Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ZY 150 624

OCT 9 1995