



## **FDA Advisory Committee Supports Efficacy and Safety of Zyprexa(R) Long-Acting Injection (LAI) for Schizophrenia Treatment**

INDIANAPOLIS, Feb 06, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- The U.S. Food and Drug Administration's (FDA) Psychopharmacologic Drugs Advisory Committee voted that, with appropriate labeling around excessive sedation events, Zyprexa(R) long-acting injection (olanzapine LAI) has been shown to be effective and acceptably safe for the treatment and maintenance treatment of schizophrenia in adults, Eli Lilly and Company (NYSE: LLY) announced today.

Zyprexa LAI is an investigational formulation that combines the atypical antipsychotic medication Zyprexa (olanzapine) with a pamoate salt, resulting in an extended delivery of up to four weeks.

"A primary barrier to the successful treatment of schizophrenia, a chronic and devastating illness, is that patients often relapse because they have trouble taking their medication on a regular basis," said Dr. John Kane, chairman, Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, N.Y. "Long-acting injectable antipsychotics can help patients derive more consistent benefits from their medications."

John Hayes, M.D., vice president of Lilly Research Laboratories, said, "Due to the chronic and severe nature of the illness and the limited number of approved long-acting formulations, we believe that, if approved, Zyprexa LAI could be an important treatment option for this patient population, who struggle with taking their medication. We are pleased with the committee's recommendation and will continue to work with the FDA in its review of our application."

The committee reviewed data from a comprehensive clinical program comprising eight studies. Results from the clinical trials showed greater symptom improvement in Zyprexa LAI-treated patients, compared with those on placebo. Due to the nature of the formulation of Zyprexa LAI, supplementation with oral antipsychotics was not needed to achieve or maintain effect in these studies.

In clinical trials, Zyprexa LAI had a safety profile similar to oral olanzapine, with the exception of post-injection excessive sedation events, which also include dizziness, confusion and altered speech. These events were seen in 0.07 percent of injections and 1.2 percent of patients, all of whom recovered fully.

To help minimize the risks associated with these excessive sedation events, Lilly included a proposed plan to manage those risks as part of its submission to the FDA. The committee also discussed the need for appropriate labeling to address the risks associated with excessive sedation events.

FDA reviewers will consider the panel's favorable recommendation in its review of the New Drug Application (NDA) that Lilly submitted for Zyprexa LAI. The FDA is not bound by its advisory committees' recommendations, but takes their advice into consideration when reviewing investigational drugs seeking approval.

### **About Long-acting Injectable Antipsychotic Medications**

Long-acting antipsychotics have been associated with improved treatment adherence and reduced treatment failures(i). By administering long-acting medications, healthcare professionals know when patients have received their medication and can immediately detect non-adherence when a patient fails to return for a scheduled injection(ii). Different from both oral and injected short-acting formulations, long-acting antipsychotics allow for stable concentrations of the active drug to remain at a therapeutic range for an extended period of time(iii).

### **About Schizophrenia**

Schizophrenia is a severe and debilitating illness often characterized by acute psychotic episodes including delusions (false beliefs that cannot be corrected by reason), hallucinations (usually in the form of non-existent voices or visions) and long-term impairments such as diminished emotion, lack of interest and depressive symptoms, such as hopelessness and suicidal thoughts. In addition to these symptoms, patients with schizophrenia are at greater risk for medical comorbidities than the general population.

### **About Oral Zyprexa**

Zyprexa is indicated in the United States for the short- and long-term treatment of schizophrenia, acute mixed and manic episodes of bipolar disorder, and maintenance treatment of bipolar disorder. Since Zyprexa was introduced in 1996, it has been prescribed to approximately 22 million people worldwide. Zyprexa is not approved for patients under 18 years of age.

Zyprexa is not approved for the treatment of patients with  
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dementia-related psychosis. Elderly patients with dementia-related  
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psychosis treated -- with atypical antipsychotic drugs are at an increased  
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risk of death compared -- with those patients taking a placebo.  
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In addition, compared to elderly patients with dementia-related psychosis taking a placebo, there was a significantly higher incidence of cerebrovascular adverse events in elderly patients with dementia-related psychosis treated with Zyprexa.

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including Zyprexa.

While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics. Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus, or who have borderline increased blood glucose level. Patients taking olanzapine should be monitored regularly for worsening of glucose control. Persons with risk factors for diabetes who are starting on atypical antipsychotics should undergo baseline and periodic fasting blood glucose testing. Patients who develop symptoms of hyperglycemia during treatment should undergo fasting blood glucose testing.

Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using olanzapine, is advised. Significant, and sometimes very high, elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight.

As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with Zyprexa. If signs and symptoms appear, immediate discontinuation is recommended. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

Also, as with all antipsychotic treatment, prescribing should be consistent with the need to minimize Tardive Dyskinesia (TD). The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

The most common treatment-emergent adverse event associated with Zyprexa in placebo-controlled, short-term schizophrenia and bipolar mania trials was somnolence. Other common events were dizziness, weight gain, personality disorder (COSTART term for nonaggressive objectionable behavior), constipation, akathisia, postural hypotension, dry mouth, asthenia, dyspepsia, increased appetite and tremor.

Full prescribing information, including a boxed warning, is available at [www.zyprexa.com](http://www.zyprexa.com).

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at [www.lilly.com](http://www.lilly.com).

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This press release contains forward-looking statements about the safety and efficacy of ZYPREXA Long Acting Injection (LAI) and reflects Lilly's current beliefs. However, as with any investigational pharmaceutical product, there are substantial risks and uncertainties in the process of research, development, regulatory milestones and commercialization. There is no guarantee that ZYPREXA LAI will be approved for the treatment of schizophrenia or that if approved, it will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

- (i) Maxine X. Patel and Anthony S. David. Why aren't depot antipsychotics prescribed more often and what can be done about it? *Advances in Psychiatric Treatment* (2005) 11: 203-211.
- (ii) Kane J.M et al. Guidelines for depot antipsychotic treatment in schizophrenia. *European Neuropsychopharmacology*, Volume 8, Number 1, 1 February 1998, pp. 55-66(12). p. 58.
- (iii) Maxine X. Patel and Anthony S. David. Why aren't depot antipsychotics prescribed more often and what can be done about it? *Advances in Psychiatric Treatment* (2005) 11: 203-211.

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