



FDA Advisory Committee Votes in Favor of Zyprexa for Two Adolescent Indications

ADELPHI, Md., June 10, 2009 /PRNewswire via COMTEX News Network/ -- ADELPHI, Md., June 10 /PRNewswire-FirstCall/ -- The U.S. Food and Drug Administration (FDA) Psychopharmacologic Drugs Advisory Committee (PDAC) voted that Zyprexa(R) (olanzapine), an atypical antipsychotic, is effective and acceptably safe for the acute treatment of schizophrenia or manic or mixed episodes associated with bipolar I disorder in adolescents aged 13-17 years old. The panel supported the FDA and Lilly's position that if Zyprexa is approved for the two indications, prescribers should consider other treatment options first for adolescent patients.

"This Committee of experts spent two days discussing the science of a difficult topic being debated in media, doctors' offices and living rooms across the country," said John Hayes, M.D., vice president of Lilly Research Laboratories. "Today's Committee vote is an important step toward providing help and hope to the many teens suffering from severe mental illness."

FDA will consider the panel's recommendations in its review of the supplemental New Drug Applications that Lilly submitted for Zyprexa. The FDA takes the advice of its Advisory Committees into consideration when deciding whether to approve new indications, but is not bound by their recommendations.

For the proposed schizophrenia indication, the panel voted 11-5, with two abstentions, that Zyprexa's effectiveness had been demonstrated, and voted 10-4, with four abstentions, that these data demonstrated acceptable safety. For the proposed indication for manic or mixed episodes associated with bipolar I disorder, the panel voted 17-0, with one abstention, that Zyprexa's effectiveness had been demonstrated, and voted 11-4, with three abstentions, that these data demonstrated acceptable safety.

The Committee examined findings from two pivotal clinical trials of Zyprexa in adolescents with schizophrenia or bipolar I disorder, including a six-week double-blind, placebo-controlled trial to assess the efficacy and safety of Zyprexa in 72 adolescents (aged 13-17 years old) with schizophrenia; and a three-week, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of Zyprexa in 107 adolescents (aged 13-17 years) with acute manic or mixed episodes associated with bipolar I disorder.

In these studies, adolescents taking Zyprexa experienced significant improvements in their schizophrenia and bipolar symptoms on various efficacy measures. Symptoms of schizophrenia include acute episodes of delusions, hallucinations and long-term impairments such as diminished emotion, lack of interest and depressive signs and symptoms(1). Manic symptoms of bipolar I disorder include long periods of euphoria, restlessness, behaving impulsively and being easily distracted(2). A mixed bipolar state occurs when symptoms of depression and mania are experienced at the same time(3).

In addition to the two placebo-controlled studies, the Committee reviewed extensive Zyprexa safety data relevant to adolescents. Increased weight, appetite, and sedation were among the most common adverse events observed in adolescents. Weight gain was greatest in adolescents who were overweight or obese when they began treatment. Significant weight gain was also observed in patients who were of normal weight at baseline.

Although no clinical trials comparing adolescents to adults were conducted, data from the adolescent trials were compared to those from the adult trials. The types of adverse events observed in adolescents treated with Zyprexa were similar to those seen in adults. The incidence and magnitude of changes in weight, prolactin, triglyceride, cholesterol and hepatic enzyme levels were greater in adolescents than adults. Sedation was also more common in adolescents than adults.

"Because weight gain and some of the metabolic changes are more likely to occur and to be more pronounced in adolescents compared to adults, we agreed with the FDA that in many cases other available treatment options should be considered before Zyprexa when treating adolescents," said Dr. Hayes.

About Schizophrenia in Adolescents

Schizophrenia affects about 1 percent of Americans(4). A substantial portion of first psychotic breaks for schizophrenia occur in adolescence. It has been estimated that 39 percent of males and 23 percent of females with schizophrenia experience onset of the disease before the age of 19(5). Studies have suggested that early-onset schizophrenia is associated with worse long-term outcomes compared to onset of illness in adulthood(6).

About Bipolar Disorder in Adolescents

Bipolar disorder affects approximately 5.7 million American adults, or about 2.6 percent of the U.S. population age 18 and older in a given year(7). It has an estimated prevalence of 0.1 percent to 2 percent among adolescents(8). Lifetime prevalence of bipolar I disorder in community samples has varied from 0.4 percent to 1.6 percent(9). It has been estimated that 20 percent of all patients with bipolar disorder experience their first manic episode during adolescence, with the peak age of onset for this group of patients occurring between 15 and 19 years of age(10). Early onset of bipolar disorder is associated with greater severity of illness and more functional impairment(11).

Safety information for Oral Zyprexa (olanzapine)

Zyprexa is indicated in adults in the United States for the acute and maintenance treatment of schizophrenia, acute mixed and manic episodes of bipolar I disorder, and maintenance treatment of bipolar I disorder.

Zyprexa is not approved for the treatment of patients with dementia-related psychosis. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

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.

The possibility of a suicide attempt is inherent in schizophrenia and bipolar I disorder. Close supervision of high-risk patient should accompany drug therapy.

As with all antipsychotic medications, a rare and potentially fatal condition known as Neuroleptic Malignant Syndrome (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.

Hyperglycemia, in some cases associated with ketoacidosis, 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 Zyprexa appears to have a greater association than some other atypical antipsychotics. Physicians should consider the risks and benefits when prescribing Zyprexa to patients with an established diagnosis of diabetes mellitus, or having borderline increased blood glucose level. Patients taking Zyprexa should be monitored regularly for worsening of glucose control. Patients starting treatment with Zyprexa should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment should undergo fasting blood glucose testing.

Undesirable alterations in lipids have been observed with Zyprexa use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using Zyprexa, is advised. Clinically significant, and sometimes very high, elevations in triglyceride levels and modest mean elevations in total cholesterol have been observed with Zyprexa use.

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

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.

Zyprexa may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia, and in some patients, syncope, especially during the initial dose-titration period. Particular caution should be used in patients with known cardiovascular disease, cerebrovascular diseases, or those predisposed to hypotension.

Other potentially serious adverse events include seizures, elevated prolactin levels, cognitive and motor impairment, body temperature elevation, and trouble swallowing.

The most common treatment-emergent adverse event associated with Zyprexa use in adults 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 boxed warning, is available at www.zyprexa.com.

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of 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.

Zyprexa(R) (olanzapine, Lilly)

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This press release contains forward-looking statements about Zyprexa. These statements reflect management's current beliefs; however, as with any pharmaceutical product there are risks and uncertainties in the process of research and development, regulatory review, and commercialization. There is no guarantee that Zyprexa will be approved for the acute treatment of schizophrenia or manic or mixed episodes associated with bipolar I disorder in adolescents, or that, if approved, it will 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.

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