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Study Demonstrated Long-Term Treatment with Zyprexa® Reduced Violent Behavior in People with Schizophrenia Compared to Risperidone

INDIANAPOLIS, Dec 14, 2004 /PRNewswire-FirstCall via COMTEX/ -- Long-term treatment with Zyprexa® (olanzapine) significantly lowered risk of violent behavior in people with schizophrenia versus risperidone (Risperdal®, Janssen), according to a study published in the December issue of the Journal of Clinical Psychiatry. The three-year naturalistic or "real world" study, the Schizophrenia Care and Assessment Program (SCAP), also showed that improved medication adherence was an important element that contributed to the reduced violence risk in patients treated with Zyprexa.

"Violent behavior, even in a small proportion of people with schizophrenia, can stigmatize all those with the disease, preventing acceptance of people with psychiatric disabilities in society, disrupting continuity of care, and limiting the effectiveness of community-based mental health services," said Jeff Swanson, Ph.D., associate professor of Psychiatry and Behavioral Sciences at Duke University Medical Center and SCAP investigator.

Unlike a traditional clinical trial, SCAP is a longitudinal observational study designed to understand the treatment provided to schizophrenia patients in community care settings. SCAP is one of the largest naturalistic studies ever conducted in the United States, consisting of 2,400 patients treated at centers across the country. SCAP investigators from Duke University Medical Center studied violent behavior in a smaller group of patients in North Carolina, one of the six states where SCAP was carried out.

Key Findings

In this non-randomized prospective study, 124 adults with schizophrenia- spectrum disorders receiving services in public-sector mental health systems in North Carolina were followed for three years. Rates of violence among people who were initiated on Zyprexa (N=59) were compared with people who were initiated on risperidone (N=65) at six-month intervals.

-- Remaining on Zyprexa for one year or more significantly lowered the risk of violent behavior

- No significant change in violence risk was found for subjects remaining on risperidone for one year or more

-- More violence-prone patients were initially switched to Zyprexa

-- The reduction in violent behavior associated with Zyprexa treatment was attributed to higher rates of medication adherence

Given the observational design of this study and the absence of random assignment to treatment conditions, it is possible that selection bias could affect these results. A patient was classified as a Zyprexa patient if he or she was prescribed Zyprexa for more than half of each six-month period during the study. Likewise a patient was classified as a risperidone patient if he or she was prescribed risperidone for more than half of each six-month period during the study.

"Data such as these can be important to healthcare professionals treating patients in community settings where nonadherence and substance abuse often further compound the risk of violent behavior," said Marvin Swartz, M.D., professor and head of the Division of Social and Community Psychiatry at Duke University Medical Center, and SCAP investigator.

Study Design

All study participants had been diagnosed with schizophrenia-spectrum disorders. The SCAP research design is naturalistic and observational; therefore, no experimental intervention or interference with usual patterns of treatment took place. Violent behavior was measured using the MacArthur Community Violence Interview, review of outpatient and inpatient medical records,

and review of arrest records for violent offenses documented in the North Carolina Department of Justice database. Medication adherence, certain, designated adverse events, patient sociodemographic characteristics and clinical variables (hospitalization history, substance abuse, psychotic symptoms and functional impairment) were assessed at six-month intervals using a patient-reported validated measure, the SCAP Health Questionnaire. Results were obtained using multivariable time series analysis controlling for selected demographic and clinical covariates. The study was sponsored by Eli Lilly and Company.

About Schizophrenia

Schizophrenia is a severe and debilitating psychosis often characterized by acute episodes of delusions (false beliefs that cannot be corrected by reason), hallucinations (usually in the form of non-existent voices) and long-term impairments such as diminished emotion, lack of interest and depressive signs and symptoms. It is usually associated with a disruption in social and family relationships.

Schizophrenia is a common severe mental illness. More than two million American adults have the disease, with more than 100,000 new cases reported each year. Symptoms of schizophrenia usually begin to appear in the teenage years or early to mid-twenties.

Important Information About Zyprexa

Zyprexa is indicated in the United States for the short-term and long-term treatment of schizophrenia, for maintenance in the treatment of bipolar disorder, and either alone or in combination with lithium or valproate (Depakote[®], Abbott) for the short-term treatment of acute mixed or manic episodes associated with bipolar disorder. In addition, on March 29, 2004, Zyprexa for injection was approved by the FDA for the control of acute agitation associated with schizophrenia and bipolar mania. Since its introduction in 1996, Zyprexa has been prescribed to more than 16 million people worldwide.

The most common treatment-emergent adverse event associated with Zyprexa in placebo-controlled, short-term schizophrenia and bipolar mania trials was drowsiness. Other common events were dizziness, weight gain, personality disorder (COSTART term for nonaggressive objectionable behavior), constipation, restlessness, episodes of low blood pressure, dry mouth, weakness, upset stomach, increased appetite, and tremor. A small number of patients experienced asymptomatic elevations of certain liver enzymes; none of these patients experienced jaundice.

Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including Zyprexa. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. All patients taking atypicals should be monitored for symptoms of hyperglycemia. Persons with diabetes who are started on atypicals should be monitored regularly for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Patients who develop symptoms of hyperglycemia during treatment should undergo fasting blood glucose testing.

Prescribing should be consistent with the need to minimize the risk of neuroleptic malignant syndrome, tardive dyskinesia, seizures and low blood pressure.

In short-term (six-week) acute bipolar mania trials in combination with lithium or valproate, the most common treatment emergent adverse event associated with Zyprexa and lithium or valproate was dry mouth. Other common events were weight gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia and abnormal burning or tingling of the skin.

Although the efficacy of Zyprexa in elderly patients with dementia has not been established in clinical trials and Zyprexa is not approved for use in this patient population, it is important to note the label for Zyprexa includes a warning for elderly patients with dementia. The warning states that strokes or mini-strokes (also called transient ischemic attacks or TIAs), including fatalities were reported in elderly patients with dementia-related psychosis participating in Zyprexa clinical trials. In addition, Lilly has completed a medical review of five placebo-controlled trials in elderly patients with dementia, and found an increased incidence of mortality from any cause in the Zyprexa group compared to patients who took placebo (3.5% vs. 1.5%). In this review, risk factors that predisposed Zyprexa patients to increased mortality included age greater than 80 years, sedation, simultaneous use of certain sedative and anti-anxiety medications (called benzodiazepines) or presence of pulmonary conditions such as pneumonia. Lilly is currently addressing this mortality data with the FDA.

Full prescribing information is available at 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 .

LillyAnswers ensures that low-income Medicare enrollees with the greatest need have complete access to the Lilly products they require. The centerpiece of the patient assistance program, the LillyAnswers card, allows seniors and people with disabilities under Medicare to pay a flat \$12 fee for a 30-day supply of certain retail distributed Lilly drugs, including Zyprexa. Since Lilly implemented LillyAnswers in 2002, hundreds of thousands of people without prescription drug insurance have received more than a half million Lilly products. LillyAnswers enrollment applications are available by calling the toll-free number: 1-877-RX-LILLY (1-877-795-4559) or online at www.lillyanswers.com . P-LLY

This press release contains forward-looking statements about the potential of Zyprexa for the treatment of schizophrenia, including the associated risk of violent behavior in some patients, and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that the product 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.