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New Study Showed No Difference in Total Treatment Costs When Comparing Those Starting Treatment with Older Conventional Antipsychotics and Those Starting Treatment with Zyprexa(R), an Atypical Antipsychotic, in the Treatment of Schizophrenia

Data also showed Zyprexa was significantly more effective than conventional antipsychotics on clinical and social measures

INDIANAPOLIS, Dec 20, 2005 /PRNewswire-FirstCall via COMTEX News Network/ -- Requiring people with schizophrenia to first fail on an older, inexpensive generic antipsychotic before allowing them to switch to the newer antipsychotic Zyprexa(R) (olanzapine) may not result in cost savings overall, according to a new study published in this month's issue of *Value in Health*. The data showed that despite higher medication costs of Zyprexa, the difference in one-year direct total costs between Zyprexa, as initial (first-line) treatment, and conventional antipsychotics as first line treatment, was small and not statistically significant. Findings indicate that any savings on medication costs were offset by the increased costs of other services associated with treatment with conventional antipsychotics including hospitalizations, crisis interventions and emergency room visits.

Researchers in this study also compared the cost-effectiveness of Zyprexa (mean modal dose 13.49 mg/day) and Risperdal(R) (risperidone) (mean modal dose 4.95 mg/day) as first-line treatment for schizophrenia and found the total costs associated with the two medications to be similar and not significantly different from each other.

This cost-effectiveness study was designed specifically to compare the clinical and social effectiveness and total direct costs of treatment with different antipsychotics, to help inform private and public payer systems' practices and policies regarding first-line antipsychotic options for treating schizophrenia.

"These data showed that regardless of whether a person was initiated on a conventional or atypical antipsychotic, the overall direct costs of treating a person with schizophrenia for one year were essentially the same," said Ralph Aquila, M.D., one of twenty-one study investigators who is the director of residential community services at St. Luke's/Roosevelt Hospital Center. "This study suggests that cost cutting efforts that require patients with schizophrenia to first fail on older, conventional antipsychotics before providing access to newer medications like Zyprexa, do not necessarily result in overall cost savings and may unnecessarily restrict access to the most optimal treatment for patients."

Attempts to contain high costs of treatment for severe mental illnesses have led to cost cutting efforts that include restricting access to more expensive antipsychotics, such as preferred drug lists, prior authorization requirements and "fail-first" treatment algorithms (where failure on a less expensive medication is required before a more expensive medication is covered). However, questions have been raised by state and federal government officials as to whether these measures actually result in overall cost savings or if any savings in medication costs may be offset by increased costs of other services.

"Finding the most effective treatment for each patient is critical, because the consequences of relapse for patients with serious mental illnesses and their families can be devastating. They have a more difficult time recovering and regaining the life that they had before," said Dr. Aquila. "The ideal approach for treating schizophrenia is to start with the most effective treatment for each individual patient. This may help them remain on that treatment longer which can lead to better functional outcomes."

Key Findings

In this one-year, multi-center, randomized, open-label study, more than 660 patients with schizophrenia were assigned to one of three treatment regimens between May 1998 and September 2001: a) Zyprexa as a first-line treatment (n=229), b) first-line treatment with conventional antipsychotics such as perphenazine, loxapine, haloperidol, thiothixene, fluphenazine (maximum of two consecutive agents before a possible switch to Zyprexa, n=214), and c) risperidone as a first-line treatment (n=221). Choice of particular conventional agent was made by the treating physician. Barring any clinically significant adverse events, all patients were to remain on their randomized treatment regimen for at least eight weeks, but could continue on their initial treatment regimen for as long as clinically indicated during the one-year trial.

Results were analyzed from the perspective of the public payer health care system and included total direct treatment costs and the treatment effectiveness for patients with schizophrenia, measured in both clinical and social terms. Total direct costs

reflected resources considered to be "mental health" or "psychiatric" (e.g., antipsychotic/psychotropic medications, psychiatric hospitalizations, outpatient visits to psychiatrists, etc.), as well as resources considered to be "non-psychiatric" (e.g., non-psychotropic medications, hospitalizations for physical illnesses, primary care physician visits, etc.). Clinical effectiveness was measured using the Brief Psychiatric Rating Scale (BPRS) and social effectiveness was measured using the Lehman Quality of Life Scale (LQLI) social relations scores.

Results showed:

- * Total one-year mean direct costs were \$20,891 for Zyprexa, \$21,283 for conventional antipsychotics, and \$21,347 for Risperdal. The differences were not statistically significant.
- * Approximately half of patients who began the study on conventional antipsychotics switched to an atypical antipsychotic, and rates of switching from the initial antipsychotic were significantly lower for Zyprexa than for the conventional antipsychotics (14% vs. 53%, $p < 0.001$) or Risperdal (14% vs. 31%, $p < 0.001$).
- * For patients who required a switch from their initial antipsychotic to another, there was a modest savings of \$195 in yearly medication costs. However, this was offset by an additional \$3,741 needed for other services.
 - More than 70% of these additional costs were for acute inpatient/outpatient services such as hospitalizations, partial hospitalizations, crisis interventions and emergency room visits.
- * When taking switching of antipsychotics into consideration, in treating schizophrenia, Zyprexa was significantly more effective than conventional antipsychotics on both clinical symptoms (BPRS) ($p=0.025$) and social relations (LQLI) ($p=0.043$), and compared to Risperdal on social relations ($p=0.002$).

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 Zyprexa

Olanzapine is indicated for the treatment of schizophrenia, for acute manic and mixed episodes of bipolar disorder, and for maintenance treatment in bipolar disorder.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Safety experience in elderly patients with dementia-related psychosis - In placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs. 1.5%, respectively). Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Cerebrovascular adverse events (CVAE), including stroke, in elderly patients with dementia - Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of CVAE in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia and diabetes mellitus - Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including olanzapine. 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 orthostatic hypotension.

The most common treatment-emergent adverse event associated with olanzapine 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.

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For full prescribing information please see www.zyprexa.com

To read the manuscript please see:

<http://www.blackwell-synergy.com/doi/full/10.1111/j.1524-4733.2006.00083.x>

This press release contains forward-looking statements about the potential of olanzapine for the treatment of schizophrenia 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.

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