



Facts About Zyprexa[®]

- Zyprexa was developed and is marketed by Eli Lilly and Company.
- To date, Zyprexa has received medical and regulatory approval and is available in more than 84 countries around the world.
- More than 14 million patients, worldwide, have been treated with Zyprexa.
- Zyprexa is available by prescription in 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg and 20 mg tablets.

Treatment of Schizophrenia

- Zyprexa was approved by the U.S. Food and Drug Administration (FDA) in October of 1996, for the treatment of schizophrenia, and was approved by the FDA in November of 2000, for long-term therapy and maintenance of treatment response of schizophrenia. Zyprexa was the first atypical antipsychotic to prove its long-term effectiveness in this patient population.
- Though its mechanism of action is unknown, it is suspected that Zyprexa chemically blocks multiple neurotransmitters in the brain, including dopamine and serotonin, which are believed to be associated with schizophrenia. Zyprexa controls the positive symptoms (hallucinations, delusions), negative symptoms (social withdrawal, lack of emotion and motivation) and affective symptoms (depression) associated with schizophrenia. Zyprexa also has been shown to improve cognition (abstract/organized thinking, insight, judgment) in schizophrenia patients.
- The efficacy of Zyprexa in treating the symptoms of schizophrenia has been shown in a series of double-blind, randomized, controlled trials conducted with nearly 3,000 patients.
- Extensive clinical trials have shown that Zyprexa has a low incidence of certain adverse events traditionally associated with previously available drugs for treating schizophrenia, including severe movement disorders (such as abnormal muscle spasms and jerking, inability to sit still), and hyperprolactinemia (a hormonal elevation that can be associated with amenorrhea, sexual dysfunction, breast engorgement).

Treatment of Bipolar Disorder

- Zyprexa was approved by the FDA in March of 2000, for the short-term treatment of acute manic episodes associated with bipolar disorder, and in July of 2003, for use in combination with lithium or valproate (Depakote[®], Abbott) for the treatment of acute manic episodes associated with bipolar disorder.
- In January of 2004, Zyprexa was approved by the FDA for maintenance in the treatment of bipolar disorder. This FDA approval recognizes that Zyprexa is an effective treatment to delay relapse into either mania or depression in patients with bipolar disorder. Zyprexa is the first treatment since lithium (1974) to be recognized by the FDA as a treatment for both acute mania and maintenance treatment in bipolar disorder and is the first and only atypical antipsychotic to be approved for maintenance treatment in bipolar disorder.

Facts About Zyprexa

Zyprexa Zydis[®]

- In April of 2000, Zyprexa Zydis (olanzapine orally disintegrating tablet) was approved as an orally disintegrating formulation of Zyprexa. Because this formulation dissolves on contact with saliva, it may be useful to physicians treating patients unable to swallow conventional tablets and may increase patients' adherence to their prescribed regimen. Zyprexa Zydis is available in doses of 5, 10, 15 and 20 mg, providing physicians with a dependable, orally disintegrating option even for acutely ill patients.

Zyprexa IntraMuscular

- In March of 2004, Zyprexa IntraMuscular (olanzapine for injection), was approved by the FDA for the control of acute agitation associated with schizophrenia and bipolar mania.
- Acute agitation is a well-recognized behavioral syndrome with a range of symptoms, including hostility, extreme excitement, poor impulse control, tension and uncooperativeness. The syndrome can occur with a number of conditions, including schizophrenia and bipolar disorder. Patients suffering from agitation in its severe forms are usually in an emergency situation and require immediate treatment to alleviate personal distress and to prevent harm to themselves and others.

Honors

- Zyprexa was named the best new product of 1996 by *Pharma Business Weekly* and the 1997 pharmaceutical product of the year by *BusinessWeek*. Zyprexa also received the prestigious U.K. Prix Galien award for outstanding achievement in pharmaceutical research. The inventors of Zyprexa (Dr. David Tupper, Dr. Jiban Chakrabarti and research chemist Terrence Hotten) received the Discoverers Award from the Pharmaceutical Research and Manufacturers of America (PhRMA) in 2000.

Important Information About Zyprexa

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. The available data are insufficient to provide reliable estimates of differences in hyperglycemia-related adverse event risk among the marketed atypical antipsychotics. 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.

Facts About Zyprexa

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.

In the Zyprexa IntraMuscular trials, adverse events included drowsiness, dizziness and muscle weakness. In addition, Zyprexa IntraMuscular was associated with infrequent decreases in blood pressure and heart rate that were clinically manageable. However, the risk of low blood pressure, slowing of heart rate, and sinus pause may be greater in non-psychiatric patients compared to psychiatric patients who are possibly more adapted to certain effects of psychotropic medications.

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.

Updated 3/15/04