



Zyprexa/Zyprexa Zydis (olanzapine)

Generic name: Olanzapine

Available strengths: 2.5 mg, 5 mg, 7.5 mg, 10 mg,
15 mg, 20 mg tablets; 5 mg, 10 mg, 15 mg, 20 mg
(rapid-dissolving tablets (Zyprexa Zydis);
10 mg/vial injection

Available in generic: No

Drug class: Second-generation antipsychotic

General Information

Zyprexa (olanzapine) is a **serotonin and dopamine antagonist** belonging to the class of second-generation antipsychotics that are often called *atypical* antipsychotics. (Refer to the handout on “Second-Generation Antipsychotics” for an explanation of how these antipsychotics work.) These agents are atypical in that they are significantly different, both in structure and pharmacology, from the older, *typical* antipsychotics medications such as Thorazine (chlorpromazine), Mellaril (thioridazine), and Haldol (haloperidol). The second-generation antipsychotics block both serotonin and dopamine receptors, whereas the typical antipsychotics are mainly dopamine-receptor antagonists. Zyprexa possesses mood-stabilizing and antipsychotic properties that are effective in treating a wide spectrum of mental disorders.

Of the second-generation antipsychotics, Zyprexa has been approved by the U.S. Food and Drug Administration for the broadest range of uses. Zyprexa is approved for the treatment of schizophrenia, for the treatment of acute mania in bipolar disorder, and for maintenance (long-term) therapy in bipolar disorder. The intramuscular form of Zyprexa is indicated for the treatment of agitation in schizophrenia and bipolar disorder. The use of a medication for its approved indications is called its *labeled* use. In clinical practice, however, physicians often prescribe medications for *unlabeled* (“off-label”) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety of those treatments. Like other second-generation antipsychotics, Zyprexa is used to treat other psychiatric disorders, including schizoaffective disorder, psychotic depression, psychosis in Alzheimer’s disease and other neuropsychiatric disorders, and refractory depression in combination with other medications.

Dosing Information

The recommended starting dosage for Zyprexa for treatment of schizophrenia is 5–10 mg/day, taken once daily, preferably in the evening or at bedtime. It may be taken without regard to meals. The dosage may be increased, usually in weekly increments of 5 mg/day. The dosage range is usually between 10 mg/day and 20 mg/day. However, dosages greater than 20 mg/day may be required for some patients.

In treatment of acute mania in bipolar disorder, the initial dosage is 10–15 mg/day, taken in a single daily dose. The dosage may be increased in increments of 5 mg/day, but not in less than 24 hours. When the acute episode is stabilized, the patient may continue maintenance therapy with Zyprexa alone (monotherapy) to prevent relapse, using a maintenance dosage of 15–20 mg/day. If Zyprexa is used in combination with another mood stabilizer, such as lithium or Depakote, the dosage is generally lowered to 10 mg/day.

Zyprexa also comes in a rapid-disintegrating tablet under the brand Zyprexa Zydis. The preparation rapidly melts in the mouth.

Common Side Effects

Frequent and bothersome side effects from Zyprexa are sedation, constipation, and dry mouth. As tolerance to the medication develops, these side effects usually subside. Taking Zyprexa in a single bedtime dose may minimize daytime sedation. For dry mouth, chewing sugarless gum or sucking on sugarless candy may promote salivation. To prevent constipation, patients should increase fluid intake and dietary fiber and should exercise regularly. Bulk laxatives or a stool softener such as Colace may be needed at times to relieve constipation.

Extrapyramidal symptoms (EPS), which are commonly associated with conventional antipsychotics, are infrequent with Zyprexa. EPS are neurological disturbances produced by antipsychotics (or other causes) in the area of the brain that controls motor coordination. These side effects include muscle rigidity, tremors, drooling, “mask-like” facial expression, shuffling gait, and muscle spasms that result in abnormal posture (**dystonia**). At dosages greater than 10 mg/day, some patients may experience **akathisia**, which is a subjective feeling of restlessness accompanied by fidgeting, pacing, or inability to sit still. EPS may be managed by decreasing the antipsychotic dosage or adding another medication (anticholinergic medication) to counteract the side effect.

Zyprexa may induce significant weight gain. This may be due to increased appetite or to some underlying metabolic changes. The major concern of excessive weight gain is the health consequence to the patient, including the potential for developing diabetes and increasing cholesterol and other lipids, which may increase the risk for cardiovascular disease. Furthermore, patients may want to stop taking their medication if they become self-conscious about putting on excessive weight. If this side effect becomes problematic, patients should not stop their medication, but should consult with their physician.

Zyprexa may block a compensatory response—the narrowing of blood vessels—that counterbalances postural change, resulting in a momentary drop in blood pressure when the person rises too rapidly, which may cause dizziness and lightheadedness. This reaction is known as **orthostatic hypotension**. Patients, especially seniors and those taking antihypertensive medications, need to be cautious and rise slowly to allow their body to adjust to the change in position, avoiding a sudden drop in their blood pressure.

Adverse Reactions and Precautions

Zyprexa may cause drowsiness and sedation and impair physical coordination and mental alertness. Patients should avoid potentially dangerous activities, such as driving a car or operating machinery, until they are sure that these side effects will not affect their ability to perform these tasks.

Tardive dyskinesia (TD) is a potential adverse reaction from antipsychotic medications. It consists of abnormal involuntary movements. It is a potentially irreversible condition that includes “pill-rolling” movements of the fingers, darting and writhing movements of the tongue, lip puckering, facial grimacing, and shoulder or neck movements. The risk of TD is believed to increase as the duration of treatment and the total cumulative amount of antipsychotic medications prescribed to the patient increases. The risk of TD associated with second-generation antipsychotics, such as Zyprexa, is significantly lower than with conventional antipsychotics.

Neuroleptic malignant syndrome (NMS) is a rare, toxic reaction to antipsychotics, including Zyprexa. The symptoms are severe muscle stiffness, rigidity, elevated body temperature, increased heart rate and blood pressure, irregular pulse, and sweating. NMS may lead to delirium and coma. It can be fatal if medical intervention is not immediately provided. There are no tests to predict whether an individual is susceptible to developing NMS when exposed to an antipsychotic. Thus NMS must be recognized early because it is a medical emergency that requires immediate discontinuation of the antipsychotic, hospitalization, and intensive medical treatment.

Zyprexa, as well as other second-generation antipsychotics, may alter glucose (sugar) metabolism and cause elevation of glucose levels (**hyperglycemia**). Patients who have excessive weight gain from Zyprexa are more susceptible to the medication’s negative impact on blood sugar and cholesterol. Patients with diabetes and individuals with a family history of diabetes should be cautious of this side effect and check glucose levels periodically while taking Zyprexa.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

Zyprexa has not been tested in women to determine its safety in pregnancy. The effects of the medication on the developing fetus in pregnant women are unknown. In animal studies, there was no evidence of harm to the fetus when exposed to Zyprexa. Animal studies, however, are not always predictive of effects in humans. Women who are pregnant or may become pregnant should discuss this with their physician. Some women may experience a recurrence of their psychosis when they stop Zyprexa. In these circumstances, the physician may discuss the need to restart the medication or seek an alternative medication or treatment.

Nursing mothers should not take Zyprexa, because small amounts will pass into breast milk and be ingested by the baby. If stopping the antipsychotic is not an alternative, breastfeeding should not be started or should be discontinued.

Possible Drug Interactions

Some medications when taken concomitantly with Zyprexa may result in drug interactions that alter their levels, which may produce undesired reactions. The possible drug interactions with Zyprexa are summarized in the table below.

Luvox (fluvoxamine)	Luvox can decrease the metabolism of Zyprexa, thus increasing blood levels of Zyprexa and the likelihood of unwanted side effects.
Tegretol (carbamazepine)	Tegretol can decrease the blood levels of Zyprexa, reducing its effectiveness in treating the symptoms of the illness.

Patients taking Zyprexa should not consume alcohol because the combination may impair thinking, judgment, and coordination.

