



Symbyax (Zyprexa [olanzapine] and Prozac [fluoxetine] combination)

Generic name: Olanzapine and fluoxetine combination
Available strengths: 6 mg/25 mg, 6 mg/50 mg,
12 mg/25 mg, 12 mg/50 mg (Zyprexa/Prozac)
Available in generic: No
Drug class: Second-generation antipsychotic and
selective serotonin reuptake inhibitor antidepressant

General Information

Symbyax is a combination medication containing the antipsychotic **Zyprexa (olanzapine)** and antidepressant **Prozac (fluoxetine)**. Zyprexa 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.) The second-generation antipsychotics block both serotonin and dopamine receptors, whereas the typical antipsychotics are mainly dopamine-receptor antagonists. Given its pharmacological properties, Zyprexa possesses mood-stabilizing and antipsychotic properties that are effective in treating a wide spectrum of mental disorders. Moreover, in addition to its indication for treatment of psychosis in schizophrenia and schizoaffective disorder, Zyprexa also received approval from the U.S. Food and Drug Administration (FDA) for the treatment of acute mania and maintenance or long-term treatment of bipolar disorder.

The antidepressant Prozac contained in Symbyax is a **selective serotonin reuptake inhibitor (SSRI)**. Prozac and other SSRI antidepressants work by blocking the reuptake of the neurotransmitter serotonin back into brain cells, thereby increasing the levels of serotonin in the brain. Depression and other mental disorders may be due to abnormally low levels of serotonin. The presumed action of Prozac and other SSRIs is to increase serotonin levels, which may help to restore those areas of the brain to normal function.

In 2004 Symbyax received an indication from the FDA for the treatment of depressive episodes in bipolar depression. Symbyax is marketed to treat the depressive episodes of bipolar disorder with Prozac and to stabilize the manic phase of the bipolar illness with Zyprexa.

Dosing Information

Symbyax comes in fixed combinations of Zyprexa and Prozac in different strengths. It is available in the combinations of 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, and 12 mg/50 mg of Zyprexa/Prozac, respectively. The recommended starting dosage for Symbyax is 6 mg/25 mg taken once a day. Dosage adjustments are made according to response and tolerability to the medication. The dosage may range from 6 mg to 12 mg of Zyprexa and 25 mg to 50 mg of Prozac, all taken in a single daily dose.

Common Side Effects

The common side effects reported with Symbyax are sleepiness, tiredness, tremor, peripheral edema (accumulation of fluid in the legs and ankles), dry mouth, increased appetite, and weight gain. As tolerance to the medication develops, these side effects should subside. Taking Symbyax in a single bedtime dose may minimize daytime sedation and drowsiness. For dry mouth, chewing sugarless gum or sucking on sugarless candy may promote salivation.

Zyprexa in Symbyax may induce **extrapyramidal symptoms (EPS)**, although these effects are very uncommon with the second-generation antipsychotics. 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.

Symbyax may increase appetite and caloric intake, causing significant weight gain. In clinical studies, the mean weight increase in patients who took Symbyax was approximately 8 pounds, compared with placebo-treated groups. 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 from putting on excessive weight. If this side effect becomes problematic, patients should not stop their medication but should consult with their physician.

Symbyax 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

Symbyax 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 associ-

ated with second-generation antipsychotics, such as Zyprexa in Symbyax, is significantly lower than with conventional antipsychotics. In rare cases, however, Prozac has been associated with TD. It is too early to determine whether the combination of Zyprexa and Prozac may increase the incidence of TD, because the condition usually requires years of exposure to the medication.

Neuroleptic malignant syndrome (NMS) is a rare, toxic reaction to antipsychotics, including Zyprexa in Symbyax. 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 Symbyax 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 Symbyax.

Antipsychotic medications, including the Zyprexa in Symbyax, may disrupt the body's ability to dissipate heat. Fatal cases from disruption of the body's ability to lower core temperature have been reported with antipsychotics, particularly the older, first-generation antipsychotics. Therefore, individuals taking Symbyax need to be cautious of conditions that may contribute to elevation in temperature, including exposure to extreme heat, dehydration, strenuous exercise, and concomitant medications, such as anticholinergic agents, which may reduce the body's ability to dissipate heat.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

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

Possible Drug Interactions

Some medications when taken concomitantly with Symbyax may result in drug interactions that alter their levels, which may produce undesired reactions. The antidepressants known as **monoamine oxidase inhibitors (MAOIs)**, such as Nardil (phenelzine), should not be taken with Symbyax. Furthermore, an MAOI should not be started for at least 2 weeks and preferably 4–5 weeks after the discontinuation of Symbyax due to the long duration of action of Prozac and its metabolites. The combination of an MAOI and Prozac may precipitate a dangerous elevation of blood pressure.

Other possible drug interactions with Symbyax are summarized in the table on the next page.

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

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| Luvox (fluvoxamine) | Luvox can decrease the metabolism of Symbyax, thus increasing blood levels of Symbyax and the likelihood of unwanted side effects. |
| Tegretol (carbamazepine) | Tegretol can increase metabolism of Zyprexa and decrease the blood levels and effectiveness of Symbyax in treating the symptoms of the illness. |
| Clozaril (clozapine) | Clozaril blood levels may be elevated by the Prozac in Symbyax, increasing the potential for toxicity. |
| Dilantin (phenytoin) | Prozac may elevate the blood levels of the anticonvulsant Dilantin, increasing the potential for toxicity from Dilantin. |
| Coumadin (warfarin) | Prozac may increase the anticoagulant effect of Coumadin and increase the risk of bleeding; the Coumadin dosage may need to be adjusted. |

Overdose

There are few data on acute overdose with Symbyax. Fatal cases have been reported with patients who overdosed on Prozac alone. The most common symptoms associated with Prozac overdose include somnolence, confusion, nausea, vomiting, rapid heart rate, and seizures. In cases of Zyprexa overdose, common signs include agitation, rapid heart rate, EPS, and reduced level of consciousness ranging from sedation to coma. Among the serious and sometimes fatal cases from acute overdose with Zyprexa, seizures, cardiac arrhythmias, respiratory depression, and cardiopulmonary arrest were reported. Acute overdose with Symbyax, which contains two active ingredients, may be potentially more hazardous than overdose with Zyprexa or Prozac alone.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought as well, because the information on the prescription label can be helpful to the treating physician in determining the number of pills ingested.

Special Considerations

- Do not discontinue Symbyax without consulting your physician.
- If you miss a dose, take it as soon as possible. If it is close to your next scheduled dose, skip the missed dose and continue on your regular dosing schedule, but do not take double doses.
- Symbyax may be taken with or without food.
- Symbyax may cause sedation and drowsiness, especially during initiation of therapy, and impair your alertness. Use caution when driving or performing tasks that require alertness.
- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of the medication.
- Keep your medication out of reach of children.
- Closely watch depressed individuals who are at risk for suicide at the outset of therapy and immediately report any signs of suicidal or violent behavior to the physician or a mental health provider.

If you have any questions about your medication, consult your physician or pharmacist.

