



Orap (pimozide)

Generic name: Pimozide

Available strengths: 1 mg, 2 mg tablets

Available in generic: No

Drug class: First-generation (conventional) antipsychotic

General Information

Orap (pimozide) belongs to a class of antipsychotics known as the **first-generation antipsychotics**, sometimes referred to as *conventional* or *typical* antipsychotics. The first-generation antipsychotics represent an older class of antipsychotics that have been the standard for treating psychotic disorders for many decades. When compared with a newer class of **second-generation antipsychotics**, these earlier antipsychotics are “typical” or “conventional” because they lack the wider spectrum of therapeutic activity. The first-generation antipsychotics are also more likely to induce side effects that cause movement disorders, such as **extrapyramidal symptoms (EPS)** and **tardive dyskinesia (TD)**, than the newer antipsychotics.

Orap is a relatively high-potency agent, compared with other first-generation antipsychotics such as Thorazine (chlorpromazine) and Mellaril (thioridazine). The higher-potency antipsychotics are less sedating and have fewer **anticholinergic side effects** but are associated with more neurological disturbances that cause EPS than are the lower-potency antipsychotics.

Orap was approved by the U.S. Food and Drug Administration for treatment of Tourette’s disorder, an inherited tic disorder that begins with simple facial tics and may progress to more complex tics, including grunting and compulsive utterances that can be publicly embarrassing and disabling for the individual. Generally, Orap is reserved for treatment of more severe cases of Tourette’s disorder that do not respond to standard treatments. The use of a drug for its approved indications is called its *labeled* use. In clinical practice, however, physicians often prescribe drugs for *unlabeled* (“off-label”) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety of the medications for these uses. Orap has limited unlabeled use and is prescribed only rarely for treatment of psychotic disorders, even though it is very similar to Haldol (haloperidol), another antipsychotic agent.

Dosing Information

The recommended starting dosage for Orap in treatment of Tourette’s disorder is 1–2 mg/day, administered in divided doses and increased slowly up to 6–10 mg/day as needed.

Common Side Effects

Orap is less sedating than the lower-potency antipsychotics, but it may induce bothersome side effects called **extrapyramidal symptoms**. These are neurological disturbances caused by antipsychotics (or a neurological disorder) in the area of the brain that controls motor coordination. When disruption occurs in a particular area of the brain, it can produce symptoms that mimic Parkinson's disease (**parkinsonism**), including muscle stiffness, rigidity, tremor, drooling, and a “mask-like” facial expression. However, unlike Parkinson's disease, which is a progressive neurological disease, parkinsonism from treatment with an antipsychotic is reversible. The Parkinson-like symptoms may be treated, and prevented, by using antiparkinson agents (also called anticholinergic agents) such as Cogentin (benztropine), Benadryl (diphenhydramine), Artane (trihexyphenidyl), and Kemadrin (procyclidine).

Akathisia is another form of EPS characterized by a subjective sense of restlessness accompanied by fidgeting, inability to sit still, nervousness, muscle discomfort, and agitation. Generally, antiparkinson agents are not effective in managing akathisia. Use of Inderal (propranolol), a *beta-blocker*, may be helpful and is sometimes prescribed by physicians.

Dystonia is a type of EPS with acute onset. The patient may develop a sudden spasm of the muscles of the tongue, jaw, and neck. **This is not an allergic reaction to the antipsychotic medication.** Although a dystonic reaction may be painful and frightening, it can be rapidly reversed with an intramuscular injection of an anticholinergic medication such as Cogentin or Benadryl. With a dystonic reaction, the patient should seek immediate medical attention and receive treatment.

Elevation of **prolactin levels** is common with conventional antipsychotics. Prolactin is a hormone produced in the area of the brain called the pituitary gland. It is normally elevated in women following childbirth, stimulating lactation, or milk production. The effects of elevated prolactin include breast enlargement and milk production (**galactorrhea**) in both women and men. Elevated prolactin is associated with impotence in men and irregular menstrual cycles or absence of menstruation in women. When side effects from elevated prolactin levels become bothersome, the alternative is to switch to one of the second-generation antipsychotic agents with no propensity to elevate this hormone.

Orap has a moderate effect on weight gain. It is unclear whether this is due to an underlying metabolic change caused by the antipsychotic or to increased appetite. Weight should be monitored closely during therapy, and if weight gain occurs, an intervention program of diet and exercise should be started.

Orthostatic hypotension and anticholinergic side effects, which occur more frequently with lower-potency antipsychotics, are usually not as troubling with higher-potency agents like Orap.

Adverse Reactions and Precautions

Orap 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.

Orap may enhance ultraviolet light absorption in the skin—a reaction known as **photosensitivity**—and predispose the person to sunburn. Patients should avoid prolonged exposure to sunlight, use sunscreen, and wear protective clothing until tolerance is developed to the medication. Under very hot conditions, patients may be predisposed to heat-related illness and **heatstroke** because antipsychotics may disrupt the body's ability to regulate temperature. Patients should take precautions to protect themselves from prolonged exposure to hot, humid weather. It is important that patients maintain adequate ventilation and stay indoors.

Tardive dyskinesia (TD) is a potential adverse reaction from antipsychotic medications. It is characterized by late-onset abnormal involuntary movements. TD is a potentially irreversible condition with symptoms that commonly include “pill-rolling” movements of the fingers, darting and writhing movements of the tongue, lip puckering, facial grimacing, and other irregular movements. The risk of TD is associated with the

duration of exposure to antipsychotic medication, and this risk increases with age. The conventional antipsychotics are associated with a greater risk of TD than the more recent second-generation antipsychotics.

Neuroleptic malignant syndrome (NMS) is a rare, toxic reaction to antipsychotics. The symptoms are severe muscle stiffness, rigidity, elevated body temperature, increased heart rate and blood pressure, irregular pulse, and profuse 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.

Antipsychotics may **slow electrical conduction in heart tissues** (myocardium). Some patients taking antipsychotics show on their **electrocardiogram (ECG)** a prolongation of the electrical impulse as it travels in the myocardium. The abnormal ECG finding, **QTc prolongation**, may signal a potential for developing an irregular heart beat (**arrhythmia**). Orap (pimozide) is associated with a greater tendency to alter the electrical impulse, and therefore it has a higher risk of causing arrhythmias, especially in individuals with cardiac disease. Patients should have ECGs before and during Orap treatment. Moreover, medications that increase this potential for cardiac risk should not be taken with Orap (see “Possible Drug Interactions”).

Antipsychotics can lower the seizure threshold and induce **seizures** in susceptible individuals, especially those with a history of seizure disorder. Patients with a seizure disorder who are receiving anticonvulsants often receive antipsychotics without any increase in seizures.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

Orap 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 Orap. 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 Orap. 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 Orap, 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 Orap may result in drug interactions that alter their levels, which may produce undesired reactions. Medications that may prolong cardiac conduction should not be taken together with Orap because the combination may increase of arrhythmias. The possible drug interactions with Orap are summarized in the table below.

Tricyclic antidepressants (TCAs)	TCAs, which may prolong cardiac conduction, in combination with Orap can have an additive effect that increases the risk for arrhythmias.
Phenothiazine antipsychotics (e.g., Thorazine)	This combination may have an additive effect of prolonging cardiac conduction, increasing the risk for arrhythmias.
Anti-arrhythmia agents	Orap must be avoided if medications for treating arrhythmias are being taken, because the combination may further depress cardiac conduction.

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Prozac (fluoxetine)	Prozac may inhibit the metabolism of Orap and increase its blood levels, which may increase the cardiac side effects and toxicity of Orap.
Erythromycin, Biaxin, Zithromax	Antibiotics belonging to the erythromycin family (macrolides) may inhibit the metabolism of Orap and increase cardiac side effects and the risk for arrhythmias.
Nizoral and Sporanox	These two antifungal agents may inhibit the metabolism of Orap and increase cardiac side effects and the risk for arrhythmias.
Cipro and Noroxin	These antibiotics, as well as others in this group (fluoroquinolones), may inhibit the metabolism of Orap and increase cardiac side effects and the risk for arrhythmias.

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

Overdose

Depression of the central nervous system (CNS) with deep somnolence, low blood pressure, EPS, and abnormal ECG results are signs of Orap overdose. More serious complications may include agitation, restlessness, convulsions, fever, arrhythmias, and coma. The risk of fatal overdose depends on the amount ingested and whether Orap was combined with other medications, especially CNS depressants.

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 your medication 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.
- Orap may be taken with or without food.
- Orap may cause sedation and drowsiness, especially during initiation of therapy, and impair your alertness. Use caution when driving or performing tasks that require alertness.
- Orap may enhance ultraviolet light absorption and increase the risk of sunburn. Use a sunscreen and avoid excessive exposure to sunlight.
- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication.
- Keep your medication out of reach of children.

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

