



Thorazine (chlorpromazine)

Generic name: Chlorpromazine

Available strengths: 10 mg, 25 mg, 50 mg,
100 mg, 200 mg tablets; 100 mg/mL oral concentrate;
25 mg/mL injection

Available in generic: Yes

Drug class: First-generation (conventional) antipsychotic

General Information

Thorazine (chlorpromazine) was the first antipsychotic used for the treatment of psychosis. Thorazine 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.

Thorazine is a relatively low-potency agent when compared with other first-generation antipsychotics such as Haldol (haloperidol) and Prolixin (fluphenazine). The low-potency antipsychotics are generally sedating and more likely to induce **anticholinergic side effects** but are less likely to cause EPS than are high-potency agents.

Thorazine is approved by the U.S. Food and Drug Administration for the treatment of psychotic disorders, such as schizophrenia, schizoaffective disorder, acute mania, and psychotic depression. In children, Thorazine is indicated for short-term treatment of severe behavioral problems marked by combativeness and explosive anger and behavior. In addition, Thorazine is indicated in treatment of nausea and vomiting and intractable hiccups. The use of a medication for its approved indication is called *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. For instance, Thorazine may be prescribed with a mood stabilizer to treat acute mania, since the mood stabilizer has a slower onset of action. After the symptoms of mania abate, Thorazine is discontinued and the mood stabilizer is continued alone.

Dosing Information

The starting dosage of Thorazine for acute psychosis may range from 400 mg/day to 1,000 mg/day, taken in divided doses, depending on whether the patient is being treated in an outpatient or inpatient setting. Thorazine is infrequently used as the single agent in treatment of schizophrenia or schizoaffective disorder. It has been replaced by better-tolerated medications. Usually, Thorazine is used in combination as an adjunct with another antipsychotic to treat acute psychosis. Thorazine's sedating properties may be useful to decrease agitation and to help the patient sleep. When Thorazine is combined with another antipsychotic, lower dosages of 100–400 mg/day are used and are often taken at bedtime or on an as-needed schedule.

Common Side Effects

When starting Thorazine, patients may experience sedation and fatigue. Taking a larger portion of the total dosage at bedtime may minimize daytime sedation. Tolerance to the sedation generally develops after about 1 week.

With higher dosages, Thorazine may induce **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.

Thorazine may induce 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.

When a medication inhibits the action of **cholinergic neurons** in the nervous system, it produces an **anticholinergic reaction**, which may produce bothersome symptoms. Because many of the antipsychotics block the normal function of cholinergic neurons, they frequently produce anticholinergic side effects. When an organ system is affected by cholinergic inhibition, it causes side effects particular to that organ. For example, when the gastrointestinal tract is affected, it may result in dry mouth, cramping, and constipation. Other anticholinergic side effects include blurred vision (when muscles of the eyes are affected) and difficulty uri-

nating (when the bladder is affected). Thorazine has more anticholinergic activity than the high-potency antipsychotics. When Thorazine is combined with other medications with significant anticholinergic activity, such as tricyclic antidepressants and antiparkinson agents, the total anticholinergic action of all the medications may produce severe symptoms because the effects are additive. Seniors and individuals with a medical condition may be particularly sensitive to anticholinergic side effects. Excessive anticholinergic activity may induce delirium, a toxic reaction characterized by impaired consciousness, confusion, and inability to sustain attention.

Thorazine 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

Thorazine 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.

Thorazine 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 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

Thorazine 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 Thorazine. 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 Thorazine. 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 Thorazine, 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 Thorazine 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 Thorazine because the combination may increase the risk of arrhythmias. The possible drug interactions with Thorazine are summarized in the table below.

Tricyclic antidepressants (TCAs)	Thorazine may increase the blood levels of TCAs, which may increase the risk for arrhythmias.
Demerol (meperidine)	The combination of Thorazine and Demerol may result in excessive sedation and hypotension.
Orap (pimozide)	Thorazine and Orap (pimozide) should never be combined. The two medications may have an additive effect on prolongation of cardiac conduction, increasing the risk of arrhythmias.
Antiparkinson agents (e.g., Cogentin, Artane, Benadryl)	The combination of Thorazine with an antiparkinson agent may increase side effects from excessive anticholinergic activity such as dry mouth, blurred vision, constipation, and confusion.
Seroquel (quetiapine)	Thorazine may significantly decrease the blood levels of Seroquel, reducing its effectiveness.

Patients taking Thorazine 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, and EPS, as well as abnormal ECGs, are frequent signs of Thorazine 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 Thorazine 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.

