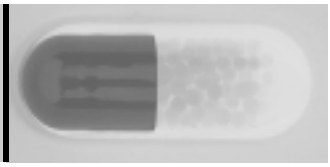

Perphenazine (Trilafon)

Generic name: Perphenazine
Available strengths: 2 mg, 4 mg, 8 mg, 16 mg tablets;
16 mg/5 mL oral concentrate
Available in generic: Yes
Drug class: First-generation (conventional) antipsychotic

General Information

Perphenazine (Trilafon) belongs to the class of antipsychotics known as the **first-generation antipsychotics,** sometimes referred to as *conventional* or *typical* antipsychotics. Perphenazine was sold under the brand Trilafon, but Trilafon has since been discontinued. Currently, only generic perphenazine is available. 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 referred to as *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.

Perphenazine is an intermediate-potency antipsychotic relative to other first-generation antipsychotics such as chlorpromazine and thioridazine, which are low-potency agents, and fluphenazine and Haldol (haloperidol), which are high-potency antipsychotics. Perphenazine is moderately sedating and less likely to lower blood pressure than the lower-potency agents. Perphenazine produces fewer EPS than the high-potency antipsychotics.

Perphenazine was approved by the U.S. Food and Drug Administration for treatment of psychotic disorders, including schizophrenia, schizoaffective disorder, and drug-induced psychosis. 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. For instance, perphenazine 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, perphenazine is discontinued and the mood stabilizer is continued alone.

Dosing Information

For treatment of acute psychosis, the hospitalized patient's starting dosage of perphenazine may be as high as 16–64 mg/day, given in divided doses. The maximum dosage should not exceed 64 mg/day. As symptoms abate, the dosage is reduced as soon as possible to a minimum effective dosage, which is usually in the range of 12–24 mg/day, given in divided doses. The dosage for seniors may be in the 8–16 mg/day range.

Common Side Effects

Perphenazine may induce bothersome side effects known as **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 also 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.

Perphenazine 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.

When a medication inhibits the action of **cholinergic neurons** in the nervous system, it produces an **anticholinergic reaction,** which may produce bothersome symptoms. Anticholinergic side effects from Perphenazine may include blurred vision, dry mouth, constipation, and difficulty with urination. Seniors and individuals with a medical condition may be particularly sensitive to anticholinergic side effects.

Perphenazine 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 the body to adjust to the change in position, avoiding a sudden drop in blood pressure. Orthostatic hypotension and anticholinergic side effects, which occur more frequently with low-potency, first-generation antipsychotics, are usually not as troublesome with the intermediate- and higher-potency agents.

Adverse Reactions and Precautions

Perphenazine may cause sedation and drowsiness, but generally these effects are not as troublesome as with the lower-potency antipsychotics like chlorpromazine and thioridazine. 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.

Perphenazine 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 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.

The FDA found that the first-generation antipsychotic medicines may be associated with an increased risk of death when used in treating elderly patients with dementia-related psychosis. The FDA now deems that all antipsychotic medications, including perphenazine, are not indicated for treating elderly patients with dementia. Physicians who prescribe antipsychotic medications to elderly patients for dementia-related psychosis should discuss this fatal risk with the patient, the patient's family, or the patient's caretaker.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

Perphenazine 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 perphenazine. 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 perphenazine. 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 perphenazine, 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 with perphenazine may result in drug interactions that alter their levels, which may produce undesired reactions. Use of medications for lowering blood pressure (antihypertensive medications), when perphenazine is also being taken, should be monitored closely because the antipsychotic medication may lower blood pressure and produce an additive effect with the antihypertensive medication.

Medications that act on the central nervous system (CNS), including benzodiazepines (e.g., Valium), antihistamines, and narcotic pain medications, may possibly increase the risk and severity of CNS-related side effects of antipsychotics, including somnolence, drowsiness, dizziness, and fatigue.

Patients taking perphenazine should not consume alcohol because the combination may worsen drowsiness and sedation and impair thinking, judgment, and coordination.

Overdose

Depression of the CNS with deep somnolence, low blood pressure, and EPS are common signs of perphenazine overdose. More serious complications may include agitation, restlessness, convulsions, fever, arrhythmias, and coma. The risk of death from the overdose depends on the amount of perphenazine ingested and whether it 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 room 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 perphenazine without consulting your physician.
- If you miss a dose, take it as soon as possible. If it is close to the next scheduled dose, skip the missed dose and continue on your regular dosing schedule. Do not take double doses.
- Perphenazine may be taken with or without food.
- Perphenazine may cause sedation and drowsiness, especially during initiation of therapy, and may impair your alertness. Use caution when driving or performing tasks that require alertness.
- Perphenazine may enhance ultraviolet light absorption and predispose to 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 the medication, and the medication may lose its therapeutic effects.
- Keep your medication out of reach of children.

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

Notes

From Chew RH, Hales RE, Yudofsky SC: *What Your Patients Need to Know About Psychiatric Medications,* Second Edition. Washington, DC, American Psychiatric Publishing, 2009