



Tranxene (clorazepate)

Generic name: Clorazepate

Available strengths: 3.75 mg, 7.5 mg, 15 mg capsules or tablets;

11.25 mg (Tranxene-SD Half Strength), 22.5 mg (Tranxene-SD)

Available in generic: Yes, except Tranxene-SD

Drug class: Benzodiazepine/anxiolytic; sedative-hypnotic

General Information

Tranxene (clorazepate) is a benzodiazepine indicated for treatment of anxiety disorders or short-term relief of symptoms of anxiety, alcohol withdrawal, and seizure disorders. The use of a drug 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. Physicians may use Tranxene outside its approved indications to treat social phobia, posttraumatic stress disorder, insomnia, and premenstrual syndrome. As with other benzodiazepines, Tranxene is associated with dependence and abuse and is regulated as a controlled substance by state and federal laws.

Tranxene’s effectiveness for treating anxiety may be explained by its pharmacological action in the brain at specific receptor sites. *Receptors* are specific sites on the nerve cell membrane that receive a signal from a neurochemical called the **neurotransmitter**. Once a neurotransmitter locks in on the receptor, the neurochemical signal is changed to an electrical or another chemical signal and travels down the neuron. The receptor sites in which benzodiazepines elicit their action are found in various regions of the brain, and the specific receptors are also known as **benzodiazepine receptors**. The coupled reaction of benzodiazepines to the receptors facilitates the inhibitory action of the neurotransmitter **γ -aminobutyric acid** (GABA) in that region of the brain. Benzodiazepines’ action on GABA receptors appears to produce their anxiolytic, sedative, and anticonvulsant actions. Tranxene is an effective anxiolytic and hypnotic medication.

Dosing Information

For treatment of anxiety, the usual starting dosage for Tranxene is 3.75 mg three times a day (11.25 mg/day), which can be administered in a single dose once a day with Tranxene-SD Half Strength in the 11.25 mg tablet. The dosage may be increased to 7.5 mg two or three times a day (15–22.5 mg/day). Patients whose symptoms are stabilized with 7.5 mg three times a day may have their medication switched to Tranxene-SD 22.5 mg tablet administered once a day. The therapeutic dosage for treating anxiety is generally in the range of 15–60 mg/day administered in divided doses. For severe anxiety and in management of acute alcohol withdrawal, the usual dosage is 15–30 mg given three to four times daily.

Common Side Effects

The common side effects reported with Tranxene are sedation and drowsiness, especially shortly after initiating therapy. Other frequent symptoms are impaired concentration and memory, feeling of dissociation (“spacey”), and impaired coordination.

Adverse Reactions and Precautions

Tranxene affects alertness and coordination, and patients should exercise caution when driving or performing other tasks requiring alertness while taking this medication. Seniors may be more adversely affected, because it may affect their coordination and reflexes and lead to falls and injury. Taking Tranxene with other central nervous system (CNS) depressants such as alcohol, narcotics, and barbiturates may compound these CNS effects.

Prolonged use of benzodiazepines can lead to dependence. When the medication is abruptly withdrawn, symptoms of withdrawal may occur. Withdrawal symptoms include headache, vomiting, impaired concentration, confusion, tremor, muscle cramps, and seizures. Benzodiazepines are centrally acting depressants, and they can depress respiration. This is particularly problematic for patients with chronic obstructive pulmonary disease and emphysema. Patients with sleep apnea—a sleep disorder in which respiration is interrupted by long pauses during the sleep cycle—should not take Tranxene or other benzodiazepines. The respiratory depressant effect of benzodiazepines may further suppress the respiratory drive in these patients and put them at risk for respiratory depression and death.

Benzodiazepines may induce paradoxical *reactions* in susceptible individuals. Instead of the expected depressant effects, the medication may produce excitement, aggression, anger, uninhibited behavior, and rage in susceptible individuals. These reactions are more likely to occur in seniors, people with brain damage, and individuals with personality and impulse-control disorders.

Possible Drug Interactions

The significant drug interactions reported with Tranxene are summarized in the table below.

Central nervous system (CNS) depressants (e.g., alcohol, narcotics, barbiturates, hypnotics) and antihistamines	Combination of Tranxene with another CNS depressant may impair coordination and breathing and increase sedation.
Tagamet (cimetidine), Serzone (nefazodone), erythromycin, Biaxin (clarithromycin), TAO (troleandomycin), Antabuse (disulfiram), Prozac (fluoxetine), Luvox (fluvoxamine), isoniazid (e.g., INH), Diflucan (fluconazole), Nizoral (ketoconazole), Sporanox (itraconazole), Cipro (ciprofloxacin), protease inhibitors (e.g., Crixivan, Norvir, Fortovase), grapefruit juice	When any of these medications, as well as grapefruit juice, are taken concurrently with Tranxene, they can inhibit the metabolism of Tranxene and increase its levels. This may enhance the adverse effects (e.g., sedation, drowsiness, respiratory depression) of the benzodiazepine. If the medication is administered concurrently with Tranxene, a dosage reduction for Tranxene may be necessary.
Oral contraceptives	The metabolism of Tranxene may be increased when taken concurrently with oral contraceptives, which may decrease the effectiveness of Tranxene.

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Lanoxin (digoxin)

Tranxene may increase the blood levels of Lanoxin, and toxicity may occur. Patients taking Tranxene and Lanoxin should have their Lanoxin levels monitored closely.

Theophylline (e.g., Theo-Dur)

Theophylline-containing medications may diminish the therapeutic effect of Tranxene.

Patients taking Tranxene should not consume alcohol because the combination may increase sedation and drowsiness.

Use in Pregnancy and Breastfeeding: Pregnancy Category D

Benzodiazepines and their metabolites are known to cross the placenta and accumulate in the fetal circulation. They are associated with risk of congenital malformations when used during pregnancy, causing cleft lip and heart deformities in the fetus. Benzodiazepines should be avoided during pregnancy, particularly in the first trimester. The use of benzodiazepines during pregnancy should be considered only when the need for the medication outweighs its risk and alternative therapies have failed.

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

Overdose

Overdoses from oral ingestion of benzodiazepines alone are generally not fatal. Most fatalities reported with benzodiazepines involve multiple medication ingestion, particularly the combination of a benzodiazepine with CNS depressants, including alcohol, narcotics, and barbiturates.

Mild symptoms of benzodiazepine overdose include drowsiness, confusion, somnolence, tiredness, impaired coordination, clumsiness in walking (ataxia), and slow reflexes. Benzodiazepine overdose, when these agents are taken alone, is rarely fatal. When multiple medications are implicated in benzodiazepine overdose, severe symptoms include difficulty breathing, slowed heart rate, low blood pressure, loss of coordination, and loss of consciousness leading to coma and, potentially, death.

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

- If you miss a dose, take it as soon as possible, but 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.
- Tranxene may be taken with or without food.
- Tranxene may cause sedation and drowsiness, especially during initiation of therapy, and impair your alertness. Use caution when driving or performing tasks that require alertness. Avoid alcohol when taking Tranxene, because alcohol may intensify these effects.

