**Brands** • Navane

*see index for additional brand names*

**Generic?** Yes

**Class**
- Conventional antipsychotic (neuroleptic, thioxanthene, dopamine 2 antagonist)

**Commonly Prescribed for** (bold for FDA approved)
- Schizophrenia
- Other psychotic disorders
- Bipolar disorder

**How the Drug Works**
- Blocks dopamine 2 receptors, reducing positive symptoms of psychosis

**How Long Until It Works**
- Psychotic symptoms can improve within 1 week, but it may take several weeks for full effect on behavior

**If It Works**
- Most often reduces positive symptoms in schizophrenia but does not eliminate them
- Most schizophrenic patients do not have a total remission of symptoms but rather a reduction of symptoms by about a third
- Continue treatment in schizophrenia until reaching a plateau of improvement
- After reaching a satisfactory plateau, continue treatment for at least a year after first episode of psychosis in schizophrenia
- For second and subsequent episodes of psychosis in schizophrenia, treatment may need to be indefinite
- Reduces symptoms of acute psychotic mania but not proven as a mood stabilizer or as an effective maintenance treatment in bipolar disorder
- After reducing acute psychotic symptoms in mania, switch to a mood stabilizer and/or an atypical antipsychotic for mood stabilization and maintenance

**If It Doesn’t Work**
- Consider trying one of the first-line atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone, amisulpride, asenapine, iloperidone, lurasidone)
- Consider trying another conventional antipsychotic
- If 2 or more antipsychotic monotherapies do not work, consider clozapine

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- Augmentation of conventional antipsychotics has not been systematically studied
- Addition of a mood-stabilizing anticonvulsant such as valproate, carbamazepine, or lamotrigine may be helpful in both schizophrenia and bipolar mania
- Augmentation with lithium in bipolar mania may be helpful
- Addition of a benzodiazepine, especially short-term for agitation

**Tests**
- Since conventional antipsychotics are frequently associated with weight gain, before starting treatment, weigh all patients and determine if the patient is already overweight (BMI 25.0–29.9) or obese (BMI ≥30)
- Before giving a drug that can cause weight gain to an overweight or obese patient, consider determining whether the patient already has pre-diabetes (fasting plasma glucose 100–125 mg/dL), diabetes (fasting plasma glucose >126 mg/dL), or dyslipidemia (increased total cholesterol, LDL cholesterol, and triglycerides; decreased HDL cholesterol), and treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management
- Monitor weight and BMI during treatment
- Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications and when initiating or switching antipsychotics
- While giving a drug to a patient who has gained >5% of initial weight, consider evaluating for the presence of pre-diabetes, diabetes, or dyslipidemia, or consider switching to a different antipsychotic
- Monitoring elevated prolactin levels of dubious clinical benefit
- Patients with low white blood cell count (WBC) or history of drug-induced
leucopenia/neutropenia should have complete blood count (CBC) monitored frequently during the first few months and thiothixene should be discontinued at the first sign of decline of WBC in the absence of other causative factors

**SIDE EFFECTS**

**How Drug Causes Side Effects**
- By blocking dopamine 2 receptors in the striatum, it can cause motor side effects
- By blocking dopamine 2 receptors in the pituitary, it can cause elevations in prolactin
- By blocking dopamine 2 receptors excessively in the mesocortical and mesolimbic dopamine pathways, especially at high doses, it can cause worsening of negative and cognitive symptoms (neuroleptic-induced deficit syndrome)
- Anticholinergic actions may cause sedation, blurred vision, constipation, dry mouth
- Antihistaminic actions may cause sedation, weight gain
- By blocking alpha 1 adrenergic receptors, it can cause dizziness, sedation, and hypotension
- Mechanism of weight gain and any possible increased incidence of diabetes or dyslipidemia with conventional antipsychotics is unknown

**Notable Side Effects**
- ∗ Neuroleptic-induced deficit syndrome
- ∗ Akathisia
- ∗ Extrapyramidal symptoms, parkinsonism, tardive dyskinesia
- ∗ Galactorrhea, amenorrhea
- ∗ Sedation
- ∗ Dry mouth, constipation, vision disturbance, urinary retention
- ∗ Hypotension, tachycardia
- ∗ Rare fine lenticular pigmentation

**Life-Threatening or Dangerous Side Effects**
- ∗ Rare neuroleptic malignant syndrome
- ∗ Rare seizures
- ∗ Rare blood dyscrasias
- ∗ Rare hepatic toxicity
- ∗ Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis

**Weight Gain**
- ∗ Reported but not expected

**Sedation**
- ∗ Occurs in significant minority

**What to Do About Side Effects**
- Wait
- Wait
- For motor symptoms, add an anticholinergic agent
- For sedation, take at night
- Reduce the dose
- Switch to an atypical antipsychotic
- Weight loss, exercise programs, and medical management for high BMIs, diabetes, dyslipidemia

**Best Augmenting Agents for Side Effects**
- Benztpine or trihexyphenidyl for motor side effects
- Sometimes amantadine can be helpful for motor side effects
- Benzodiazepines may be helpful for akathisia
- Many side effects cannot be improved with an augmenting agent

**DOSING AND USE**

**Usual Dosage Range**
- 15–30 mg/day

**Dosage Forms**
- Capsule 2 mg, 5 mg, 10 mg

**How To Dose**
- Initial 5–10 mg/day; maximum dose generally 60 mg/day; higher doses may be given in divided doses

**Dosing Tips**
- When thiothixene is dosed too high, it can induce or worsen negative symptoms of schizophrenia
• Lower doses may provide the best benefit with fewest side effects in patients who respond to low doses
• Treatment should be suspended if absolute neutrophil count falls below 1,000/mm³

**Overdose**
• Muscle twitching, sedation, dizziness, CNS depression, rigidity, weakness, torticollis, dysphagia, hypotension, coma

**Long-Term Use**
• Some side effects may be irreversible (e.g., tardive dyskinesia)

**Habit Forming**
• No

**How to Stop**
• Slow down-titration (over 6–8 weeks), especially when simultaneously beginning a new antipsychotic while switching (i.e., cross-titration)
• Rapid discontinuation may lead to rebound psychosis and worsening of symptoms
• If antiparkinson agents are being used, they should be continued for a few weeks after thiothixene is discontinued

**Pharmacokinetics**
• Initial elimination half-life approximately 3.4 hours
• Terminal elimination half-life approximately 34 hours

**Drug Interactions**
• Respiratory depression may occur when thiothixene is combined with lorazepam
• Additive effects may occur if used with CNS depressants
• May decrease the effects of levodopa, dopamine agonists
• Some patients taking a neuroleptic and lithium have developed an encephalopathic syndrome similar to neuroleptic malignant syndrome
• Combined use with epinephrine may lower blood pressure
• May increase the effects of antihypertensive drugs except for guanethidine, whose antihypertensive actions thiothixene may antagonize

**Other Warnings/Precautions**
• If signs of neuroleptic malignant syndrome develop, treatment should be immediately discontinued
• Use cautiously in patients with alcohol withdrawal or convulsive disorders because of possible lowering of seizure threshold
• Antiemetic effect can mask signs of other disorders or overdose
• Do not use epinephrine in event of overdose, as interaction with some pressor agents may lower blood pressure
• Use cautiously in patients with glaucoma, urinary retention
• Observe for signs of ocular toxicity (pigmentary retinopathy, lenticular pigmentation)
• Avoid extreme heat exposure
• Do not use in Parkinson’s disease or Lewy body dementia

**Do Not Use**
• If patient has CNS depression, is in a comatose state, has circulatory collapse, or there is presence of blood dyscrasias
• If there is a proven allergy to thiothixene

**SPECIAL POPULATIONS**

**Renal Impairment**
• Use with caution

**Hepatic Impairment**
• Use with caution

**Cardiac Impairment**
• Thiothixene may cause or aggravate EKG changes

**Elderly**
• Some patients may tolerate lower doses better
• Although conventional antipsychotics are commonly used for behavioral disturbances in dementia, no agent has been approved for treatment of elderly patients with dementia-related psychosis
• Elderly patients with dementia-related psychosis treated with antipsychotics are at an increased risk of death compared to placebo, and also have an increased risk of cerebrovascular events
**Children and Adolescents**
- Safety and efficacy have not been established in children under age 12
- Generally consider second-line after atypical antipsychotics

**Pregnancy**
- Controlled studies have not been conducted in pregnant women
- There is a risk of abnormal muscle movements and withdrawal symptoms in newborns whose mothers took an antipsychotic during the third trimester; symptoms may include agitation, abnormally increased or decreased muscle tone, tremor, sleepiness, severe difficulty breathing, and difficulty feeding
- Reports of extrapyramidal symptoms, jaundice, hyperreflexia, hyporeflexia in infants whose mothers took a phenothiazine during pregnancy
- Psychotic symptoms may worsen during pregnancy and some form of treatment may be necessary
- Atypical antipsychotics may be preferable to conventional antipsychotics or anticonvulsant mood stabilizers if treatment is required during pregnancy
- Thiothixene should generally not be used during the first trimester
- Thiothixene should be used during pregnancy only if clearly needed

**Breast Feeding**
- Unknown if thiothixene is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- *Recommended either to discontinue drug or bottle feed*

**Potential Disadvantages**
- Patients with tardive dyskinesia
- Children
- Elderly

**Primary Target Symptoms**
- Positive symptoms of psychosis
- Negative symptoms of psychosis

**Pearls**
- *Although not systematically studied, may cause less weight gain than other antipsychotics*
- Conventional antipsychotics are less expensive than atypical antipsychotics
- Patients have very similar antipsychotic responses to any conventional antipsychotic, which is different from atypical antipsychotics where antipsychotic responses of individual patients can occasionally vary greatly from one atypical antipsychotic to another
- Patients with inadequate responses to atypical antipsychotics may benefit from a trial of augmentation with a conventional antipsychotic such as thiothixene or from switching to a conventional antipsychotic such as thiothixene
- However, long-term polypharmacy with a combination of a conventional antipsychotic such as thiothixene with an atypical antipsychotic may combine their side effects without clearly augmenting the efficacy of either
- For treatment-resistant patients, especially those with impulsivity, aggression, violence, and self-harm, long-term polypharmacy with 2 atypical antipsychotics or with 1 atypical antipsychotic and 1 conventional antipsychotic may be useful or even necessary while closely monitoring
- In such cases, it may be beneficial to combine 1 depot antipsychotic with 1 oral antipsychotic
- Although a frequent practice by some prescribers, adding 2 conventional antipsychotics together has little rationale and may reduce tolerability without clearly enhancing efficacy

**Potential Advantages**
- For patients who do not respond to other antipsychotics
Suggested Reading
