
THIORIDAZINE (Mellaril) Fact Sheet [G]

Bottom Line:

Thioridazine prolongs the cardiac QT interval more than any other antipsychotic, rendering it too risky to use for the majority of patients.

FDA Indications:

Schizophrenia (not for first-line use).

Off-Label Uses:

Anxiety, insomnia.

Dosage Forms:

Tablets (G): 10 mg, 25 mg, 50 mg, 100 mg.

Dosage Guidance:

Start 50–100 mg TID, ↑ by 50–100 mg/day increments every three to seven days and adjust to lowest effective dose. Dose range 200–800 mg/day divided BID–QID; max FDA-approved dose is 800 mg/day due to ocular pigmentation at high doses.

Monitoring: ECG if cardiac disease.

Cost: \$

Side Effects:

- Most common: EPS, headache, sedation, drowsiness, dry mouth, constipation, blurred vision, dizziness, prolactin elevation (sexual side effects, amenorrhea, galactorrhea).
- Serious but rare: QT prolongation and torsades de pointes (highest risk of all antipsychotics); ocular pigmentation and degenerative retinopathies.
- Pregnancy/breastfeeding: Some risk in pregnancy; relatively safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 receptor antagonist.
- Metabolized primarily by CYP2D6; $t_{1/2}$: 24 hours. May inhibit CYP2D6. Poor metabolizers of CYP2D6 metabolize the drug more slowly; may have increased effects.
- CYP2D6 inhibitors (eg, fluoxetine, paroxetine, quinidine) may increase thioridazine levels. Caution with substrates of CYP2D6 as thioridazine may increase their levels and effects.

Clinical Pearls:

- Thioridazine is a low-potency first-generation antipsychotic; this leads to less EPS and to more sedation, orthostasis, and anticholinergic side effects compared to high-potency agents (eg, haloperidol, fluphenazine).
- Efficacy has not been studied in refractory schizophrenia, but thioridazine is indicated only for and should be reserved for use only in patients who have failed to respond to other medications. This is due to the significant risks associated with thioridazine, particularly QT prolongation.

Fun Fact:

Thioridazine can kill antibiotic-resistant bacteria such as *Staphylococcus aureus* (including MRSA) and extensively drug-resistant *Mycobacterium tuberculosis*. Researchers are studying how thioridazine does this (latest studies show a weakening of bacterial cell walls) in order to develop drugs that can target resistant bacteria.