PERPHENAZINE (Trilafon) Fact Sheet [G]

Bottom Line:

Perphenazine, first introduced in 1957, is an older first-generation agent that enjoyed a big boost in popularity after the 2005 CATIE trial found it to be as effective as most second-generation agents with minimal weight gain or metabolic problems. It has become a favorite go-to antipsychotic for many clinicians—an effective, well-tolerated, and inexpensive alternative to second-generation antipsychotics.

FDA Indications:

Schizophrenia (children ≥12 years); severe nausea and vomiting.

Off-Label Uses:

Bipolar disorder; behavioral disturbances; impulse control disorders.

Dosage Forms:

Tablets (G): 2 mg, 4 mg, 8 mg, 16 mg.

Dosage Guidance:

- Schizophrenia: Start 4–8 mg TID (8–16 mg BID–QID for hospitalized patients); adjust to lowest effective dose. Dose range 8–16 mg BID–QID; max FDA-approved dose for non-hospitalized patients is 24 mg/day, but hospitalized psychotic patients may be dosed up to 64 mg/day.
- Dose timing: Most patients take perphenazine BID, and the usual strategy is to give a larger amount at night due to sedation. If needed, you can dose it all at HS.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:

- Most common: EPS, headache, drowsiness, dry mouth, prolactin elevation (sexual side effects, amenorrhea, galactorrhea).
- Serious but rare: Tachycardia (especially with sudden marked increase in dose).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 receptor antagonist.
- Metabolized primarily by CYP2D6; t ½: 9–12 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 perphenazine levels. Caution with substrates of 2D6 as perphenazine may increase their levels and effects.

Clinical Pearls:

- Perphenazine is an intermediate-potency first-generation antipsychotic; this leads to less EPS compared to high-potency agents (eg, haloperidol, fluphenazine) and to less sedation, less orthostasis, and fewer anticholinergic side effects compared to low-potency agents (eg, chlorpromazine).
- Fewer metabolic effects (weight gain, glucose, lipids) than some antipsychotics.
- Based on an 18-month randomized trial of 1,493 patients with schizophrenia (CATIE trial), perphenazine appears similar in efficacy and EPS compared to second-generation antipsychotics (olanzapine, quetiapine, risperidone, ziprasidone).

Fun Fact:

Perphenazine has long been available in a formulation with amitriptyline (a tricyclic antidepressant) called Triavil. This combination antipsychotic/antidepressant was first available in 1965, foreshadowing the next such combination drug (Symbyax) by 38 years.