PERPHENAZINE (Trilafon) Fact Sheet [G]

BOTTOM LINE:
Well-tolerated and inexpensive alternative to second-generation antipsychotics, especially when trying to avoid EPS and metabolic side effects; however, efficacy data in kids are more limited compared to newer agents.

PEDIATRIC FDA INDICATIONS:
Schizophrenia (12+ years).

ADULT FDA INDICATIONS:
Schizophrenia; 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.

PEDIATRIC DOSAGE GUIDANCE:
Ages >12: Start 4 mg BID; 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 (adults).

MONITORING: Prolactin, lipids, glucose, EPS, abnormal movements.

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).

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, duloxetine, quinidine) may increase perphenazine levels. Caution with substrates of 2D6 as perphenazine may increase their levels and effects.

EVIDENCE AND CLINICAL PEARLS:
- No clinical trial data in children or adolescents with schizophrenia, but FDA indicated and used in kids by some clinicians based on experience as well as results from efficacy studies in adults.
- Based on an 18-month randomized trial of 1,493 adult patients with schizophrenia (CATIE trial), perphenazine appears similar in efficacy and EPS compared to second-generation antipsychotics (olanzapine, quetiapine, risperidone, ziprasidone).
- Perphenazine is an intermediate-potency conventional (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.

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.