MIRTAZAPINE (Remeron) Fact Sheet [G]

BOTTOM LINE:
Second- or third-line agent due to lack of data. Weight gain and sedation may limit its use in many kids. It may be useful in depressed patients with anxiety or insomnia, those who have had sexual side effects with other antidepressants, and those who may benefit from appetite stimulation.

PEDIATRIC FDA INDICATIONS:
None.

ADULT FDA INDICATIONS:
Major depression.

OFF-LABEL USES:
Panic disorder; PTSD; GAD; insomnia; nausea; appetite stimulant; methamphetamine use disorder.

DOSAGE FORMS:
- **Tablets (G):** 7.5 mg, 15 mg, 30 mg, 45 mg.
- **Orally disintegrating tablets (G):** 15 mg, 30 mg, 45 mg.

PEDIATRIC DOSAGE GUIDANCE:
- Very limited dosing guidance in children and adolescents.
- Start 7.5 mg or 15 mg QHS, ↑ by 15 mg/day every one to two weeks. Max 45 mg/day.

MONITORING: Weight.

COST: $

SIDE EFFECTS:
- Most common: Somnolence, increased appetite, weight gain, perhaps offset by stimulating effects of higher dosages.
- Serious but rare: Agranulocytosis or severe neutropenia (with or without infection) reported very rarely.

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:
- Noradrenergic (via central presynaptic alpha-2 adrenergic receptor antagonist activity) and specific serotonergic (via postsynaptic 5HT2 and 5HT3 antagonist effects) antidepressant.
- Metabolized primarily through CYP1A2, 2D6, and 3A4; t ½: 20–40 hours.
- Avoid use with MAOIs. Caution with inducers of 1A2 or 3A4 (eg, carbamazepine), which could reduce efficacy of mirtazapine.

EVIDENCE AND CLINICAL PEARLS:
- Two unpublished eight-week randomized trials of mirtazapine 15–45 mg/day in outpatient children and adolescents with depression found no significant reduction in depressive symptoms compared to placebo.
- One open-label 85-day study of mirtazapine 30–45 mg/day in 24 adolescents with depression showed marked efficacy on depression, anxiety, and sleep as well as good tolerability (sedation, weight gain, and increased appetite were most common side effects).
- Twenty-six subjects with pervasive developmental disorder (PDD) ages 4–24 years were treated with mirtazapine 7.5–45 mg/day in an open-label trial, showing only modest benefit for symptoms associated with autism and other PDD.
- If patients experience too much sedation at initial lower dose, increase dose; mirtazapine has increased noradrenergic effect relative to antihistaminergic effect at higher doses.
- Two small studies in adult men with methamphetamine use disorder have shown promising effects with reducing use.

FUN FACT:
Esmirtazapine, the (S)-enantiomer, was under development for the treatment of insomnia and hot flashes associated with menopause, but the company pulled the plug in 2010.