RAMELTEON (Rozerem) Fact Sheet [G]

Bottom Line:
Ramelteon is a melatonin receptor agonist. Compared to other hypnotics, ramelteon poses a lower risk for respiratory depression and hangover effect (morning grogginess). It's a good agent to have in your bag of tricks, but consider the possibility of rare hormonal effects. Also consider that over-the-counter melatonin (which ramelteon mimics) may do the same job, possibly at a lower price.

FDA Indications:
Insomnia (sleep onset).

Off-Label Uses:
Jet lag; shift-work sleep disorder.

Dosage Forms:
Tablets (G): 8 mg.

Dosage Guidance:
Start, target, and maximum dose 8 mg QHS, 30 minutes before bedtime. Avoid administering with high-fat meal (delays therapeutic effect by 45 minutes).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Headache, somnolence, fatigue, dizziness, nausea.
- Serious but rare: Anaphylaxis, angioedema, complex sleep-related behavior (sleep driving, cooking, eating, phone calls), increased prolactin, abnormal cortisol or testosterone levels.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Melatonin-1 and melatonin-2 receptor agonist.
- Metabolized primarily through CYP1A2 (major), and to a lesser extent CYP2C9 and CYP3A4; t ½: 1–2.6 hours.
- Avoid concomitant use with CNS depressants (additive effects). Exercise caution in patients taking potent CYP1A2 inhibitors (eg, fluvoxamine), which could increase ramelteon's effects.

Clinical Pearls:
- Because ramelteon's mechanism of action relates to melatonin receptors and regulation of circadian rhythms, it does not cause patients to "feel" sedated. Often patients say that it doesn't start working for several days—however, clinical trials have shown efficacy from the first night of use. It's good to warn patients about this ahead of time, or they may conclude it's ineffective after a single night and stop using it.
- No evidence of abuse potential or physical dependence.
- Hormonal alterations occur very rarely and usually with high-dose (16 mg in one study) and longer-term use (six to 12 months). If unexplained amenorrhea, galactorrhea, decreased libido, or fertility problems occur, consider evaluating patient's prolactin or testosterone levels.

Fun Fact:
Another melatonin agonist, agomelatine, has been studied as an antidepressant, partly because circadian rhythms are disrupted in depression. It is approved overseas, but the manufacturer scrapped its development in the US.