MELATONIN Fact Sheet [G]

Bottom Line:
Melatonin is secreted by the pineal gland, and its rise in serum levels correlates with the time course of natural sleep. Short-term melatonin treatment appears to only modestly reduce the time it takes to fall asleep (about 12 minutes, which might not be considered clinically relevant) and does not appear to significantly improve overall sleep time. However, some patients report minor improvement in subjective feelings of sleep quality. It is cheaper than the melatonin agonist ramelteon (Rozerem); however, like ramelteon, it lacks good long-term safety data, especially with regard to effects on hormones.

FDA Indications:
None.

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

Dosage Forms:
Supplied over the counter (OTC) in various forms including liquid, tablet, capsule, sublingual, and time-release formulations; usually in 0.5 mg, 1 mg, 2.5 mg, 3 mg, 5 mg, and 10 mg.

Dosage Guidance:
- Insomnia (adults): 0.5–20 mg in early evening. Emerging data suggest lower doses are effective; start low (0.5–1 mg) and gradually increase to desired effect ("normal" melatonin levels vary widely among individuals, and the same dose can induce different levels depending on age or health).
- Jet lag: 1–3 mg on day of departure at a time that corresponds to the anticipated bedtime at arrival destination, followed by 1–3 mg at bedtime for next three to five days.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Generally well tolerated in the short term. Drowsiness, headaches, and dizziness most common but at similar rates to placebo; next-day grogginess or irritability (higher doses); vivid dreams or nightmares (higher doses).
- Serious but rare: No serious side effects reported; however, long-term human studies have not been conducted. Theoretically, melatonin may alter other hormones (inhibiting ovulation in women and gonadal development in children and adolescents); avoid use in women who are pregnant or are attempting to become pregnant, and use caution in children.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Melatonin receptor agonist.
- Metabolized primarily through CYP1A2, may inhibit CYP1A2; t ½: 35–50 minutes.
- Some suggest melatonin may reduce glucose tolerance and insulin sensitivity and may increase efficacy of calcium channel blockers for blood pressure.

Clinical Pearls:
- Melatonin is secreted from the pineal gland in a 24-hour circadian rhythm. It rises at sunset and peaks in the middle of the night, regulating the normal sleep/wake cycle.
- Melatonin should only be taken in its synthetic form; the "natural" form comes from ground-up cow pineal glands and may spread disease (eg, mad cow disease).
- Melatonin taken at bedtime doesn't seem to affect nocturnal sleep. Taken in the early evening, it appears to be similar to temazepam in hypnotic effect.
- Although melatonin products have been available OTC in the US since the mid-1990s, many countries require a prescription, and some do not permit its sale. Of note, several studies over the years have found the melatonin content of supplements on the market varies widely from what is listed on the label, with most containing 20%, 30%, 50%, or even 250% more than listed on the label.
- The American Academy of Sleep Medicine took a stand in 2022 and advised parents to seek medical advice before giving melatonin to children and adolescents given the increase in associated emergency room visits and calls to poison centers.

Fun Fact:
Foods containing melatonin include cherries, bananas, grapes, rice, cereals, herbs, olive oil, wine, and beer.