TASIMELTEON (Hetlioz) Fact Sheet [G]

Bottom Line:
Tasimelteon is a melatonin receptor agonist approved for non-24-hour sleep-wake disorder (N24SWD), which occurs primarily in blind people. Due to its high price (even for the new generic version), you may want to consider ramelteon instead. While ramelteon hasn't been studied in patients with N24SWD, it's reasonable to try because it is so similar pharmacologically yet much more affordable.

FDA Indications:
N24SWD.

Off-Label Uses:
None recommended; potentially may be used for insomnia, jet lag, shift-work sleep disorder.

Dosage Forms:
- **Capsules (G):** 20 mg.
- **Oral suspension (Hetlioz LQ):** 4 mg/mL.

Dosage Guidance:
Start 20 mg QHS at the same time every night.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $$$$$

Side Effects:
- Most common: Headache, increased LFTs, nightmares or unusual dreams.
- Serious but rare: None reported.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Melatonin receptor agonist (at both MT1 and MT2 receptors).
- Metabolized primarily by CYP1A2 and 3A4; t ½: 1 hour.
- Smoking may reduce tasimelteon levels by 40% and lower its efficacy. Caution with 3A4 inhibitors and inducers.

Clinical Pearls:
- Like ramelteon, tasimelteon binds melatonin receptors. Tasimelteon has greater affinity for the MT2 receptor, whereas ramelteon has greater affinity for the MT1 receptor. Both are fairly non-selective, though (meaning they both bind to both MT1 and MT2), so making a clinical distinction is difficult.
- Approved as an orphan drug (a drug for rare diseases that affect fewer than 200,000 people).
- N24SWD is a circadian rhythm disorder commonly seen in blind patients with no light perception. Due to absence of environmental input, these patients experience a constant gradual shift of their sleep cycles by roughly 30 minutes per day, realigning with the 24-hour clock only once every 48 days.
- Should be used daily to maintain therapeutic effect.

Fun Fact:
The advocacy group Public Citizen accused the FDA of allowing tasimelteon's manufacturer to list N24SWD as the drug's indication without specifying that it was for use in totally blind people with N24SWD, the originally filed indication for consideration. Rather than correcting the error and adjusting the drug's label, the FDA sent out a press release officially expanding the approved indication to any patients with N24SWD (there are sighted individuals with this disorder, likely with a genetic basis).