SUVOREXANT (Belsomra) Fact Sheet

Bottom Line:

Suvorexant is an orexin receptor antagonist, and as such it treats insomnia differently from existing agents (though lemborexant and daridorexant have since followed in its footsteps). Other than a new mechanism of action, suvorexant doesn't have any clear advantages. It is no more effective than benzos or Z-drugs, and it has a similar abuse liability. We're concerned that next-day impairment is a potential side effect at the highest approved dose of 20 mg, particularly since sleepless patients may decide on their own to take even higher doses. It's not a first-line hypnotic.

FDA Indications:

Insomnia (sleep onset and sleep maintenance).

Dosage Forms:

Tablets: 5 mg, 10 mg, 15 mg, 20 mg.

Dosage Guidance:

Start 10 mg QHS, 30 minutes before bedtime and with at least seven hours remaining before planned awakening time. If tolerated but not effective, may increase to max 20 mg QHS. For more rapid onset, patients should wait at least an hour after a meal before taking it. Avoid administering within an hour of a high-fat meal (delays therapeutic effect by about 1.5 hours).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $$$$

Side Effects:

- Most common: Somnolence, headache, abnormal dreams, dry mouth.
- Serious but rare: Impaired alertness and motor coordination, including impaired driving; dose-related worsening depression or suicidal ideation; sleep paralysis (inability to speak or move for up to a few minutes during the sleep-wake transition), hypnagogic/hypnopompic hallucinations (including vivid and disturbing perceptions), and cataplexy-like symptoms (leg weakness for seconds up to a few minutes both in the nighttime and the daytime) reported, especially at higher doses.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- "DORA" or dual orexin (OX1 and OX2) receptor antagonist.
- Metabolized primarily through CYP3A4, with minor contribution from 2C19; t ½: 12 hours.
- Caution with CYP3A4 inhibitors and inducers; suvorexant dose adjustment recommended. Caution with alcohol and other CNS depressants.

Clinical Pearls:

- Suvorexant, like other DORAs, has a unique mechanism of action. Unlike other hypnotics, it does not act by stimulating GABA or melatonin receptors or by blocking histamine. Instead, suvorexant blocks orexin receptors (orexins are neurotransmitters that promote wakefulness).
- Schedule IV controlled substance. One study found that drug abusers "liked" suvorexant as much as Ambien.
- Suvorexant is contraindicated in patients with narcolepsy.
- The incidence of suicidal ideation reported with suvorexant seemed to be dose related, unlike lemborexant. However, all patients taking suvorexant should be monitored for suicidality, particularly those with depression.
- Risk of next-day impairment increases with dose; caution patients taking 20 mg against next-day driving and other activities requiring mental alertness.
- Suvorexant's package label was updated in 2020 to include findings on its use in 285 patients with mild to moderate Alzheimer's disease and insomnia. Suvorexant improved total sleep time and was well tolerated, with somnolence (4% compared to 1% for placebo), dry mouth (2% compared to 1% for placebo), and falls (2% compared to 0% for placebo) as the most common side effects.

Fun Fact:

Merck expected to gain FDA approval for suvorexant in summer 2013. However, the FDA expressed concerns about safety with the proposed 30–40 mg dosing range and denied approval. It was finally approved in August 2014 at lower doses.