LEMBOREXANT (Dayvigo) Fact Sheet

Bottom Line:
Lemborexant was the second orexin receptor antagonist to win FDA approval. 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 10 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.

Dosage Guidance:
Start 5 mg QHS, 30 minutes before bedtime and at least seven hours before planned awakening time. If tolerated but not effective, may increase to max 10 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; 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 CYP3A5; t ½: 17–19 hours.
- Caution with CYP3A4 inhibitors and inducers; lemborexant dose adjustment recommended. Caution with alcohol and other CNS depressants.

Clinical Pearls:
- Lemborexant, 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, lemborexant blocks orexin receptors (orexins are neurotransmitters that promote wakefulness).
- Schedule IV controlled substance. Data in recreational drug users found they "liked" lemborexant more than placebo and as much as zolpidem and suvorexant.
- Lemborexant is contraindicated in patients with narcolepsy.
- Incidence of suicidal ideation or behavior was 0.3% (10 mg) and 0.4% (5 mg) compared to 0.2% in patients taking placebo. Closely monitor and assess patients for suicidality, especially those with depression.
- Risk of next-day impairment increases with dose; caution patients taking 10 mg against next-day driving and other activities requiring mental alertness.

Fun Fact:
Eisai, the drug company that pursued FDA approval and now markets Dayvigo, bought the rights to this medication in 2015 from Purdue Pharma, the company that brought us OxyContin and pleaded guilty to criminal charges related to the opioid epidemic.