

Optimizing Insomnia Therapy

Overview

Effective insomnia management involves accurate diagnosis, identifying comorbidities, selecting appropriate non-pharmacologic and pharmacologic interventions, and ensuring safe use of hypnotics. Lemborexant, a dual orexin receptor antagonist (DORA), represents an alternative to benzodiazepines (BZDs) and Z-drugs and has demonstrated efficacy in clinical studies. Data from short- and long-term trials support its safety and tolerability profile, including preservation of sleep architecture and low observed rates of withdrawal symptoms.^{1,2}

Indication

Lemborexant (DAYVIGO™) is indicated for the treatment of insomnia characterized by difficulty falling asleep and/or staying asleep.^{3,8}

The recommended dose is 5 mg nightly, taken immediately before bedtime with at least 7 hours available for sleep. Avoid taking with or immediately after meals, as this may delay onset.³

Precautions

Patients Requiring Caution

Use with increased vigilance in patients with:³

- Mild to moderate hepatic impairment (max 5 mg)
- Severe renal impairment
- Organic brain disorders
- Moderate–severe respiratory impairment (non-OSA/COPD)
- Moderate–severe OSA or COPD (long-term safety not established)

Important Safety Notes

Residual next-day impairment may occur (somnolence, reduced attention, slowed reflexes). Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms may rarely occur. Complex sleep behaviors (e.g., sleepwalking, sleep-driving) require immediate discontinuation.³

Monitor for worsening depression or suicidal ideation.³

Contraindications

Lemborexant should not be used in patients with:³

- Narcolepsy
- Known hypersensitivity to lemborexant
- Severe hepatic impairment
- Concomitant use with strong or moderate CYP3A inhibitors/inducers

Drug Interactions

CYP3A-Mediated Interactions

Lemborexant is mainly metabolized by CYP3A.³

Drug Category	Interaction	Recommendation
Strong/moderate CYP3A inhibitors (e.g., itraconazole)	Markedly increased lemborexant exposure	Contraindicated
Strong/moderate CYP3A inducers (e.g., rifampicin, phenytoin)	Greatly decreased exposure and efficacy	Contraindicated
Weak CYP3A inhibitors	Increased exposure	Max dose 5 mg once nightly

Other Interactions

- CYP2B6 substrates (bupropion, methadone): DAYVIGO™ may decreased their effect; consider dose adjustment.
- CNS depressants (benzodiazepines, opioids, antipsychotics, alcohol): additive CNS depression; dosage adjustment may be needed.^{3,8.}
- Alcohol significantly increased lemborexant exposure (Cmax +35% / AUC +70%) and impairs cognition; avoid use.

Common Side Effects

Across 884 subjects, adverse events occurred in 28.2%, most commonly:³

- Somnolence (10.7%)
- Headache (4.2%)
- Malaise (3.1%)

Less frequent effects include dizziness, sleep paralysis, abnormal dreams/nightmares, hallucinations, nausea, dry mouth, abdominal pain, palpitations, parasomnias, and disturbance in attention.³

Long-term clinical trials with treatment durations of up to 12 months demonstrated maintained efficacy and a safety profile consistent with shorter-term use, with infrequent and generally mild withdrawal symptoms and no evidence of clinically meaningful rebound insomnia at the population level..^{2,4}

Switching From Benzodiazepines to Lemborexant

Switching from BZDs to lemborexant is appropriate when patients experience insufficient benefit, BZD-related risks (falls, dependence, cognitive impairment), or require safer long-term therapy.^{5,6}

In clinical studies, lemborexant was associated with low withdrawal symptom scores (T-BWSQ <3), stable efficacy over 12 months, and no evidence of clinically significant rebound insomnia following discontinuation.^{2,4}

Recommended Switching Methods

1. Direct Switch

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Best for: low doses, short use (<2–4 weeks), low dependence risk

How:

- Stop BZD
- Start Lemborexant 5 mg the same night

Evidence:

Direct switching was well-tolerated in psychiatric populations with no major withdrawal⁵

2. Add-On Then Taper (Preferred Method)

Best for: long-term use, medium to high doses, older adults, anxiety-prone patients

How:

- Start Lemborexant 5 mg at bedtime
- Maintain current BZD dose for 3–7 nights
- Begin taper 10–25% per week
- Discontinue BZD once minimal dose reached

Evidence:

Stabilizing sleep with LEM first reduces rebound insomnia and improves taper success (SLIM study; Japanese Expert Consensus).^{5,7}

3. Taper First then Start Lemborexant (“Taper & Wait”)

Best for: high BZD doses, short-acting BZD (alprazolam), or strong withdrawal history

How:

- Gradually taper BZD to low dose
- Stop BZD for 1–2 nights
- Initiate Lemborexant 5 mg

Evidence:

Consistent with ASAM benzodiazepine tapering guidelines and Petunjuk Teknis.^{8,9}

BZD Tapering Principles

- Reduce 5–25% every 1–2 weeks; slower for high doses or long-term use
- Consider switching to a long-acting BZD (diazepam) for smoother taper
- Avoid abrupt cessation (risk of seizures, severe withdrawal)
- Educate patients on temporary rebound insomnia
- Monitor for anxiety, agitation, palpitations, severe insomnia⁹

Why Lemborexant Is a Suitable Switch Target (Evidence)

Multiple trials & systematic reviews report:^{1,2,4,5}

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- Improved sleep onset & maintenance vs placebo and zolpidem
- Stable long-term efficacy up to 12 months
- Low observed withdrawal symptoms and no evidence of clinically meaningful rebound insomnia in clinical studies
- Preserved sleep architecture (Increased NREM & REM)
- A favorable safety profile in older adults, including assessments of balance, cognition, and driving performance
- Lower observed misuse potential compared with benzodiazepines and Z-drugs, based on available clinical and post-marketing data

References:

1. Rosenberg, R. et al. (2019). Comparison of lemborexant with placebo and zolpidem ER in older adults with insomnia disorder. JAMA Network Open.
2. Kärppä, M. et al. (2020). Long-term efficacy and tolerability of lemborexant in adults with insomnia disorder (SUNRISE-2). Sleep.
3. DAYVIGO™ Product Information Leaflet (2025). PT Eisai Indonesia
4. Dash, A. et al. (2022). Efficacy and safety of lemborexant over 12 months in Asian adults. Sleep Med X.
5. Horikoshi, S. et al. (2023). Switching to lemborexant for the management of insomnia in mental disorders (SLIM Study). J Clin Sleep Med.
6. De Crescenzo, F. et al. (2022). Comparative effects of pharmacological interventions for insomnia. The Lancet.
7. Takaesu, Y. et al. (2023). Japanese Expert Consensus on Treatment Strategy for Insomnia. Frontiers in Psychiatry.
8. Perhimpunan Dokter Spesialis Kedokteran Jiwa Indonesia (PDSKJI). (2025). Petunjuk teknis penggunaan lemborexant untuk penanganan insomnia di Indonesia.
9. American Society of Addiction Medicine (2024). Benzodiazepine Tapering Guidelines.