Transitioning to Lemborexant for Insomnia Therapy: Practical Strategies for Clinicians

WEBINAR HIGHLIGHTS

Held in September 2024, this event focused on the evidence for de-prescribing benzodiazepines and Z-drugs, and the rationale for initiating and transitioning to orexin receptor antagonist therapy with Lemborexant in the management of insomnia. The webinar was chaired by **Dr Ng Beng Yeong**, Consultant Psychiatrist and Director of the Ng Beng Yeong Psych Medicine Clinic Ltd in Singapore.

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Starting Lemborexant, and Switching From Sedative-Hypnotics To Lemborexant: When, Why And How?

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Challenges of benzodiazepine and Z-drug misuse: A case for de-prescribing

It is common among many of Dr Ram's patients, particularly those middle-aged, to misuse benzodiazepines and Z-drugs in a desperate attempt to improve their sleep. As a result, his patients often seek higher doses or they frequently transition between various hypnotics, leading to tolerance and ongoing dissatisfaction with their medications. Even with increased doses, their sleep quality can remain poor, which prompts Dr Ram to consider de-prescribing benzodiazepines and Z-drugs from these patients.

Dr Ram's general strategies for switching hypnotics

Direct Switch: The first insomnia medication is discontinued, and the new medication is initiated the next day at the standard therapeutic dose. Dr Ram states that this method can potentially carry a greater risk of withdrawal symptoms.

Cross Taper: This involves gradually reducing the dose of the first insomnia medication while introducing a new medication at a lower or staggered dose, which is then slowly increased.

Taper and Wait: This method slowly tapers off the current medication until it is fully discontinued, followed by a waiting period of 1–2 days before starting the new insomnia medication. This pause allows time for the previous medication, especially those with longer half-lives, to clear from the system.

Expert recommendations on tapering benzodiazepines

A 2023 review article, authored by five US-based sleep experts, examined the literature on de-prescribing, tapering, and switching insomnia medications, and evaluated the quality of the evidence.[1] The experts collectively recommended that benzodiazepines should generally be tapered when discontinuing or transitioning to another insomnia medication.[1] **A reduction of 10–25% over weeks to months ensures a smooth and safe transition**.[1] For benzodiazepines with short half-lives or for patients on higher doses, a more cautious approach is needed, while patients on benzodiazepines with longer half-lives or lower doses can transition more quickly.[1]

In addition, trials included in Cochrane reviews have indicated that psychosocial interventions, such as cognitive-behavioral therapy (CBT) and motivational interviewing, can improve the effectiveness of benzodiazepine tapering.[2]

Recommended Z-drug de-prescribing method

The review article states that discontinuing Z-drugs is typically manageable with a gradual delay, and it is recommended that **a pause of 1-2 days in administration is applied before the next insomnia therapy is initiated**.[1] However, for supratherapeutic doses, a 25% reduction per week over four weeks is advised.[1]

Why transition to Lemborexant?

Approximately 50–60% of Dr Ram's patients on benzodiazepines and Z-drugs successfully transition to Lemborexant. Dr Ram considers Lemborexant to be a "true game changer" in the pharmacological treatment of insomnia, due to its highly specific antagonism of orexin receptors,[3] distinguishing it from benzodiazepines and Z-drugs.

In his experience, Lemborexant's selectivity of orexin leads to a much more favorable side effect profile, with cognitive impairments, such as the sluggishness commonly associated with long-term use of benzodiazepines and Z-drugs, largely absent. In addition, phase 3 studies demonstrated that Lemborexant is associated with less postural instability compared to zolpidem in elderly patients who woke during the middle of the night,[4,5] suggesting a significantly lower risk of falls. Dr Ram believes that this makes Lemborexant a far more attractive long-term option for his insomnia patients.

Dr Ram answers commonly asked questions about starting Lemborexant

What is the best patient profile for Lemborexant?

For Dr Ram, there isn't a specific patient profile where benzodiazepines are preferred over Lemborexant. In fact, Lemborexant is now his first choice of drug for treating insomnia due to its low abuse potential, low risk of dependence, its efficacy, and in Dr Ram's experience, its ability to be discontinued with much more ease and certainty compared to benzodiazepines or Z-drugs.

What is the usual starting dose of Lemborexant?

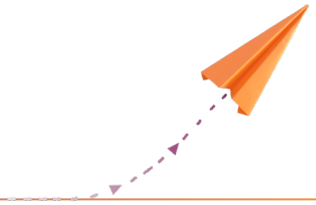
The recommended starting dose is 5 mg. Around 90% of Dr Ram's patients respond well at this dose, achieving good sleep. Only a small number of patients, particularly those who are refractory to other hypnotic classes, may require an increase to 10 mg.

Are there any patients who should avoid Lemborexant?

The only absolute contraindication is narcolepsy.[3] In addition, when a patient has significant anxiety symptoms that are impacting their sleep, Dr Ram often opts for other hypnotics, usually coupled with a selective serotonin reuptake inhibitor (SSRI). For most patients, where anxiety levels are not extremely high, Dr Ram uses Lemborexant as his first choice for treating insomnia.

Counselling patients about de-prescribing

When de-prescribing hypnotics, Dr Ram notes that it is crucial to explain to patients why it's being done, the potential benefits, and what effects they might experience in the first few weeks. Most patients of his patients are open to the idea but many are concerned about memory impairment, having read or learned online that long-term use of common sleeping pills, such as benzodiazepines, can lead to this side effect.



Selected Q&A

Is Lemborexant better for new patients or more suitable as a second-line option?

Dr Ram: It is excellent for new patients because it is effective and can be used with lessened concerns about dependence. I initially used it primarily during de-prescribing, but now I frequently prescribe it to drug-naïve patients. The only instance where I hesitate to use it is in cases of severe anxiety that disrupt sleep; in those situations, I prefer to prescribe a benzodiazepine with the understanding that it will be tapered off once the SSRIs begin to take effect.

What percentage of your patients are on Lemborexant 10 mg?

Dr Ram: Approximately 90% of my patients on Lemborexant are prescribed 5 mg.

When should I increase the dosage of Lemborexant to 10 mg, and how long should I wait if 5 mg isn't sufficient?

Dr Ram: Many people are understandably impatient about achieving restful sleep and may not want to wait 4 to 6 weeks. I typically recommend that patients take 5 mg for seven to ten days. If there are no improvements in that time frame, I suggest increasing the dosage.

Dr Ng: Some patients have reported that with 5 mg, they only manage to sleep for two hours. In those cases, after a couple of nights, I advise them to increase the dosage to 10 mg, as that amount can often make a difference.

What are the signs for stopping benzodiazepines / Z-drugs and starting Lemborexant?

Dr Ram: The decision to stop benzodiazepines should be based on specific factors. Key reasons include dissatisfaction with sleep quality, a desire to increase the dose, frequent switching between different benzodiazepines and Z-drugs, the use of multiple medications, adverse effects like falls, or substance misuse. If any of these issues are present, I would recommend stopping or cross-tapering benzodiazepines and Z-drugs, and transitioning to Lemborexant.

Do you discontinue Lemborexant if a patient experiences nightmares?

Dr Ng: We first discuss the severity of the nightmares with the patient. If the nightmares are intense and traumatizing, I would discontinue Lemborexant. However, if the nightmares are mild and manageable, some patients may choose to continue it. Additionally, for patients with PTSD, nightmares often diminish over time, especially when combined with SSRIs.

Which antidepressants are most effective when combined with Lemborexant to enhance its clinical effect?

Dr Ram: I primarily combine Lemborexant with SSRIs, particularly escitalopram and sertraline, as they are my go-to antidepressants. However, there isn't conclusive data to suggest a particular antidepressant offers the greatest benefit in combination with Lemborexant.

References

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