June 2021

# pad Refills

**Your dose of drug information in between details**

## Drug information question: What is lemborexant (Dayvigo) and how does it differ from other hypnotics for insomnia, such as zopiclone?

**Conclusion: Lemborexant is a central nervous system (CNS) depressant but differs pharmacologically from other medications currently approved for insomnia. It is unknown whether it offers any efficacy or safety advantages compared to other commonly prescribed medications, such as zopiclone.**

The BC Provincial Academic Detailing (PAD) Service's 2020-2021 topic Medications for Insomnia offers participants the opportunity to discuss:

- The strength of recommendations for and against specific medications in contemporary clinical practice guidelines
- Prescribing principles applicable to medications for insomnia
- Drug information relevant to the prescribing, deprescribing and monitoring of medications for insomnia

We frequently receive this question during academic detailing sessions: ***What is lemborexant and how does it differ from medications such as zopiclone?***

Lemborexant (Dayvigo) was approved by Health Canada in 2020. Like zopiclone, it is approved for both sleep onset and sleep maintenance insomnia.[1,2] Our literature search did not identify randomized clinical trials directly comparing lemborexant to zopiclone, so we are unable to evaluate its relative efficacy and safety. Here are a few key points:

a) Pharmacology.[1,3,4] Lemborexant is the second medication approved by Health Canada in a class of hypnotics called orexin receptor antagonists. The first, suvorexant (Belsomra), was approved in 2018 but the manufacturer decided not to market it in Canada. Health Canada describes the pharmacology of the class as follows: antagonism of the orexin neuropeptide signalling system in the hypothalamus, thereby interfering with wakefulness.

b) CNS depressant.[1,5] Sedation is the most common adverse event (somnolence, lethargy, fatigue, sluggishness). The lowest approved dose (5 mg) is recommended because of a clear relationship between higher doses and adverse events, whereas efficacy does not clearly increase with the higher dose (10 mg). Lemborexant should not be co-prescribed with other hypnotics.

c) Efficacy.[1,4-6] Two pivotal efficacy trials compare lemborexant to a placebo over 1 and 6 month treatment periods in people with chronic insomnia. Compared to the improvement that occurred in the placebo group during the trials, lemborexant reduced **time to sleep onset** by 4 and 8 minutes. The length of **time people were awake during the night** was reduced by 13 and 25 minutes compared to a placebo. The relevance of these differences is difficult to interpret given the lack of agreement on a minimal clinically-important difference.

d) Adverse Events of Special Interest.[1] Lemborexant can cause narcolepsy-like adverse events. This includes sleep paralysis (inability to move or speak for up to several minutes), cataplexy-like symptoms (sudden leg weakness) and hallucinations during sleep-wake transitions.

e) Drug Interactions.[1,7] Lemborexant is metabolized by CYP3A4 and is susceptible to interactions with medications such as amiodarone, amlodipine, carbamazepine, clarithromycin, diltiazem, fluoxetine and phenytoin. Lemborexant may affect other medications metabolised by CYP2B6, such as bupropion and methadone. Alcohol should be avoided: a single dose of alcohol can increase lemborexant concentrations up to 70%.

[1]Health Canada Lemborexant; [2]Health Canada Zopiclone; [3]Health Canada Suvorexant; [4]Drug Shortages Canada Belsomra; [5]US FDA 2019 Lemborexant Review; [6]CADTH 2018 Insomnia Review; [7]BC Provincial Academic Detailing Service 2020 Medications for Insomnia



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