October 2021

pad Refills

Your dose of drug information in between details

Drug information question: How does eszopiclone (Lunesta®) differ from zopiclone?

Conclusion: It is unclear if eszopiclone differs meaningfully from zopiclone for efficacy or safety outcomes but it is costlier.

The BC Provincial Academic Detailing (PAD) Service's 2020-2021 topic Medications for Insomnia addresses:

- 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

Zopiclone (Imovane®) was approved by Health Canada in 1990.[1] It is a racemic mixture of mirror-image molecules (enantiomers). Thirty years later, in 2020, eszopiclone (Lunesta®) was approved by Health Canada and is the single S-enantiomer or "left hand" molecule that comprises 50% of the racemate zopiclone.[2] There are other common examples of single enantiomers: escitalopram from citalopram, dexlansoprazole from lansoprazole, esomeprazole from omeprazole, dextroamphetamine from amphetamine, desvenlafaxine from venlafaxine, levofloxacin from ofloxacin.

A 2021 systematic review identified 185 randomized clinical trials (RCTs) directly comparing single enantiomers to the racemic precursor drug.[3] The researchers concluded that it is uncommon for the newer single-enantiomer drug to demonstrate an efficacy or safety advantage when compared to the racemic drug: roughly one in seven RCTs report an advantage in an efficacy or safety outcome. The review did identify one RCT comparing eszopiclone to zopiclone:[4]

- The stated objective of the trial was to determine whether eszopiclone is non-inferior (not significantly worse) than zopiclone.
- The primary efficacy outcome reported in the RCT was participants' subjective assessment of their insomnia severity however this was an unexplained change from the originally-stated primary efficacy outcome.[5]
- Insomnia severity scores improved in both treatment groups from baseline and were comparable at the end of four weeks of treatment: eszopiclone 7.4 versus zopiclone 7.8 (Insomnia Severity Index: score ranges from 0 to 28).
- The short four-week length of the trial precludes drawing conclusions on many relevant safety outcomes such as the relative risk of dependence, withdrawal, misuse and other serious adverse events.

Zopiclone and eszopiclone are gamma-aminobutyric acid ($GABA_A$) agonists which share some of the pharmacologic features of benzodiazepines.[6,7] Health Canada's prescribing information indicates that, compared to zopiclone, eszopiclone binds differently to various subunits within the $GABA_A$ receptor.[2] The agency does not comment on the clinical relevance of this pharmacologic difference.[2] The European Medicines Agency (EMA) determined however that there was insufficient evidence to establish a meaningful difference between eszopiclone and zopiclone and did not grant eszopiclone the status of a novel drug.[8] The drug company subsequently decided not to market eszopiclone in Europe, citing compromised commercial viability.[9]

In British Columbia, zopiclone costs approximately $0.15 per tablet whereas eszopiclone costs approximately $1.70 a tablet.[10] Though slight differences in pharmacokinetic parameters exist, patients receiving either of these medications may experience next day impairment and must be advised to avoid driving or other activities that require full alertness for at least 12 hours after taking a dose.[1,2]

[1]Health Canada Zopiclone; [2]Health Canada Eszopiclone; [3]LONG JAMA Network Open 2021 (PMID: 33956134); [4]PINTO Clinics 2016 (PMID: 26872077); [5]ClinicalTrials.gov NCT01100164; [6]US FDA 2004 Eszopiclone Pharmacology Review; [7]WHO 2006 Zopiclone Review; [8]EMA 2009 Eszopiclone Review; [9]EMA 2009 Eszopiclone Marketing Withdrawn; [10]BC PAD Medications for Insomnia

BC Provincial Academic Detailing Service
Email: PAD@gov.bc.ca
Web: www.bcpad.ca