



Drug information question: Is quetiapine a safer alternative to zopiclone for insomnia?

Conclusion: The evidence for quetiapine in the treatment of insomnia is limited. Drawing conclusions regarding the comparative safety of quetiapine to zopiclone is not possible. Monitor for somnolence, weight gain, hypotension, syncope and extrapyramidal symptoms which can occur early in therapy at initial doses.

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.

High quality trials are needed to determine the effectiveness of quetiapine for insomnia.

- Quetiapine (Seroquel®, Seroquel XR®) is approved by Health Canada for the treatment of schizophrenia, bipolar disorder and major depressive disorder.^{1,2}
- It interacts with a broad range of neurotransmitter receptors: dopamine, serotonin, histamine, adrenergic.^{1,2}
- Common adverse events include somnolence and sedation.^{1,2}
- In a 2020 [Canadian Agency for Drugs in Technology and Health](#) review, the quality of evidence for quetiapine across sleep outcomes (sleep onset latency, total sleep time, wake after sleep onset, sleep quality, sleep satisfaction, sleep efficiency, insomnia severity, fatigue, quality of life) was low, critically-low or entirely absent.³

Monitor for potential adverse events associated with quetiapine.

- Our literature search did not identify clinical trials or cohort studies comparing the safety of quetiapine to zopiclone nor did our search identify formal dose-response analyses for quetiapine-associated adverse events.
- The Health Canada prescribing information for [quetiapine](#) indicates that somnolence, weight gain, hypotension, syncope and extrapyramidal symptoms can occur early in therapy at initial doses.^{1,2}
 - Use of the smallest effective dose, for the shortest duration, with periodic reassessments is advised.^{1,2}
- Advisories from Health Canada and the US Food and Drug Administration for atypical antipsychotics as a class include: increased risk of respiratory depression or sedation when combined with opioids, urinary retention, new or worsening sleep apnea, increased risk of death in older adults with dementia (cardiovascular, pneumonia).⁴⁻⁷
- In 2017, Health Canada updated the prescribing information for quetiapine to include the potential for misuse, tolerance, physical dependence and advised caution when prescribing quetiapine to people with a history of substance or alcohol use disorder.^{1,2,8}
- To minimize the risk of withdrawal symptoms, a taper is recommended when quetiapine is discontinued.^{1,2}

Quetiapine has the potential to interact with other medications.

- CYP3A4 inhibitors (e.g., macrolide antibiotics, azole antifungals, antiretrovirals, calcium channel blockers) can increase quetiapine levels six-fold.^{1,2,9}
- Other potential pharmacodynamic interactions include: QT prolongation and additive or opposing effects with anticholinergic medications, cholinesterase inhibitors and antiparkinson medications.^{1,2,9}
- See our [Handout](#) for Medications for Insomnia: Drug Interaction Overview.

¹Health Canada Drug Product Database Seroquel; ²Health Canada Drug Product Database Seroquel XR; ³CADTH 2020 Insomnia Evidence Review; ⁴US FDA 2016 opioid respiratory depression sedation; ⁵Health Canada 2016 urinary retention; ⁶Health Canada 2016 sleep apnea; ⁷Health Canada 2005 dementia mortality; ⁸Health Canada 2017 quetiapine misuse; ⁹BC PAD Service Insomnia Medications 2020