Therapeutics Initiative
Better prescribing. Better health.

THERAPEUTICS LETTER 158
August - September 2025

Understanding insomnia treatment

PLAIN LANGUAGE SUMMARY

What is insomnia?

Insomnia means having trouble falling asleep or staying asleep. It can affect health, mood, and daily activities.

What can be done about longstanding sleep problems (chronic insomnia)?

When people have chronic insomnia (lasting for more than three months), doctors will often explain "sleep hygiene" methods for improving sleep. For example, avoiding coffee or looking at bright screens in the evening. However, sleep hygiene often doesn't work well for people who have longstanding insomnia.

What is now seen as a better way to treat chronic insomnia?

Experts now recommend Cognitive Behavioural Therapy for Insomnia (CBT-I). This is a type of therapy that helps people to first notice, and then change, the kinds of thoughts and actions that keep them awake. It's now seen as the first thing to try for long-term insomnia. It can be started immediately using a self-guided technique. Helpful resources are available.

What about sleeping pills? Do they help?

Research studies show these drugs only help a little for short periods of time. For example, they might help people fall asleep a little bit faster or sleep a little bit longer (often only about 15-20 minutes).

Are there risks to taking sleeping pills?

Yes. Research shows while 1 in 12 people who take them fall asleep a bit sooner and may sleep about 15-20 minutes longer, harms are common. These harms include "morning after" drowsiness that can cause motor vehicle crashes and injuries from falls. When they are used for a long time, dependence on these drugs can develop (habituation), including serious trouble trying to stop them.

What if sleeping pills are prescribed?

- Medications should be used only for shorter sleep problems (no more than 1 week).
- Start with low doses, especially for people 65 or older.
- Understand that sleepiness can continue the next day, with a need to restrict activities.
- Keeping a "sleep diary" to track sleep hours for one week before and one week after starting a sleeping pill helps the doctor or nurse practitioner and the patient know if the drug is working

What if sleeping pills have been used for a long time or at high doses?

- To avoid withdrawal effects, the dose should be tapered slowly to the smallest dose that works. Never prescribe or use doses higher than those recommended.

THE UNIVERSITY OF BRITISH COLUMBIA

Therapeutics Initiative
The University of British Columbia
Department of Anesthesiology, Pharmacology & Therapeutics
2176 Health Sciences Mall, Vancouver, BC, Canada V6T 1Z3

T +1 604.822.0700
F +1 604.822.0701
E info@ti.ubc.ca

ISSN 2369-8691

Therapeutics Initiative
Better prescribing. Better health.

Improving how we prescribe zopiclone and trazodone for insomnia

ABSTRACT

Background:

Chronic insomnia presents a significant clinical challenge. Current guidelines recommend cognitive behavioural therapy (CBT-I) as first-line treatment for chronic and recurring insomnia lasting longer than three months. Advice about sleep hygiene, formerly a standard recommendation, lacks evidence of effectiveness. However, zopiclone and trazodone are commonly prescribed in British Columbia, often beyond approved indications, or at doses that exceed evidence-based ceilings. Randomized controlled trials show modest benefits from these drugs, but efficacy is limited to short-term use. They cause minor or serious harms as frequently as benefits, leading to concerns about overprescribing and the safety of long-term use.

Aims:

This *Therapeutics Letter* aims to identify the lowest effective doses for initial zopiclone and trazodone prescriptions, based on RCT evidence on sleep outcomes and their harm-benefit ratios. It proposes a practical tapering strategy for clinicians to help patients already taking excessive doses of zopiclone or trazodone to achieve the lowest effective dose, to minimize habituation and adverse effects.

Recommendations:

Emphasize CBT-I as the first-line therapy for **chronic insomnia**. Patients should complete a 1-week sleep diary before and after receiving any prescription medication for insomnia. If pharmacological treatment is considered for **acute insomnia**, prescribe hypnotics only short term (<7 days). Initiate zopiclone at 3.75 mg/day, and do not exceed 7.5 mg/day (5 mg/day for people over 65), and warn patients about next-day impairment. For trazodone, evidence does not support doses above 50 mg/day; efficacy may wane within two weeks. For patients on long-term or high doses, a gradual taper to the lowest effective dose should be attempted.

Keywords: Cognitive Behavioral Therapy; Deprescriptions; Drug Utilization; Hypnotics and Sedatives; Off-Label Use; Patient Safety; Sleep Hygiene; Sleep Initiation and Maintenance Disorders; Substance Withdrawal Syndrome; Trazodone; Zopliclone.

Multiple experts and primary care clinicians reviewed the draft of this Therapeutics Letter for factual accuracy, and to ensure it is relevant to clinicians.

The UBC TI is funded by the BC Ministry of Health to provide evidence-based information about drug therapy. We neither formulate nor adjudicate provincial drug policies.

ISSN 2369-8691

Therapeutics Initiative
Better prescribing. Better health.

THERAPEUTICS LETTER 158
August - September 2025

Improving how we prescribe zopiclone and trazodone for insomnia

Vignette: *A 64-year-old retired office manager whom you've treated for years takes both zopiclone 15 mg/d and trazodone 100 mg/d nightly. Yet still she complains that "I don't ever seem to sleep – not a wink!" Your office is overflowing with people complaining of sore backs, ears, and runny noses.* ***What should you do?***

Summary and conclusions

- **Randomized controlled trials (RCTs) of zopiclone and trazodone demonstrate small improvements in sleep metrics for about 1 in 12 people (NNT=12).**
- **In RCTs minor or serious harms were as common as sleep benefits (NNH=8 for zopiclone and NNH=12 for trazodone).**
- **Before and after any prescription for insomnia, patients should complete a 1-week sleep diary.**
- **If you prescribe zopiclone, begin with Health Canada's recommended starting dose of 3.75 mg, and do not exceed 7.5 mg (5 mg in older patients). Always warn patients about "morning after" sedation and driving risk – and document the warning.**
- **RCTs do not clarify a minimal effective dose of trazodone for insomnia. No evidence supports exceeding 50 mg/day.**
- **Trazodone's initial effect for sleep attenuates within 2 weeks.**
- **For patients already taking zopiclone or trazodone, reduce to the lowest dose consistent with good overall clinical care.**

Insomnia: a chronic therapeutic challenge

Clinicians face a dilemma when a patient complains: "I can't sleep." We are taught to take a thorough history, including identifying and correcting breaches of sleep hygiene, such as spending too much time in bed, sedentarism, and napping. However, for **chronic insomnia**, there is no evidence that advice about sleep hygiene is effective. Both European and United States guidelines now recommend cognitive behavioural therapy (CBT-I).[1,2]

CBT-I includes behavioural and psychological techniques that are very different from what was traditionally recommended for sleep hygiene. Evidence-based CBT-I is available in print and digital self-help formats, as therapist-directed treatment, and in hybrid versions. It is now recommended as first-line therapy for recurrent and **chronic insomnia** lasting >3 months.[3]

But many patients expect to leave the clinic with a prescription. In 1995 *Therapeutics Letter* #11 cautioned about over-prescribing of sedative hypnotics, and how easy it is for patients to become dependent on them.[4] *Letter #54*, published in 2004, showed that British Columbians, especially older females, were using more benzodiazepines than ever. An expert reviewer expressed concern that "*other drugs used as sedative/hypnotics, such as antihistamines, antidepressants and antipsychotics, may be more harmful than benzodiazepines and Z drugs.*"[5] The warning was prescient, as long-term prescriptions for drugs such as quetiapine and mirtazapine became common.

This *Therapeutics Letter* focuses on 2 pharmacological options used to treat **acute insomnia**. Like advice on sleep hygiene, they are recommended only for very short-term use (days).[6] Trazodone is not approved in Canada for treatment of insomnia. CBT-I is both a more effective and a safer strategy than drug treatment for chronic insomnia.[1]

As of 2024, zopiclone and trazodone are the drugs most often prescribed for insomnia in BC. Often, this is for purposes not approved by Health Canada, or at doses exceeding a ceiling above which additional benefit is unlikely.[6-8] **Can we make prescribing safer, and reduce habituation and long-term use of sedative/hypnotics?**

Relying on available evidence from randomized controlled trials (RCTs), this *Letter* has 2 goals:

- Identify the lowest effective dose for a first prescription of zopiclone or trazodone.
- Suggest a strategy for patients already taking excessive doses to achieve the lowest effective dose.

THE UNIVERSITY OF BRITISH COLUMBIA

Therapeutics Initiative
The University of British Columbia
Department of Anesthesiology, Pharmacology & Therapeutics
2176 Health Sciences Mall, Vancouver, BC, Canada V6T 1Z3

T +1 604.822.0700
F +1 604.822.0701
E info@ti.ubc.ca

ISSN 2369-8691

How do clinical trials measure sleep?

Like patients in primary care, volunteers in randomized clinical trials (RCTs), typically self-report their own "sleep metrics." **Unlike most patients, research participants are expected to complete a comprehensive sleep diary.** Standard self-reported experimental measures include:

- sleep quality: using a measure such as the Insomnia Severity Index;
- sleep latency: the delay between going to bed and falling asleep;
- time awake: the duration of awakenings from sleep;
- total sleep time.

To avoid "first contact prescribing" for sleep complaints, it may be common sense to ask patients to complete a 1-week sleep diary before considering treatment, as well as immediately after any initial prescription.[9,10]

How well does zopiclone work in RCTs?

Far more British Columbians use zopiclone than the other "Z-drugs" licensed in Canada (eszopiclone and zolpidem). Zopiclone is a racemic drug, with "left" and "right" mirror image configurations. S-zopiclone (eszopiclone, Lunesta) is the pharmacologically active enantiomer, accounting for half of any zopiclone dose in milligrams. It is twice as potent as racemic zopiclone; otherwise they are indistinguishable. Given the popularity of zopiclone as BC's most prescribed drug treatment for insomnia, readers may be surprised by evidence available from RCTs.

Compared with a placebo, acute treatment with zopiclone **improved overall sleep quality for about 1 in 12 people**.[11,12] A 2018 Cochrane systematic review (SR) of 14 RCTs (N=4,732), including 7 for primary insomnia, found that eszopiclone (effectively zopiclone) reduced sleep latency by a mean of 12 minutes. It decreased mean time awake - after volunteers fell asleep - by 17 minutes more than placebo. Compared with placebo, this amounts to an average increase of about 29 minutes in total sleep time.[13]

Is there a maximum effective (ceiling) dose?

Multiple RCTs compared zopiclone dose-responses at 2.5 mg to 15 mg per night. Generally, doses >7.5 mg did not further improve sleep metrics.[14-20] The Canadian product monograph states clearly that the 7.5 mg ceiling dose "***should not be exceeded***."[21] For people >65, it recommends a maximum dose of 5 mg.[22]

Harms from zopiclone

It is important to balance the improved sleep quality noticed by some patients with safety. Zopiclone (like other Z-drugs) is associated with dose-dependent adverse events, including motor vehicle accidents, falls, and fall-related injuries.[23,24] Next-day impairments include "hangover" effects related to zopiclone's mean elimination half-life of about 7 hours (or longer in people >65).[23,25] Effects of a 7.5 mg dose are comparable to driving with a blood alcohol concentration (BAC) of 0.05% - above the legal driving limit in BC.[26-27] Consumer information in the revised product monograph and a 2014 Health Canada health professional risk communication warn patients not to drive within 12 hours of a bedtime dose - along with multiple other sobering precautions.[21,22] The 2022 network meta-analysis found that for acute insomnia, the number needed to harm (NNH) was ~8.[11]

Many British Columbians take excessive doses

During 2023, about 132,000 British Columbians received prescription zopiclone. **Half were age 65 or older, of whom 60% received doses exceeding the evidence-informed ceiling dose.** Paradoxically, amongst people under age 65, only about 10% received doses >7.5 mg/day. **Of all first prescriptions to British Columbians for zopiclone during 2023, 75% exceeded 3.75 mg/day.**[28]

Use of zopiclone in BC nearly doubled from 2002 to 2012, but declined after 2015. Use of trazodone doubled by 2020, but may have stabilized. Other sedatives (e.g., mirtazapine and quetiapine) have probably replaced zopiclone for many British Columbians.

Annual Use of Zopiclone and Trazodone in British Columbia (per 1000 population)

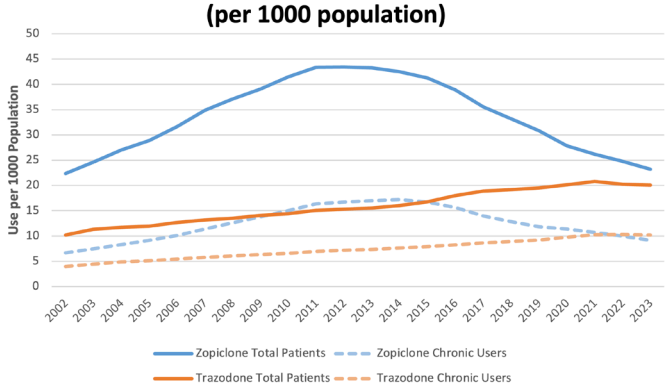

Table: Mean self-reported sleep measures and pharmacokinetics for zopiclone and trazodone

Drug	Cautious starting dose	Evidence-informed ceiling dose	Reduction in mean delay of sleep onset	Increase in mean total sleep time	Time to onset and peak effect	Half-life	References
Zopiclone	Age <65: 3.75 mg	Age <65: 7.5 mg	12 minutes	29 minutes	Onset: <0.5 hours Peak: 1-1.5 hours	4-6 hours	21, 22
	Age ≥65: 3.75 mg	Age ≥65: 5 mg					
Trazodone	12.5 to 25 mg	50 mg	n/a*	n/a*	Onset: 0.5-2.5 hours Peak: 0.5-1 hours	4-10 hours	29, 34, 35
	Lower doses warranted in elderly patients						

** We cannot quantify the magnitude of effect, because of conflicting information from RCTs.*

Multiple experts and primary care clinicians reviewed the draft of this Therapeutics Letter for factual accuracy, and to ensure it is relevant to clinicians.

The UBC TI is funded by the BC Ministry of Health to provide evidence-based information about drug therapy. We neither formulate nor adjudicate provincial drug policies.

Inter-dose withdrawal can be mistaken for anxiety or restlessness

Zopiclone's elimination half-life may be appealing for **short-term or occasional use**, despite the well-recognized harm of next-day sedation, because it is shorter than some other sedatives. However, during regular daily use, the same property can be problematic. The product monograph warns: "An increase in daytime anxiety and/or restlessness has been observed during treatment.... This may be a manifestation of inter-dose withdrawal."[21]

Trazodone

Trazodone was marketed in the early 1980s as an antidepressant; but its sedating properties were soon recognized as disadvantageous during the day. Subsequently, it was reincarnated in off-label (unapproved) use at lower doses as a hypnotic, primarily for antidepressant-associated insomnia. Use expanded to include many people with primary insomnia. Trazodone is not approved for insomnia in Canada, the USA, or the United Kingdom.

How well does trazodone work for sleep in RCTs?

RCTs for insomnia used small sample sizes and a variety of outcome measures. Results were often inconsistent and unsuitable for meta-analysis. When consistent, their clinical significance is questionable.[11,29-32] A 2022 network meta-analysis of RCTs in acute insomnia indicates that compared with placebo, about 1 in 12 people achieve improved sleep quality from trazodone.[11] Based on published data from RCTs, we cannot quantify the magnitude of changes in other sleep metrics.

Trazodone soon loses its efficacy for insomnia. In a RCT that compared trazodone 50 mg with zolpidem 10 mg or placebo, trazodone was less effective than zolpidem after 1 week. After week 2, trazodone was no more effective than placebo.[33] In 2017 the American Academy for Sleep Medicine's clinical practice guideline for pharmacologic treatment of chronic insomnia found no evidence that trazodone improves quality of sleep; it recommended against using trazodone for insomnia.[6]

Is a ceiling dose known?

No well-designed RCTs assessed the dose response of trazodone in primary insomnia. In depressed people with sleep problems, a dose-response study (N=75) found no difference in total sleep time between doses of 50 mg, 75 mg, or 100 mg. The patients were already taking the sedative antidepressant imipramine at about 50 mg/day.[34]

A 1983 study compared trazodone kinetics after a single dose of 100 mg in volunteers age 23 to 30 vs older volunteers age 64 to 74. The elimination half-life and time-concentration exposure were doubled in the older group, who also experienced more prolonged sedation.[35]

Harms from trazodone

In people **age 65 or older treated for depression**, meta-analysis of 2 large cohort studies concluded that compared with no drug treatment, trazodone was associated with an increased risk of falls (RR 1.79, 95%CI 1.60, 1.97).[36] The larger cohort, comprising 60,476 people diagnosed with depression in British general practices, identified 2,573 people prescribed trazodone from 1996 through 2007. Their adjusted hazard ratio for death was 1.82 (95%CI 1.59-2.08).[37]

Less information is available about adverse events when trazodone **is used for insomnia**. Of 3 RCTs that evaluated trazodone's efficacy for **primary insomnia** (N=331), only 1 assessed safety.[29-31] For treatment of **any type of insomnia**, only 2 of 7 RCTs reported adverse events.[30] One RCT comparing trazodone 50 mg/night with placebo found that trazodone caused impairments of short-term memory and verbal learning.[38] Other studies found trazodone no safer than benzodiazepines or antipsychotics, with similar risks of falls and fall-related injuries.[39-41] The 2022 network meta-analysis of drug treatment found that for **acute insomnia**, the number needed to harm with trazodone (NNH~12) was similar to the number needed to treat for benefit (NNT~12).[11]

Avoid prescribing cascades

What if prescription of a sleep medication arises from an adverse effect of another prescribed drug (a prescribing cascade), or from self-administered non-prescription substance use? Insomnia is an important adverse effect of alcohol, cocaine, amphetamines, and prescription stimulants. It should also be considered in people taking antidepressants, (including duloxetine or SSRIs) and cholinesterase inhibitors such as donepezil.[43]

Strategic prescribing

Given the modest expected efficacy of hypnotics - but the risk of habituation - how can we improve clinical practice? A "strategic prescribing" approach is analogous to current advice on cautious prescribing of opioids for chronic non-cancer pain. **Looking ahead** may protect patient safety by minimizing adverse effects, or habituation and potential difficulty in stopping a drug.

Common sense suggests establishing goals of therapy for individual patients in plain language. Specify potential harms clearly, and emphasize intermittent, short-term use. "Strategic prescribing" could include documenting discussion with a patient and instruction to:

- Begin with a pre-treatment sleep diary, and follow-up soon after treatment begins.
- **Specify and record objective goals and measures** of therapeutic success or failure, such as the time to fall asleep, total sleep time, number of awakenings, and morning alertness vs somnolence.
- **First line therapy is CBT-I, which can be started immediately** using a self-guided technique when a trained therapist is not available. **If necessary, use a hypnotic only intermittently**, dispensed from a short-term prescription.
- **Record safety issues**: cognitive impairment, falls, motor vehicle crashes, and other accidents (including at work).

Start low and revisit goals and effects within one week

Evidence from RCTs does not clarify the duration of an adequate therapeutic trial. But based on the elimination half-lives of zopiclone (and other Z-drugs) and trazodone, a 3- to 5-day trial is clinically reasonable. **Initial prescriptions exceeding 7 days are not**. Start with the lowest dose to

Multiple experts and primary care clinicians reviewed the draft of this Therapeutics Letter for factual accuracy, and to ensure it is relevant to clinicians.

The UBC TI is funded by the BC Ministry of Health to provide evidence-based information about drug therapy. We neither formulate nor adjudicate provincial drug policies.

assess efficacy, and to take advantage of the placebo effect. Given the approximate NNT of 12 for a clinically useful response, **limit your expectations as a prescriber – and those of your patients.** What if a short low-dose trial is unsuccessful? Clinical logic could suggest stopping the drug. A clinical alternative is a similarly brief trial at a higher dose, but **below** the approved maximum. However, this strategy is not supported by experimental evidence. **Prolonged trials are not rational.**

Never renew without considering dose reduction or deprescribing

Should we reduce doses even for patients with no obvious clinical problems? Long-term risks associated with hypnotic sedatives are not necessarily obvious, especially in telehealth assessment. Adverse effects affecting safety may develop only after years, whether due to reduced physiological reserve or to potential inter-dose withdrawal phenomena.

For people already habituated to a sedative/hypnotic, identifying the lowest effective dose can be challenging. Quality improvement studies indicate that patients often perceive prescribers as lacking understanding about insomnia. But when presented with viable options, most patients will consider alternatives.[43-45]

Requests for refills are an opportunity to discuss with patients why it is **always good practice to reassess the prescription** and consider tapering or deprescribing:

- Is this patient still "not sleeping well?"
- Is there evidence or potential for harm?
- Is the dose unreasonably high?

Achieving the lowest effective dose

Tailor the rate of dose reduction to the individual patient. Over half of patients can tolerate a relatively rapid taper.[46] However, about one-third may require a more cautious approach - for example, at least 2 weeks between each dose reduction, and a gradual taper such as reduction by ¼ of a tablet per interval.

Troublesome withdrawal symptoms may require extending intervals to 3 to 4 weeks. Patients need to understand that withdrawal symptoms can mimic their original symptoms of insomnia, or include physical symptoms (restlessness, twitching) and psychological symptoms (confusion, anxiety). If withdrawal symptoms are severe, resuming the original dose may be unavoidable.

Vignette resolution: *After expressing empathy for your patient's symptoms, you ask her to complete a 7-day sleep diary to discuss within 2 weeks at a specific appointment. The diary shows that she sleeps longer at night than she realized, which she finds reassuring. She acknowledges that she's been napping and going to bed early, hoping to catch up on sleep. But then she ends up lying awake feeling frustrated. Based on the* ***10 Tips for a Better Night's Sleep****,[47] she agrees to avoid naps, set a later bedtime, and rise at the same time each day.*

You explain why dose reductions are prudent, and she agrees to try reducing both zopiclone and trazodone gradually over the next 3-6 months. Several months later, having reduced doses at each of several visits, she is down to zopiclone 3.75 mg/day and trazodone 25 mg/day. You are both pleasantly surprised that her sleep is greatly improved.

Family and friends say she is much more alert during the day – ***something you document prominently in her record.*** *The welcome success inspires you to review other patients' prescriptions thoughtfully, whenever they request renewals.*

Data References and Disclaimer

The British Columbia (BC) Ministry of Health approved access to and use of BC data. The following data sets were used: *PharmaNet, Medical Services Plan, Discharge Abstract Database, National Ambulatory Care Reporting System, Client Roster.* All inferences, opinions and conclusions drawn in this manuscript are those of the authors and do not reflect the opinions or policies of the data stewards.

References

1. Riemann D, Espie CA, Altena E, et al. *The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023.* Journal of Sleep Research. 2023; 32(6):e14035. DOI: 10.1111/jsr.14035
2. Edinger JD, Arnedt JT, Bertisch SM, et al. *Behavioral and psychological treatments for chronic insomnia disorder in adults: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment.* J Clin Sleep Med. 2021; 17(2):263-98. DOI: 10.5664/jcsm.8988
3. Stanford Medicine. *Cognitive Behavioral Therapy for Insomnia (CBTI): Sleep Restriction.* Stanford Medicine Health Care. 2025; https://stanfordhealthcare.org/medical-treatments/c/cognitive-behavioral-therapy-insomnia/procedures/sleep-restriction.html
4. Therapeutics Initiative. *To Sleep or Not to Sleep: Here Are Your Questions.* Therapeutics Letter. 1995 Nov-Dec; 11:1-2. https://ti.ubc.ca/letter11
5. Therapeutics Initiative. *Use of Benzodiazepines in BC – Is it consistent with recommendations?* Therapeutics Letter. 2004 Nov-Dec; 54:1-2. https://ti.ubc.ca/letter54
6. Sateia MJ, Buysse DJ, Krystal AD, et al. *Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline.* Journal of Clinical Sleep Medicine. 2017; 13(2):307–349. DOI: 10.5664/jcsm.6470
7. Qaseem A, Kansagara D, Forciea MA, et al. *Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians.* Annals of Internal Medicine. 2016; 165(2):125–33. DOI: 10.7326/M15-2175
8. Morin CM, Benca R. *Chronic insomnia.* Lancet. 2012; 379(9821):1129–41. DOI: 10.1016/ S0140-6736(11)60750-2
9. Maich KHG, Lachowski AM, Carney CE. *Psychometric Properties of the Consensus Sleep Diary in Those With Insomnia Disorder.* Behavioral Sleep Medicine. 2018; 16(2):117–134. DOI: 10.1080/15402002.2016.1173556
10. Kales A, Soldatos CR, Kales JD. *Taking a sleep history.* Am Fam Physician. 1980; 22(2):101-7. PMID: 7405778
11. De Crescenzo F, D'Alo GL, Ostinelli EG, et al. *Comparative effects of pharmacological interventions for the acute and long-term management of insomnia disorder in adults: a systematic review and network meta-analysis.* Lancet. 2022; 400(10347):170–184. DOI: 10.1016/S0140-6736(22)00878-9
12. BC Provincial Academic Detailing (PAD) Service. *Medications for Insomnia: Evidence to Practice.* 2020 Dec; https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/provincial-academic-detailing-service/pad_insomnia_handout.pdf

Multiple experts and primary care clinicians reviewed the draft of this Therapeutics Letter for factual accuracy, and to ensure it is relevant to clinicians.

The UBC TI is funded by the BC Ministry of Health to provide evidence-based information about drug therapy. We neither formulate nor adjudicate provincial drug policies.

13. Rösner S, Englbrecht C, Wehrle R et al. *Eszopiclone for insomnia.* Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD010703. DOI: 10.1002/14651858.CD010703.pub2
14. Dehlin O, Rundgren A, Borjesson L, et al. *Zopiclone to geriatric patients. A parallel double-blind dose-response clinical trial of zopiclone as a hypnotic to geriatric patients - a study in a geriatric hospital.* Pharmacology. 1983; 27 Suppl 2:173–8. DOI: 10.1159/000137924
15. Dundee JW, Elwood RJ, Hildebrand PJ, Singleton M. *Dose-finding and premedication studies with zopiclone.* Pharmacology. 1983; 27 Suppl 2:210–5. DOI: 10.1159/000137929
16. Lader M, Denney SC. *A double-blind study to establish the residual effects of zopiclone on performance in healthy volunteers.* Pharmacology. 1983; 27 Suppl 2:98–108. DOI: 10.1159/000137916
17. Nicholson AN, Stone BM. *Zopiclone: sleep and performance studies in healthy man.* Pharmacology. 1983; 27 Suppl 2:92–7. DOI: 10.1159/000137915
18. Billiard M, Besset A, de Lustrac C, Brissaud L. *Dose-response effects of zopiclone on night sleep and on nighttime and daytime functioning.* Sleep. 1987; 10 Suppl 1:27–34. DOI: 10.1093/sleep/10.suppl_1.27
19. Lamphere JK, Roehrs TA, Zorick FJ, et al. *The dose effects of zopiclone.* Human Psychopharmacology. 1989; 4(1):41–6. DOI: 10.1002/hup.470040107
20. Nair NP, Schwartz G, Dimitri R, et al. *A dose-range finding study of zopiclone in insomniac patients.* International Clinical Psychopharmacology. 1990; 5 Suppl 2:1–10 PMID: 2201721
21. Sanofi-Aventis Canada. *Product Monograph: Imovane (zopiclone).* 2018; https://pdf.hres.ca/dpd_pm/00047597.PDF
22. Health Canada. *IMOVANE (zopiclone) - New Dosage Recommendations to Minimize the Risk of Next-Day Impairment - For Health Professionals.* 2014; https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/42253a-eng.php
23. Gunja N. *In the Zzz Zone: The Effects of Z-Drugs on Human Performance and Driving.* Journal of Medical Toxicology: Official Journal of the American College of Medical Toxicology. 2013; 9(2):163–71. DOI: 10.1007/s13181-013-0294-y
24. Brandt J, Leong C. *Benzodiazepines and Z-Drugs: An Updated Review of Major Adverse Outcomes Reported on in Epidemiologic Research.* Drugs in R&D. 2017; 17(4):493–507. DOI: 10.1007/s40268-017-0207-7
25. Mets MA, de Vries JM, de Senerpont Domis LM, et al. *Next-day effects of ramelteon (8 mg), zopiclone (7.5 mg), and placebo on highway driving performance, memory functioning, psychomotor performance, and mood in healthy adult subjects.* Sleep. 2011; 34(10):1327–34. DOI: 10.5665/SLEEP.1272
26. McElroy H, O'Leary B, Adena M, et al. *Comparison of the effect of lemborexant and other insomnia treatments on driving performance: a systematic review and meta-analysis.* Sleep Advances: a Journal of the Sleep Research Society. 2021; 2(1):zpab010 DOI: 10.1093/sleepadvances/zpab010
27. HealthLinkBC. *Canada's Guidance on Alcohol and Health.* Government of BC. 2024 Aug 19; https://www.healthlinkbc.ca/mental-health-substance-use/substance-use/alcohol-use
28. BC Ministry of Health [creator] (2024): *Medical Services Plan (MSP) Payment Information File.* BC Ministry of Health [publisher]. MOH (2023); BC Ministry of Health [creator] (2024): *PharmaNet.* BC Ministry of Health [publisher]. MOH (2023); BC Ministry of Health [creator] (2024): *Discharge Abstract Database.* BC Ministry of Health [publisher]. MOH (2023); BC Ministry of Health [creator] (2024): *National Ambulatory Care Reporting System.* BC Ministry of Health [publisher]. MOH (2023); BC Ministry of Health [creator] (2024): *Client Roster.* BC Ministry of Health [publisher]. MOH (2023);. https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central
29. Jaffer KY, Chang T, Vanle B, et al. *Trazodone for Insomnia: A Systematic Review.* Innovations in Clinical Neuroscience. 2017; 14(7–8):24–34. PMID: 29552421
30. Yi XY, Ni SF, Ghadami MR, et al. *Trazodone for the treatment of insomnia: a meta-analysis of randomized placebo-controlled trials.* Sleep Medicine. 2018; 45:25–32. DOI: 10.1016/j.sleep.2018.01.010
31. Zheng Y, Lv T, Wu J, Lyu Y. *Trazodone changed the polysomnographic sleep architecture in insomnia disorder: a systematic review and meta-analysis.* Scientific Reports. 2022; 12(1):14453. DOI: 10.1038/s41598-022-18776-7
32. Everitt H, Baldwin DS, Stuart B, et al. *Antidepressants for insomnia in adults.* Cochrane Database of Systematic Reviews 2018, Issue 5, Art. No.: CD010753. DOI: 10.1002/14651858.CD010753.pub2
33. Walsh JK, Erman M, Erwin CW, et al. *Subjective hypnotic efficacy of trazodone and zolpidem in DSMIII–R primary insomnia.* Human Psychopharmacology. 1998; 13(3):191–198. DOI: 10.1002/(SICI)1099-1077(199804)13:3%3C191::AID-HUP972%3E3.0.CO;2-X
34. Mashiko H, Niwa S, Kumashiro H, et al. *Effect of trazodone in a single dose before bedtime for sleep disorders accompanied by a depressive state: dose-finding study with no concomitant use of hypnotic agent.* Psychiatry & Clinical Neurosciences. 1999; 53(2):193–4. DOI: 10.1046/j.1440-1819.1999.00532.x
35. Bayer AJ, Pathy MS, Ankier SI. *Pharmacokinetic and pharmacodynamic characteristics of trazodone in the elderly.* British Journal of Clinical Pharmacology. 1983; 16(4):371–6. DOI: 10.1111/j.1365-2125.1983.tb02180.x
36. Ruxton K, Woodman RJ, Mangoni AA. *Drugs with anticholinergic effects and cognitive impairment, falls and all cause mortality in older adults: A systematic review and meta-analysis.* British Journal of Clinical Pharmacology 2015; 80(2):209-20. DOI: 10.1111/bcp.12617
37. Coupland CA, Dhiman P, Barton G, et al. *A study of the safety and harms of antidepressant drugs for older people: a cohort study using a large primary care database.* Health Technology Assessment (Winchester England) 2011; 15(28):1-202, iii-iv. DOI: 10.3310/hta15280
38. Roth AJ, McCall WV, Liguori A. *Cognitive, psychomotor and polysomnographic effects of trazodone in primary insomniacs.* Journal of Sleep Research. 2011; 20(4):552–8. DOI: 10.1111/j.1365-2869.2011.00928.x
39. Anonymous. *American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults.* Journal of the American Geriatrics Society. 2023; 71(7):2052–2081. DOI: 10.1111/jgs.18372
40. Bronskill SE, Campitelli MA, Iaboni A, et al. *Low-Dose Trazodone, Benzodiazepines, and Fall-Related Injuries in Nursing Homes: A Matched-Cohort Study.* Journal of the American Geriatrics Society. 2018; 66(10):1963–1971. DOI: 10.1111/jgs.15519
41. Watt JA, Gomes T, Bronskill SE, et al. *Comparative risk of harm associated with trazodone or atypical antipsychotic use in older adults with dementia: a retrospective cohort study.* CMAJ Canadian Medical Association Journal. 2018; 190(47):E1376–E1383. DOI: 10.1503/cmaj.180551
42. McCarthy L, Savage R, Dalton K, et al. *ThinkCascades: A Tool for Identifying Clinically Important Prescribing Cascades Affecting Older People.* Drugs & Aging. 2022; 39(10):829–840. DOI: 10.1007/s40266-022-00964-9
43. Araujo T, Jarrin DC, Leanza Y, et al. *Qualitative Studies of Insomnia: Current State of Knowledge in the Field.* Sleep Medicine Reviews. 2017; 31:58–69. DOI: 10.1016/j.smrv.2016.01.003
44. Dyas JV, Apekey TA, Tilling M, et al. *Patients' and clinicians' experiences of consultations in primary care for sleep problems and insomnia: a focus group study.* British Journal of General Practice. 2010; 60(574):e180-200. DOI: 10.3399/bjgp10X484183
45. Vincent N, Lionberg C. *Treatment preference and patient satisfaction in chronic insomnia.* Sleep. 2001; 24(4):411–7. DOI: 10.1093/sleep/24.4.411
46. Horowitz M, Taylor DM. *The Maudsley Deprescribing Guidelines: Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs.* 2024 January; Wiley-Blackwell. ISBN: 978-1-119-82302-5
47. National Sleep Foundation. *10 Tips for a Better Night's Sleep.* National Sleep Foundation 2025; https://www.thensf.org/sleep-tips/

Multiple experts and primary care clinicians reviewed the draft of this Therapeutics Letter for factual accuracy, and to ensure it is relevant to clinicians.

The UBC TI is funded by the BC Ministry of Health to provide evidence-based information about drug therapy. We neither formulate nor adjudicate provincial drug policies.