



# Therapeutic Brief

# 31

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## Topic 31: Insomnia management – reviewing the risk of hypnotics

Benzodiazepines and the benzodiazepine receptor agonists (hypnotics) are commonly prescribed for short-term management of insomnia but patients often use them for much longer.<sup>1,2</sup>

Adverse effects associated with the use of these medicines such as confusion, memory and other cognitive impairment, falls, incontinence and motor vehicle accidents often outweigh any benefits.<sup>3</sup> Non-drug strategies, such as behavioural and cognitive therapies, are effective, offer sustained benefits and should be considered the first-line and ongoing treatment for insomnia.<sup>4-6</sup> Involving patients in the discussion about the risks of these medicines can increase their willingness to trial reduction and cessation.

Insomnia can be a complex problem to manage. Where possible, underlying causes such as pain, sleep apnoea, restless legs syndrome and depression should be identified and managed.<sup>1,7</sup> In Veterans' MATES Topic 18, many veteran respondents with sleeping difficulties (72%) indicated they would be willing to try non-drug options; and over two-thirds of those using sleeping tablets reported they were willing to reduce the amount they were using. This therapeutic brief highlights the risks and adverse effects associated with benzodiazepines (temazepam, oxazepam, nitrazepam, flunitrazepam, triazolam and diazepam) and benzodiazepine receptor agonists (zopiclone and zolpidem).<sup>4</sup> It is recognised that some of the medicines are used for indications other than insomnia but they are still associated with the same risks and adverse effects. The therapeutic brief also suggests practical ways to reduce the use of these medicines in patients who are willing to do so.

### How effective are hypnotics?

Hypnotics have limited effectiveness and can modify the quality of sleep.<sup>8</sup> On average, they are associated with only small improvements in sleep latency (4.2 minutes) and sleep duration (62 minutes when used for 14 days or less).<sup>9</sup> Tolerance to hypnotics can develop within a few days to a few weeks of daily use, which may lead to dose escalations and a higher risk of adverse effects. Dependence may lead to withdrawal symptoms (e.g. muscle pain, tremors, seizures, hallucinations and nightmares) and rebound insomnia upon cessation.<sup>1,4</sup>

Although non-drug strategies are considered first line, hypnotics may be considered for the short-term management of insomnia.<sup>5</sup> If they are prescribed, hypnotics should be prescribed at the lowest effective dose, used intermittently and for the shortest possible time (e.g. 2 to 4 times per week and for fewer than 2 weeks).<sup>5,7,10</sup> Clinicians are advised to agree a cessation date with their patients at the time of initial prescribing. In all situations, the possible benefits need to be weighed against the risk of adverse effects.

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- 2 What are the risks?
- 3 Reduction and discontinuation
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### Key points

- > Many veterans report they are willing to reduce their use of sleeping tablets.
- > The consultation to re-prescribe a hypnotic is an opportunity to review its appropriateness.
- > Discuss with your patient their willingness to reduce hypnotic use and negotiate a withdrawal plan.
- > Review potential for harm in all patients prescribed hypnotics. Consider the risk of cognitive impairment, falls and functional incontinence.

## What are the risks?

Benzodiazepines and benzodiazepine receptor agonists are associated with a range of adverse effects, therefore the risks associated with ongoing treatment need to be discussed with the patient when these medicines are first prescribed. In those patients who have taken hypnotics long-term, the consultation to re-prescribe the hypnotic is an opportunity to review these risks. Cognitive decline and increased frailty may lead to additional risk (e.g. falls, incontinence, confusion) over time in long-term users. Some studies have linked hypnotic use to an increased risk of death although the exact causes are unknown.<sup>11-13</sup> **Therefore, it is important to review these risks before writing each prescription.**

Benzodiazepines and benzodiazepine receptor agonists have similar adverse effect profiles.<sup>4,14</sup>

### Issues to consider include:

#### Urinary incontinence

Hypnotics can increase the risk of functional incontinence, especially in older people.<sup>15</sup> The use of hypnotics should be reviewed in patients with a history of urinary incontinence to identify whether the hypnotic could be a contributing factor (see Topic 26: Urinary incontinence. <https://www.veteransmates.net.au/topic-26-therapeutic-brief>).

#### Cognitive impairment

- Hypnotics can contribute to cognitive impairment (e.g. short term memory loss and slowed reaction times) with both short and long-term use.<sup>3</sup>
- Discontinuation of hypnotic medicines can lead to improved cognition, including improved accuracy and speed of information processing, faster reaction times and increased alertness.<sup>16</sup>
- Use of hypnotics should be reviewed in patients with dementia, since they are predisposed to cognitive impairment (see Topic 25: Dementia. <https://www.veteransmates.net.au/topic-25-therapeutic-brief>).

#### Falls

- The risk of falls and fractures increases with both short and long-acting hypnotics.<sup>3,17</sup> This increased risk persists beyond 30 days.<sup>17</sup>
- Taking multiple medicines<sup>18</sup> in addition to hypnotics, such as antipsychotics (including prochlorperazine), antidepressants, antihypertensives, diuretics, sedatives and anti-Parkinson medications can have additive effects on falls risk (see Topic 20: Reducing the risk of falls. <https://www.veteransmates.net.au/topic-20-therapeutic-brief>). Use of hypnotics should be reviewed in patients with a history of falls, or who are taking other multiple falls risk medicines in addition to their hypnotic.

#### Physical function and mobility

- Hypnotics may impair physical function (e.g. decreased mobility and impaired ability to perform activities of daily living).<sup>19,20</sup> This may represent a threat to independent living.

#### Driving

- Hypnotics have been associated with double the risk of motor vehicle accidents in older persons.<sup>3,16</sup> Long-acting benzodiazepines and zopiclone are associated with almost double the risk of road traffic accidents in all age groups.<sup>21</sup>
- Hypnotic users should be advised about the risks to driving arising from impaired reaction time, attention and vigilance.<sup>22</sup>

#### Non-drug strategies

Veterans' MATES Topic 18 includes information about non-drug strategies as well as recommending a sleep diary (<https://www.veteransmates.net.au/topic-18-therapeutic-brief>). Information to assist GPs in the selection and implementation of cognitive and behavioural strategies has been produced by the Drug and Alcohol Services South Australia ([www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet](http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet)).

**See Further Information.**

### What about other medicines?<sup>4,8,23</sup>

Other medicines with sedative properties are sometimes used to manage insomnia in the presence or absence of psychiatric co-morbidity. These medicines may include antidepressants (e.g. mirtazapine, tricyclic antidepressants and agomelatine), sedating antihistamines and antipsychotics. Each of these medicines has its own adverse effect

profile. Adverse effects may include cognitive impairment and falls injuries.

Melatonin prolonged-release tablets (Circadin<sup>®</sup>) are marketed only for people over 55 years of age (for up to 13 weeks), however the long-term safety and efficacy are not well studied. Non-prescription preparations of melatonin are available but most contain subtherapeutic doses.

Many over the counter herbal medicines, including valerian, chamomile, hops, catnip, lavender and passiflora, available in different product forms, have been advocated for insomnia. Evidence is limited and routine use is not recommended. Most herbal medicines sold in Australia do not require proof of efficacy prior to marketing.

## Reduction and discontinuation

Many patients can successfully cease long term hypnotics by following a gradual dose reduction schedule.<sup>16</sup> Patients embarking on a reduction program are more likely to be successful if they are motivated, well-supported and adequately prepared with accurate information about what to expect and take part in planning the discontinuation strategy.<sup>5,24</sup> In some cases, referral to a specialist sleep clinic, sleep physician or psychologist may be necessary.

### A guide to help patients to reduce or discontinue hypnotics<sup>8,23</sup>

1

Develop a hypnotic withdrawal plan with the patient, including goals, scheduled dose reductions and timing. Advise on the management of withdrawal symptoms (e.g. a temporary dose increase if symptoms occur), use of cognitive and behavioural strategies, and avoidance of alcohol as a substitute.

2

Outline a realistic dose reduction schedule (will depend on doses in use). For example, for doses such as 10mg temazepam each night, withdrawal could consist of 5mg nightly for 2 weeks, then reduce to when-required use only. Seek specialist advice if discontinuing large doses, multiple hypnotics or in complex cases.

3

Be sure to titrate the dose according to the severity of rebound insomnia and withdrawal symptoms. Discuss with patients about possible withdrawal symptoms and advise they are usually transient. If withdrawal symptoms occur, rather than revert to the original regimen, allow the patient about a week to stabilise before the next dose reduction.

4

Review patients frequently (weekly or as determined by patient need) and monitor sleep, mood, withdrawal symptoms and use of other substances (alcohol, nicotine). Ongoing support, education and reassurance for patients and their family/carers can increase the success rate. Reinforce the need to continue behavioural and cognitive strategies.

5

Encourage the patient to try again if discontinuation is unsuccessful.<sup>25</sup>



## What to discuss with your patient

### Explain limited effectiveness of hypnotics

Hypnotics have some benefits but these are limited and often not sustained. For example, a study found no difference in sleep ratings between patients who withdrew from benzodiazepines and those who continued to use them.<sup>16</sup>

### Explain the type, nature and expected duration of withdrawal symptoms and rebound insomnia

Withdrawal symptoms including rebound insomnia, anxiety, irritability, nightmares, sweating and seizures have been reported as early as the first night of ceasing a short-acting hypnotic (e.g. zolpidem) and up to 1 to 2 weeks after cessation of longer acting hypnotics e.g. diazepam.<sup>7,26</sup>

In most cases, withdrawal symptoms usually last for only 1 to 3 days.<sup>5,7</sup> Gradual reduction of dose and/or frequency even after short-term use may help minimise withdrawal symptoms.

### Explain age-related changes and normality of broken sleep

Sleep requirements and patterns change throughout life.<sup>27</sup> Sleep quality and sleep efficiency (total sleep time/total bed time) decrease with normal ageing: average total sleep time drops by 27 minutes per decade from mid-life until the eighth decade.<sup>28</sup> Segmented sleep may be the natural pattern in tune with our inherent circadian rhythms and the natural environment.<sup>29,30</sup> It is normal to have brief awakenings each night and patients might require considerably less than eight hours of sleep per night.

### Advise not to substitute with alcohol

Alcohol does not help due to limited hypnotic efficacy, short half-life and its tendency to cause rebound insomnia.

### Discuss non-drug strategies and engage patients in their own management

Non-drug therapies have many benefits. Concurrent and ongoing behavioural and cognitive therapies can maximise the chance of successful cessation.<sup>31,32</sup> Non-drug therapies may provide longer lasting improvements in sleep after a hypnotic is stopped. Behaviour therapy has been found to result in a greater decrease in sleep latency than pharmacotherapy.<sup>6</sup>





## Further information on:

- non-drug strategies see the insert to Topic 18: Insomnia management: Effective approaches for a common problem <https://www.veteransmates.net.au/topic-18-therapeutic-brief>
- insomnia management information produced by Drug and Alcohol Services South Australia [www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+topics/substance+misuse+and+dependence/sleep+problems+--+insomnia+management+kit](http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+topics/substance+misuse+and+dependence/sleep+problems+--+insomnia+management+kit)
- medicines that may affect urinary incontinence see Topic 26: Urinary incontinence <https://www.veteransmates.net.au/topic-26-therapeutic-brief>
- managing insomnia for patients with dementia see Topic 25: Dementia <https://www.veteransmates.net.au/topic-25-therapeutic-brief>
- medicines that can increase falls risk see Topic 20: Reducing the risk of falls <https://www.veteransmates.net.au/topic-20-therapeutic-brief>

**Consider a medicines review\*** for patients prescribed hypnotics for insomnia treatment. The accredited pharmacist can help assess factors that may affect sleep and provide patient education to assist with withdrawal of hypnotics.

\* Home Medicines Review (HMR) or Residential Medication Management Review (RMMR)

## References

- Woodward M. Sleep in older people. *Rev Clin Gerontol* 2012; 22 (2): 130-49.
- Iliffe S, Curran HV, Collins R, et al. Attitudes to long-term use of benzodiazepine hypnotics by older people in general practice: findings from interviews with service users and providers. *Aging Ment Health* 2004; 8 (3): 242-8.
- Glass J, Lancotot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ* 2005; 331 (7526): 1169.
- Rossi S (Editor). *Australian Medicines Handbook*. Adelaide: Australian Medicines Handbook Pty Ltd 2012.
- Psychotropic Expert Group. *Therapeutic Guidelines: Psychotropic*. Version 6. Melbourne: Therapeutic Guidelines Limited; 2008.
- Smith MT, Perlis ML, Park A, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry* 2002; 159 (1): 5-11.
- Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008; 4 (5): 487-504.
- NPS - Better Choices Better Health. NPS News 24: Benzodiazepines, complementary medicines and non-drug treatments for insomnia. 2002 [accessed March 5 2012]; Available from: [http://www.nps.org.au/health\\_professionals/publications/nps\\_news/archive/NPS\\_News\\_24](http://www.nps.org.au/health_professionals/publications/nps_news/archive/NPS_News_24)
- Holbrook AM, Crowther R, Lotter A, et al. Meta-analysis of benzodiazepine use in the treatment of insomnia. *CMAJ* 2000; 162 (2): 225-33.
- Kamel NS, Gammack JK. Insomnia in the elderly: cause, approach, and treatment. *Am J Med* 2006; 119 (6): 463-9.
- Hublin C, Partinen M, Koskenvuo M, et al. Sleep and mortality: a population-based 22-year follow-up study. *Sleep* 2007; 30 (10): 1245-53.
- Mallon L, Broman JE, Hetta J. Is usage of hypnotics associated with mortality? *Sleep Med* 2009; 10 (3): 279-86.
- Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. *BMJ Open* 2012; 2 (1): e000850.
- National Institute for Clinical Excellence. *Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia*. Technology Appraisal 77. London; 2004.
- Landi F, Cesari M, Russo A, et al. Benzodiazepines and the risk of urinary incontinence in frail older persons living in the community. *Clin Pharmacol Ther* 2002; 72 (6): 729-34.
- Curran HV, Collins R, Fletcher S, et al. Older adults and withdrawal from benzodiazepine hypnotics in general practice: effects on cognitive function, sleep, mood and quality of life. *Psychol Med* 2003; 33 (7): 1223-37.
- Ray WA, Thapa PB, Gideon P. Benzodiazepines and the risk of falls in nursing home residents. *J Am Geriatr Soc* 2000; 48 (6): 682-5.
- Deandrea S, Lucenteforte E, Bravi F, et al. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology* 2010; 21 (5): 658-68.
- Gray SL, LaCroix AZ, Hanlon JT, et al. Benzodiazepine use and physical disability in community-dwelling older adults. *J Am Geriatr Soc* 2006; 54 (2): 224-30.
- Ried LD, Johnson RE, Gettman DA. Benzodiazepine exposure and functional status in older people. *J Am Geriatr Soc* 1998; 46 (1): 71-6.
- Barbone F, McMahon AD, Davey PG, et al. Association of road-traffic accidents with benzodiazepine use. *Lancet* 1998; 352 (9137): 1331-6.
- Drug and Alcohol Services South Australia (DASSA). *Benzodiazepines, Opioids and Driving*. 2006 [accessed March 5 2012]; Available from: [http://www.dassa.sa.gov.au/webdata/resources/files/Benzo\\_literature.pdf](http://www.dassa.sa.gov.au/webdata/resources/files/Benzo_literature.pdf)
- NPS - Better Choices Better Health. NPS News 67: Addressing hypnotic medicines use in primary care. 2010 [accessed March 5 2012]; Available from: [http://www.nps.org.au/health\\_professionals/publications/nps\\_news/current/nps\\_news\\_67](http://www.nps.org.au/health_professionals/publications/nps_news/current/nps_news_67)
- Khong E, Sim MG, Hulse G. Benzodiazepine dependence. *Aust Fam Physician* 2004; 33 (11): 923-6.
- Tiller J. The management of insomnia: an update. *Aust Prescr* 2003; 26 (4): 78-81.
- Grunstein R. Insomnia. Diagnosis and management. *Aust Fam Physician* 2002; 31 (11): 995-1000.
- Ohayon MM, Carskadon MA, Guilleminault C, et al. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep* 2004; 27 (7): 1255-73.
- Van Cauter E, Leproult R, Plat L. Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA* 2000; 284 (7): 861-8.
- Brown WA. Broken sleep may be natural sleep. *Psychiatric Times* Mar 1, 2007 [accessed March 5 2012]; Available from: <http://www.psychiatristimes.com/display/article/10168/55271>
- Wehr TA. In short photoperiods, human sleep is biphasic. *J Sleep Res* 1992; 1 (2): 103-7.
- Morin CM, Bastien C, Guay B, et al. Randomized clinical trial of supervised tapering and cognitive behavior therapy to facilitate benzodiazepine discontinuation in older adults with chronic insomnia. *Am J Psychiatry* 2004; 161 (2): 332-42.
- Parr JM, Kavanagh DJ, Cahill L, et al. Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis. *Addiction* 2009; 104 (1): 13-24.