

## Standard of Practice

### Prescribing Benzodiazepines & Z-Drugs (including Zopiclone & other drugs)

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Standards of Practice of Medicine set out the requirements related to specific aspects for the quality of the practice of medicine. Standards of Practice of Medicine provide more detailed information than contained in the *Regulated Health Professions Act*, Regulations, and Bylaws. All members must comply with Standards of Practice of Medicine, per section 86 of the *Regulated Health Professions Act*.

This Standard of Practice of Medicine is made under the authority of section 82 of the *Regulated Health Professions Act* and section 15 of the CPSM Standards of Practice Regulation.

#### PREAMBLE

This Standard establishes the standard of practice and ethical requirements of all members in relation to prescribing benzodiazepines and/or Z-Drugs for maximum safety for all patients whether in the community or in a health care facility. **This Standard does not apply to the use of these drugs in the treatment of cancer, palliative and end-of-life patients, seizure disorders, bipolar/psychotic disorder, and acute alcohol withdrawal.** Medical evidence of the risk to benefit ratio of prescribing benzodiazepines and/or Z-Drugs is altered over time, so prescribing these drugs must be in accordance with current medical knowledge. This Standard recognizes that in prescribing benzodiazepines and/or Z-Drugs each member exercises their clinical judgment, which is to be that of a member acting reasonably in the circumstances with current medical knowledge.

## STANDARD OF PRACTICE

### 1. GENERAL

- 1.1. Reasonable efforts are to be used to optimize non-pharmacological treatment modalities first (i.e., Cognitive Behaviour Therapy, improved sleep habits, elimination of caffeine, etc.) if available, and then optimize non-benzodiazepines or non-Z-Drug treatment modalities.
- 1.2. To mitigate risk of harm the member must use reasonable efforts to review the patient's current and past medications utilizing DPIN or eChart or consult with a pharmacist to obtain DPIN. This will mitigate the risk of harmful drug interactions and combinations and will prevent patients from obtaining prescriptions from multiple providers.
- 1.3. Members must prescribe the lowest effective dosage of benzodiazepines or Z- Drugs for the shortest possible duration and only exceed the maximum recommended dosage in exceptional circumstances and document this.
- 1.4. Long term use must be supported by current clinical evidence. Benzodiazepines and Z- Drugs may be appropriate for certain uncommon indications.
- 1.5. Discuss the following with the patient and document it in the medical record:
  - 1.5.1. Treatment goals including specific and realistic goals and an eventual possible discontinuation strategy;
  - 1.5.2. Non-pharmacological therapies;
  - 1.5.3. The modest benefit of long-term benzodiazepines and Z-Drugs;
  - 1.5.4. Risks associated with treatment; and
  - 1.5.5. The impairment caused by these drugs, particularly the dangers of driving, operating heavy machinery, or performing safety sensitive tasks, providing child or elder care if impaired.
- 1.6. Alprazolam (Xanax) has been identified as a drug with significant risks of abuse and diversion in Manitoba and should be avoided and/or replaced.
- 1.7. Members must carefully consider all concurrent medical conditions in the context of decisions to prescribe or continue to prescribe these medications:
  - 1.7.1. Heart failure, obesity, sleep apnea, chronic lung disease, alcohol and substance use disorders and renal or hepatic insufficiency and other chronic conditions or pregnancy compound the risk of these medications in unique ways.
  - 1.7.2. Patients must be regularly screened for the presence or emergence of mental health disorders (particularly mood and substance use disorders) which may complicate management.

- 1.8. In the course of managing patient care on these drugs (particularly while tapering), a substance use disorder may develop or reveal itself, and physicians must be able to appropriately diagnose and manage the patient's care needs. Appropriate care management can include referral to a physician with expertise and can include slow tapering of benzodiazepines and Z-Drugs to minimize the effects of withdrawal. Periodically attempt a trial of slow tapering (and if possible, collaborate with a trusted pharmacist identified by the patient). Use tapering guidelines and equivalency tables referred to in the Contextual Information attached to this Standard of Practice. Appropriate care management does not include abruptly discontinuing or an ultra rapid decrease of these drugs after long term use. Where tapering is not feasible, if there is documented benefit to the patient outweighing the potential harms, then continue with the treatment. Tapering of long term benzodiazepines and/or Z-Drugs is difficult, though possible.
- 1.9. Combining benzodiazepines and/or Z-Drugs with themselves or with other medications compounds risk of harm:
  - 1.9.1. If prescribing benzodiazepines and/or Z-Drugs, physicians must consider potential drug interactions with prescribed, over the counter, and recreational psychoactive substances including alcohol, opioids, gabapentin, and other benzodiazepines, dimenhydrinate and diphenhydramine, and document their advice to patients to avoid these;
  - 1.9.2. If patients with complex care needs are receiving multiple sedating medications, the physician must consider seeking the opinion of relevant consultants such as psychiatrists, pain specialists, addiction medicine specialists, pharmacists, and others to work toward a collaborative medication regimen that minimizes risk as much as possible.
  - 1.9.3. Only in exceptional circumstances prescribe opioids together with benzodiazepines and/or Z-Drugs. Patients must be informed of the increased risk of death with this combination, and the discussion documented.
  - 1.9.4. Only in exceptional circumstances prescribe two or more benzodiazepines and/or Z-Drugs concurrently unless in the context of a taper.
- 1.10. Members must be aware of and comply with statutory reporting duties in the context of disease or disability, including a treatment regimen, that is expected to cause impairment to any relevant authorities (e.g. the MPI Registrar of Motor Vehicles).

## 2. PRESCRIPTION WRITING

- 2.1. Explicit instructions must be provided to the patient regarding appropriate use, quantity, and number of days the supply is intended to last. A dispensing interval, indicating the number of days the supply is anticipated to last, must be noted on the prescription (e.g. dispense X tablets every Y days).

2.2. Only write a prescription for a maximum of three months, with dispensing to be authorized for no more than a one-month supply unless it is for infrequent use. On an exceptional basis, members may authorize a dispensing interval of up to three months for patients:

2.2.1. in remote communities; and

2.2.2. travelling, if the patient has been on a stable long-term prescription.

### 3. OLDER ADULT PATIENTS – ADDITIONAL

3.1. For older adult patients recognize that new starts of benzodiazepines and Z-Drugs must be carried out with extreme caution and not be used as first choice for insomnia, agitation, or delirium, nor for managing behaviours arising from dementia and delirium.

3.2. Ensure that dosing takes into consideration declining renal, hepatic and cognitive function and polypharmacy in older adult patients.

3.3. In prescribing for older adult patients, the member must recognize and discuss with the patient additional risks, including but not limited to:

3.3.1. Falls and subsequent fractures related to sedation, confusion, drowsiness and postural instability;

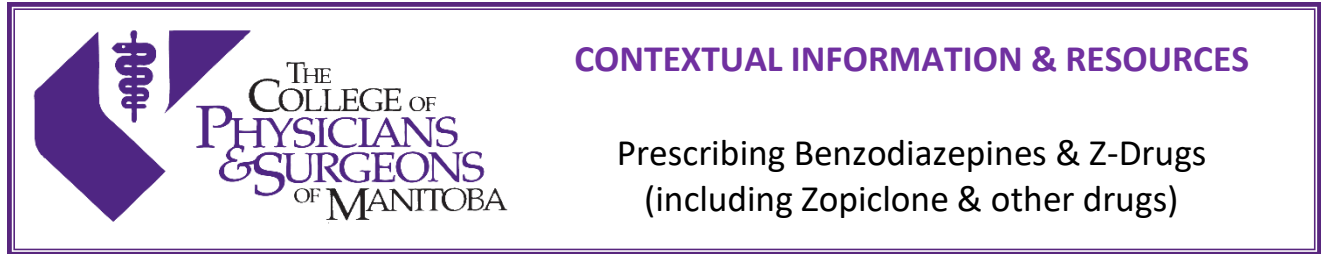
3.3.2. Impairment of psychomotor skills, judgment, and coordination increases the risk of motor vehicle and other accidents;

3.3.3. Negative effects on cognition, memory, delirium and a possible link to cognitive decline and dementia.

### 4. APPLICABLE DRUGS FOR THIS STANDARD

Benzodiazepines		Z-Drugs
Alprazolam (Xanax®)	Lorazepam (Ativan®)	Eszopiclone
Bromazepam (Lectopam®)	Midazolam (Versed®)	Zolpidem
Chlordiazepoxide (Librium®)	Nitrazepam (Mogadon®)	Zopiclone
Clobazam *to be started by Neurologists only	Oxazepam (Serax®)	
Clonazepam (Rivotril®)	Potassium-Clorazepate	
Diazepam (Valium®)	Temazepam (Restoril®)	
Flurazepam (Dalmane®)	Triazolam (Halcion®)	

See next page for Contextual Information and Resources



## Background

Medical evidence of the risk to benefit ratio of prescribing benzodiazepines and/or Z-Drugs has altered over time, so prescribing these drugs must be in accordance with current medical knowledge. Drugs of dependence have important therapeutic uses, but there is a need to ensure the supply of these medicines is clinically appropriate. In the past two decades clinical guidelines have recommended against long-term use of benzodiazepines and Z-Drugs. The conditions where benzodiazepines are most commonly prescribed (anxiety and insomnia) remain sources of debate in medical circles. Physicians must consider multiple factors when prescribing benzodiazepines. Good clinical judgment and an evidence-based approach remain key to safe and appropriate prescribing. The Standard tries to strike the best balance between the benefits benzodiazepines and Z-drugs provide for many patients with the risk posed to some patients.

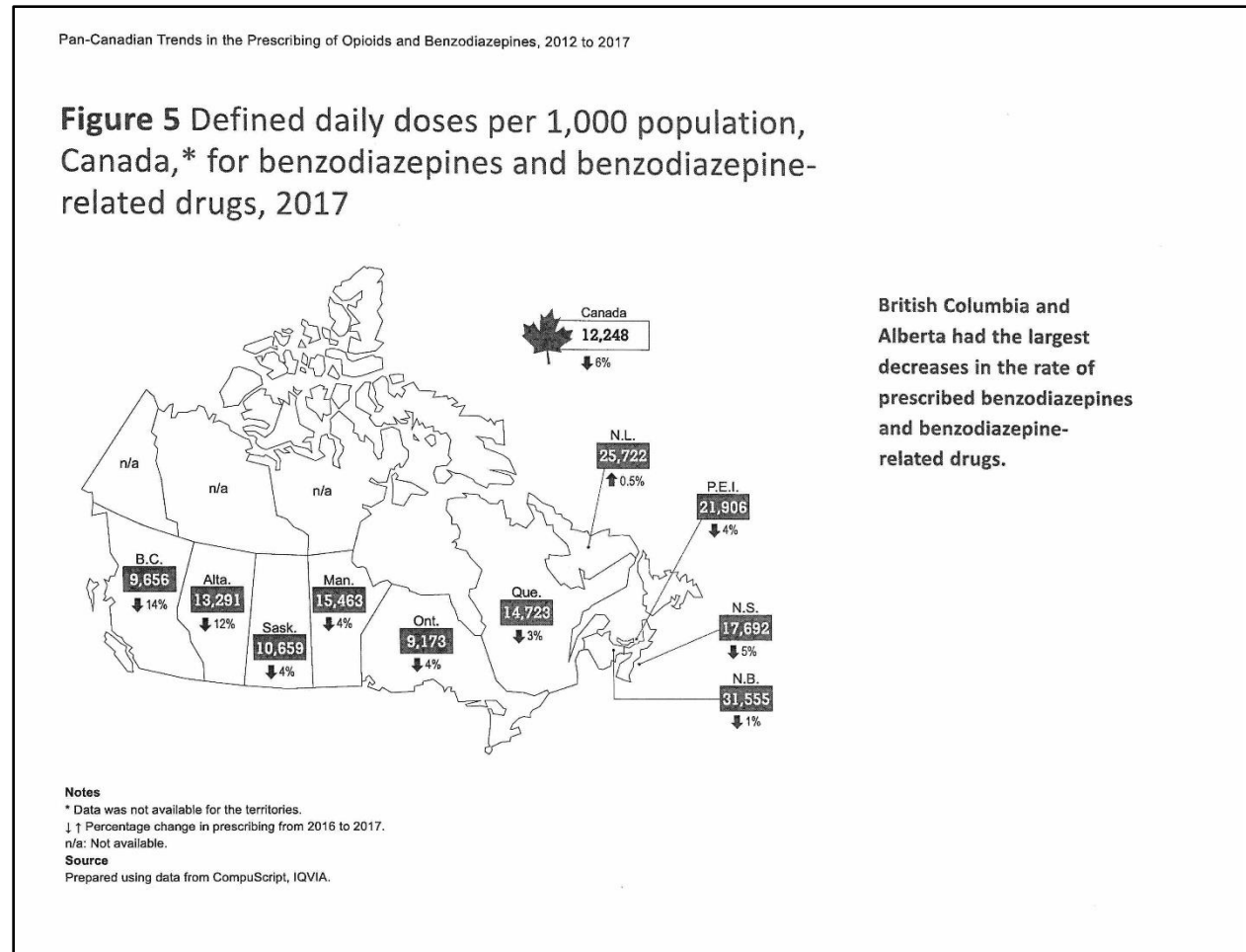
## Risks of Benzodiazepines in Manitoba

CPSM participates in the Adult Inquest Review Committee of the Chief Medical Examiner to review all deaths involving prescription medications. These reviews indicate deaths from other drugs are climbing rapidly while opioid deaths have levelled off. Alprazolam and Gabapentin, as well as diphenhydramine, have become significant drugs of abuse in Manitoba.

- Alprazolam is the benzodiazepine that contributed to the largest number of overdose deaths last year.
- Most opioid deaths can be attributed to one or more opioids combined with other drugs, often benzodiazepines and/or Z-Drugs.
- The two drug classes that were the top contributors to opioid overdoses were benzodiazepines and antidepressants from 2014-2017.
- Alprazolam, Zopiclone, and/or SSRIs contributed in total to 11, 9, and 8 drug overdose deaths respectively from 2016-2018.

The lessons learned from this provincial death data should transform physician prescribing practices. The Standard is to urge physicians to **be mindful of polypharmacy - the overall risk may outweigh the benefit from individual medications. Opioids, benzodiazepines, antidepressants, Z-Drugs, antipsychotics, and gabapentin all interact with each other often contributing to these deaths.**

Outside of Atlantic Canada, Manitoba has the highest rate of prescribing benzodiazepines and related drugs, at 50% higher than neighbouring Ontario and Saskatchewan. In 2017 there were 15,463 defined daily doses per 1000 population for these drugs.



A study in Manitoba in 2016 concluded that a limited segment of the population that received benzodiazepine prescriptions was classified as sustained users, and a smaller proportion of that group escalated to doses higher than those recommended by product monographs and clinical guidelines. <https://ps.psychiatryonline.org/doi/full/10.1176/appi.ps.201500380>

## Risks of Benzodiazepines in General

Benzodiazepines and Z-Drugs carry significant risk such as:

- Sedation, confusion, drowsiness and postural instability contributing to the risk of falls and subsequent fractures;
- Impairment of psychomotor skills, judgment, and coordination increasing the risk of motor vehicle accidents;
- Negative effects on cognition and memory, delirium, drug-related pseudo dementia and a possible link to cognitive decline and Alzheimer's disease;

- Dependency and abuse potential;
- Risky interaction with medications or herbals;
- Sleep automatism (in the case of Z-Drugs), including food binging, and even driving while asleep or in a sleep-like state.

The Standard recognizes that:

- Initiating benzodiazepines and/or Z-Drugs in hospital substantially increases the risk of long-term use and dependency.
- Cognitive behavioural therapy, brief behavioural interventions and tapering protocols have a proven benefit in sedative-hypnotic discontinuation and are also beneficial in improving sleep.
- The number needed to treat with a benzodiazepine and/or Z-Drugs to get improved sleep is 13, whereas the number needed to harm is only 6. [BMJ: doi: 10.1136/bmj.38623.768588.47(published 11 November 2005)]

### Risks of Benzodiazepines in the Elderly

Benzodiazepines and/or Z-Drugs have been identified as problematic medications for use in older adults and carry significant risks. Large scale studies consistently show that the risk of motor vehicle accidents, falls and hip fractures, leading to hospitalization and death, can more than double in older adults taking benzodiazepines and/or Z-Drugs. Older patients, their caregivers and their health care providers should recognize these potential harms when considering treatment strategies for insomnia, agitation or delirium.

Benzodiazepines and Z-Drugs carry significant risks beyond those for the general patient population:

- Sedation, confusion, drowsiness and postural instability contributing to the risk of falls and subsequent fractures;
- Further impairment of psychomotor skills, judgment, and coordination increasing the risk of motor vehicle accidents;
  - Negative effects on cognition and memory, delirium, drug-related pseudo dementia and a possible link to cognitive decline and Alzheimer's disease.

### Driving or Operating Heavy Machinery and Benzodiazepines and Z-Drugs

MPI, in its Drug Impaired Driving educational sessions for physicians and other health professionals, highlights the potential perils associated with driving among individuals who are prescribed benzodiazepines and Z-drugs. This is reflected in the CMA Guide for determining medical fitness to operate motor vehicles, which also highlights the peril associated in combination with alcohol.

MPI's advice to prescribers is for any patient provided with a new prescription or an increase in dosage that they should temporarily stop driving until they can be reassessed by the prescriber (please note that this would generally not call for a notification of MPI in accordance with the

mandatory reporting requirement). The prescriber can determine whether it is reasonable to resume driving when the clinical reassessment is conducted. Should some degree of functional impairment be suspected at the time of reassessment, the prescriber should, at that point, report to MPI with an appropriate recommendation, which could be that the patient's driver license be suspended or that a functional driving assessment be conducted.

The same applies with necessary modifications to patients who operate heavy machinery. Such patients should also be provided with a note indicating they should not operate such equipment for either a limited time period or until reassessment.

### Application of Standard

This Standard applies to Benzodiazepines and what are known as the Z-Drugs (Zopiclone, Zolpidem, Zaleplon, and Eszopiclone) because of the similarity of these drugs in prescribing for similar medical conditions, risks, addictions (abuse and diversion), and use.

### BENZODIAZEPINE RECEPTOR AGONIST EQUIVALENCY ESTIMATES

(Diazepam 10 mg as reference)

	Ashton	Kalvik et al.	Shader & Greenblatt	Alessi-Severini et al.
<b>Diazepam</b>	<b>10 mg</b>	<b>10 mg</b>	<b>10 mg</b>	<b>10 mg</b>
Alprazolam (Xanax®)	0.5 mg	1 mg	1 mg	1 mg
Bromazepam (Lectopam®)	5 mg	6-12 mg	NA	10 mg
Chlordiazepoxide (Librium®)	25 mg	20-50 mg	50 mg	20 mg
Clobazam	20 mg	NA	NA	20 mg
Clonazepam (Rivotril®)	0.5 mg	1-2 mg	0.5 mg	0.5 mg
Potassium Clorazepate	15 mg	15 mg	15 mg	NA
Flurazepam (Dalmane®)	30 mg	30 mg	30 mg	30 mg
Lorazepam (Ativan®)	1 mg	1-2 mg	2 mg	2 mg
Oxazepam (Serax®)	20 mg	30 mg	30 mg	20 mg
Nitrazepam (Mogadon®)	10 mg	10-20 mg	10 mg	10 mg
Temazepam (Restoril®)	20 mg	20-30 mg	30 mg	30 mg
Triazolam (Halcion®)	0.5 mg	0.5 mg	0.25 mg	0.25 mg
Zaleplon	20 mg	NA	NA	20 mg
Zolpidem	20 mg	NA	10 mg	NA
Zopiclone	15 mg	NA	NA	7.5 mg

Ashton H. benzo.org.uk : Benzodiazepine Equivalence Table. <http://www.benzo.org.uk/bzequiv.htm>. Published 2007. Kalvik A., Isaac P., Janecek E. Benzodiazepines: Treatment of anxiety, insomnia and alcohol withdrawal. *Pharmacy connection* Sept/ Oct 1995 20-32. Shader RI, Greenblatt DJ. *J Clin Psychopharmacol*. 1997;17(4):331. Alessi-Severini S, Bolton JM, Enns MW. Sustained Use of Benzodiazepines and Escalation to High Doses in a Canadian Population. *Psychiatric Serv*. 2016;67(9):1012-1018.



## Tapering

Gradual dose reduction is the central tenet in discontinuing benzodiazepine and Z-Drugs and supervision is the preferred tapering strategy. Patient preference is not a valid reason to defer tapering.

Various taper plans, suggestions, and schedules are included in the resources above.

## Working with the Pharmacist

With a high level of knowledge of dosage forms, equivalencies, tapering tools, and the potential for compounding intermediate dosage forms when necessary, as well as the most frequent contact with shared patients, pharmacists can and should often play an active role in planning and providing feedback during and after benzodiazepine and Z-drug tapers. Some pharmacists can assist in preparing tapering schedules.

Furthermore, collaborating and communicating with the pharmacist especially when tapering is in progress is beneficial because the pharmacy maintains ongoing documentation on patient interactions and any issues/concerns they may have noted over time. Providing the pharmacy with a patient care plan for tapering will keep all healthcare providers informed, especially if the patient contacts the pharmacist if they are experiencing any withdrawal symptoms or are requesting early refills. Randomized controlled trials have shown sedative-hypnotics deprescribing rates of 43% when pharmacists and physicians worked in collaboration.<sup>1</sup>

Consider a tripartite agreement with the patient-pharmacist-physician. Having a patient use only one pharmacy for their prescriptions helps the pharmacist know and assess the patient and enables the physician to inform the pharmacist in advance of special requests.

## Suggested Resources

[\*Managing Benzodiazepine Use in Older Adults\*](#) by the Centre for Effective Practice in Ontario is an **excellent clinical tool** which can be adapted for other ages.

[\*Deprescribing Benzodiazepine Receptor Agonists: Evidence Based Clinical Practice Guideline\*](#) issued by the College of Family Physicians of Canada is a helpful resource.

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<sup>1</sup> Martin P, Tamblyn R, Benedetti A, Ahmed S, Tannenbaum C. Effect of a Pharmacist-Led Educational Intervention on Inappropriate Medication Prescriptions in Older Adults: The D-PRESCRIBE Randomized Clinical Trial. JAMA 2018;320:1889-98

[\*\*Prescribing Drugs of Dependence in General Practice Part B\*\*](#), by the Royal Australian College of General Practitioners includes a framework for accountable prescribing of benzodiazepines in a practical guide that physicians can use to minimise harm and maximise benefits to patients. There are terrific **resources** included such as examples of responses to patient requests for benzodiazepines, communications with patients, practice policies and forms, patient agreements, drug and alcohol assessment tool, and a GP Guide to Insomnia.

[\*\*Canadian Guidelines on Benzodiazepine Receptor Agonist Use Disorder Among Older Adults\*\*](#) has useful guidance on either preventing the development of Benzodiazepine use disorder or optimally assessing and treating older patients who have developed such a disorder. The tapering guidance is helpful and can be applicable for other ages.

[\*\*Patient Pamphlet: Insomnia and Anxiety in Older People\*\*](#): – Sleeping pills are usually not the best solution.

[\*\*Toolkit: Less Sedatives for Your Older Relatives\*\*](#) – A toolkit for reducing inappropriate use of benzodiazepines and sedative-hypnotics among older adults in hospitals.

[\*\*Toolkit: Drowsy Without Feeling Lousy\*\*](#) – A toolkit for reducing inappropriate use of benzodiazepines and sedative-hypnotics among older adults in primary care.

[\*\*www.mysleepwell.ca\*\*](http://www.mysleepwell.ca) has an online hub of cognitive behaviour therapy for insomnia.

[\*\*Ementalhealth.ca\*\*](http://Ementalhealth.ca) has information for both patients and physicians.