Benzodiazepines: Use and Taper

Benzodiazepines (BZDs) are one of the largest and most widely prescribed psychotropic compounds. As of July 2015, the use of prescription sedatives among the Canadian general population was about 10%.[1] In Alberta alone, in 2013 there were over 560,000 prescriptions for benzodiazepines and a third of these were for individuals aged 60 or over.[2]

While use in the short-term may be effective and indicated in some clinical settings, long-term use of BDZ and Z-drugs has little proven efficacy and poses serious risks. This applies in particular to susceptible populations, such as the elderly who are more sensitive to the effects of these medications[3,4]. **BZDs and Z-drugs have been identified as potentially inappropriate medications for use in older adults[4,5] and carry significant risks such as**:

- Sedation, confusion, drowsiness and postural instability contributing to the risk of falls and subsequent fractures[6-8];
- Impairment of psychomotor skills, judgement and coordination increasing the risk of motor vehicle accidents[9, 10];
- Negative effects on cognition and memory, delirium, drug-related pseudo dementia and a possible link to cognitive decline and Alzheimer's disease[11,12];
- Dependency and abuse potential[11];
- Risky interactions with medications or herbals; and,
- Sleep automatism (in the case of z-drugs), including food binging, and even driving while still asleep or in a sleep-like state[10].

Clinicians should meticulously weigh the pros and cons, consider concomitant medications, assess risk of addiction and rule-out the possibility of diversion before prescribing BDZs or Z-drugs. Advanced age, concomitant use of alcohol or opioids, liver dysfunction and reduced renal function can increase the associated risk of toxicity and adverse events. As such, if prescribed at all, the dose for BDZ and Z-drugs in seniors should be lowered to about half the established defined daily dose (DDD) for adults.

Cautions that may preclude use include:

- Pregnancy (category D);
- Active substance abuse, including alcohol;
- Certain pre-existing health or mental conditions; e.g. sleep apnea, COPD or myasthenia gravis;
- Elderly patients, especially with a fall history;
- Hypersensitivity reactions.

Prescribers should assess family and personal history of medical/nonmedical abuse prior to prescribing in all patients.

Red-Flags for Abuse or Addiction include:

- Rapid escalation of drug use;
- Deteriorating function despite increasing dose;
- Dishonesty with respect to prescriptions which may present as frequent reports of loss or theft of medications and/or routine early refill requests;
- Involvement with law-enforcement;
- Non-oral route of use;
- Active addiction to another substance; and,
- Diversion or other drug-dealing behavior.

Alcohol potentiates the depressant effects of sedatives and consumption should be discussed if these are prescribed. The low-risk drinking guidelines advise per day consumption of no more than: 14 drinks per week for men; 9 drinks per week for women; and, 2 daily drinks for either gender[13]. Avoidance of these medications in patients using other sedating drugs or alcohol is the safer, and often more appropriate, choice.

Continuous daily use of BDZ and related compounds can lead to tolerance and dependence even at therapeutic doses within a few weeks[11]. As a result, their discontinuation can result in withdrawal symptoms. This applies even to patients who are not abusing the drug as physical dependence develops with extended use. Psychological dependence can also occur and may present as excessive worry about securing sufficient supply, reluctance to stop or reduce use, low self-confidence and a perceived inability to cope without the medication[14,15]. These factors can contribute to making discontinuation a challenging process, both for the patient and the clinician. Contemplating the benefits and risk-reduction from discontinuation can help with motivation in these cases. Referral may also be an option. Once these medications are stopped, withdrawal signs may appear in 1-2 days for short-acting; or, in 2-4 days for long-acting BDZs. These symptoms may persist for weeks, especially in patients who have a personal or family history of substance abuse.

Withdrawal symptoms may present as:

- **Minor:** Anxiety, irritability, insomnia, nausea, vomiting, tremors, dizziness, diaphoresis, visual distortion, tinnitus; Or,
- **Major:** agitation, confusion, disorientation, delirium, depersonalization, seizures, unstable vital signs.

To reduce the risk of severe withdrawal, which can be life threatening, abrupt discontinuation following long-term use is generally not indicated and a gradual taper of BDZ is recommended when clinically appropriate. Indications to taper off BDZs include addiction, adverse effects, advanced age or concurrent use of alcohol or opioids.

BDZ use for longer than 4-6 weeks should be cautiously approached. While it may be indicated for certain treatment resistant and/or severe chronic psychiatric conditions or in terminal illness, long-term use should be uncommon in practice as it has limited value for many patients and carries significant risks. In fact, unmonitored long-term use of BDZs, as mono- or poly-therapy, has been identified in research as a 'red-flag' for misuse and/or malpractice[16]. If used long-term, it is preferable to use the lowest effective dose with regular attempts to revisit the need for therapy and to re-evaluate the risks vs. benefit for the patient. Non-pharmacological measures and lower-risk therapeutic alternatives should be fully explored and the rationale for continued BDZ use, if applicable, should be well-documented in the patient's chart. BDZ should ideally be prescribed by a single prescriber responsible for the patient's therapy and be dispensed from a single pharmacy as much as possible.

The table below lists some **alternatives to consider before prescribing BDZs:**

Anxiety disorders	➢ Cognitive behavior therapy (CBT), psychotherapy ➢ SSRIs, SNRIs, Buspirone, Pregabalin
Insomnia	➢ CBT for insomnia, sleep restriction, sleep hygiene ➢ Doxepin, trazodone, other sedating antidepressants(if co-existing depression), melatonin

Improved cognitive and psychomotor functioning and a renewed feeling of well-being have been reported following successful discontinuation of BDZs[17,18]. Various strategies to reduce benzodiazepine prescribing in primary practice have been studied and range from minimalist interventions such as patient discontinuation letters, to more intensive approaches that include psychotherapy and/or pharmacological augmentation[18-20]. BDZ tapering guidelines and equivalencies excerpted from the National Opioid Use Guideline Group (NOUGG)[21] are appended to this document.

In conclusion, short-term use of BDZ may be indicated and can be effective. Responsible prescribing generally includes discontinuation of BDZs after this short-term use in most cases. In the rare situations that may require extended use, due diligence with regular reassessment and attempts to taper off BDZs, whenever indicated, is warranted.

Suggested Resources:

http://www.topalbertadoctors.org/cpgs/8640793
Towards Optimized Practice Adult Insomnia Guidelines

https://www.cma.ca/en/Pages/cpg-details.aspx?cpgId=14645&la_id=1
Canadian practice guidelines for the management of anxiety, post-traumatic stress and obsessive compulsive disorder

RACGP-Prescribing_drugs_of_dependence_in_general_practice
Australian Benzodiazepine Guidelines

http://www.benzo.org.uk/manual/bzsched.htm
Compound specific slow tapering samples

cbt.ca/
CBT workshops with option of Certificate in Medical CBT

http://deprescribing.org/news/empower-trial-empowering-older-adults-to-reduce-benzodiazepine-use/
EMPOWER benzodiazepine brochure for patients

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Benzodiazepine Tapering

1. BENEFITS of Benzodiazepine Tapering

- Lower the risk of future adverse drug-related risks such as falls.
- Increased alertness and energy.

2. APPROACH to Tapering

- Taper slowly: slow tapers are more likely to be successful than fast tapers.
- Use scheduled rather than p.r.n. doses.
- Halt or reverse taper if severe anxiety or depression occurs.
- Schedule follow-up visits q. 1–4 weeks depending on the patient's response to taper.
- At each visit, ask patient about the benefits of tapering (e.g., increased energy, increased alertness).

3. PROTOCOL for Outpatient Benzodiazepine Tapering

3.1 Initiation

- Can taper with a longer-acting agent, e.g., diazepam/clonazepam, or taper with agent that patient is taking. (Diazepam can cause prolonged sedation in elderly and those with liver impairment.)
- Insufficient evidence to strongly support the use of one particular benzodiazepine for tapering.
- Convert to equivalent dose in divided doses (see equivalence table below).
- Adjust initial dose according to symptoms (equivalence table is approximate).

3.2 Decreasing the Dose

- Taper by no more than 5 mg diazepam equivalent/week.
- Adjust rate of taper according to symptoms.
- Slow the pace of the taper once dose is below 20 mg of diazepam equivalent (e.g., 1–2 mg/week).
- Rx: dispense daily, 2x weekly, or weekly depending on dose and patient reliability.

3.3 Another Approach

Taper according to the proportional dose remaining: Taper by 10% of the dose every 1–2 weeks until the dose is at 20% of the original dose; then taper by 5% every 2–4 weeks.

Source: Adapted from Kahan 2002

SEE GUIDELINE, PART B, RECOMMENDATION 6

Benzodiazepine Equivalent Table

Source: Adapted from Kalvik 1995; Canadian Pharmacists Association 1999.

Benzodiazepine	Equivalent to 5 mg diazepam (mg) *
Alprazolam (Xanax®)**	0.5
Bromazepam (Lectopam®)	3–6
Chlordiazepoxide (Librium®)	10–25
Clonazepam (Rivotril®)	0.5–1
Clorazepate (Tranxene®)	7.5
Flurazepam (Dalmane®)	15
Lorazepam (Ativan®)	0.5–1
Nitrazepam (Mogadon®)	5–10
Oxazepam (Serax®)	15
Temazepam (Restoril®)	10–15
Triazolam (Halcion®)**	0.25

* Equivalences are approximate. Careful monitoring is required to avoid over-sedation, particularly in older adults and those with impaired hepatic metabolism.

**Equivalency uncertain.

SEE GUIDELINE, PART B, RECOMMENDATION 6