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, in 2013 alone, 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 these medications has very little proven benefit and poses serious risks. This applies in particular to susceptible populations, such as the elderly.

BZDs and Z-drugs have been established as potentially inappropriate medications for use in older adults[3] and carry **significant risks** for the general population such as:

- Sedation, drowsiness and lethargy contributing to the risk of falls;
- Impairment of psychomotor skills, judgement and coordination increasing the risk of vehicle accidents;
- Effects on cognition and memory impairment
- Dependency and abuse potential;
- Increased dementia, and possibly Alzheimer's disease risk;
- Interactions with other medications; and,
- Sleep automatism (in the case of z-drugs), including food binging, and even driving while still asleep or in a sleep-like state.

Clinicians should meticulously weigh the pros and cons of use, consider concomitant medications, assess risk of addiction and rule-out the possibility of diversion before making the decision to prescribe these medications. Advancing age, alcohol and/or opioid use, liver dysfunction and reduced kidney function, all increase the associated risk of toxicity.

Cautions that may preclude use include:

- Pregnancy (category D);
- Active substance abuse, including alcohol;
- Medical and mental health problems that may be exacerbated by use; for instance, sleep apnea, COPD or myasthenia gravis;
- Older age, with or without organ compromise;
- Long term use; and,
- 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. [4] Avoiding use is best if a patient's on other sedating drugs or is using alcohol.

Continued use of BDZ and related compounds can lead to tolerance and dependence, even at therapeutic doses, following only a few weeks of daily use. As a result, their discontinuation can result in withdrawal symptoms. This would also apply to patients not abusing the drug who have developed physically dependence with long-term use. When stopped, withdrawal symptoms may appear in 1-2 days for short-acting; and, in 2-4 days for long-acting BDZs. Symptoms may persist for weeks, especially in patients with a personal or family history of substance abuse. Withdrawal can result in minor symptoms, or, may become major and potentially life-threating.

Withdrawal symptoms may present as:

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

To reduce the risk of severe symptoms of withdrawal, abrupt discontinuation after 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 tapering guidelines and equivalencies from the National Opioid Use Guideline Group[5] are excerpted for inclusion, and follow this document.

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

Anxiety disorders	-Cognitive behavior therapy, psychotherapy -SSRIs, TCAs and Buspirone
Insomnia	-Proper sleep hygiene -Cognitive behavior therapy -TCAs (trazodone, amitriptyline, doxepin) and other sedating antidepressants(mirtazapine)

BDZ use longer than 4-6 weeks should be cautiously approached. While it may rarely 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 most 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.[6] If used long-term, it is preferable to avoid short-acting agents and to use the lowest effective dose with regular attempts to revisit the need for therapy and re-evaluate its risk vs. benefit to 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 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.

In conclusion, while BDZ use in short-term may be indicated and effective, this rarely applies to long-term use which is often also relatively unsafe. Responsible prescribing generally dictates discontinuation of BDZs after short-term use in most patients; or, regular reassessment and gradual taper off BDZs, whenever indicated, in rarer situations requiring longer use.

References:

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3. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel (2012), American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society*, 60: 616–631. doi: 10.1111/j.1532-5415.2012.03923.x
4. Butt, P., Beirness, D., Cesa, F., Gliksman, L., Paradis, C., & Stockwell, T. (2011). Alcohol and health in Canada: A summary of evidence and guidelines for low-risk drinking. Ottawa, ON: Canadian Centre on Substance Abuse.
5. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Canada: National Opioid Use Guideline Group (NOUGG); 2010 [cited 2016 Feb 29]. Available from: http://nationalpaincentre.mcmaster.ca/opioid
6. Dell'Osso B, Albert U, Atti AR, et al. Bridging the gap between education and appropriate use of benzodiazepines in psychiatric clinical practice. *Neuropsychiatric Disease and Treatment.* 2015;11:1885-1909. doi:10.2147/NDT.S83130.
7. Longo, Lance P., Johnson B. Addiction: Part 1. Benzodiazepines - Side Effects, Abuse Risk and Alternatives. Am Fam Physician. 2000 Apr 1;61 (7):2121-8

Suggested Resources:

RACGP-Prescribing drugs of dependence in general practice, Part B
Australian Guidelines

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

http://www.topalbertadoctors.org/cpgs/8640793
TOP Adult Insomnia Guidelines

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4120194/
Canadian practice guidelines for management of anxiety, posttraumatic stress and obsessive-compulsive disorders

www.cbtforinsomnia.com
Resources for cognitive behavioral therapy including tools for patient access

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