Compilation of International Recommendations for Prescribing Benzodiazepine Receptor Agonists

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Preface

In modern society, work-related stress, changing lifestyles, and a rapidly evolving information environment continue to affect people's mental health and sleep quality. With an aging population and the rising prevalence of chronic diseases, insomnia and anxiety have become major global health concerns. Sleep and emotional well-being are closely interrelated and frequently influence one another; when symptoms persist and interfere with daily life, they may progress into conditions such as insomnia disorder and anxiety disorder, exerting a marked impact on individual health and quality of life.

Benzodiazepines and Z-drugs, both classified as benzodiazepine receptor agonists (BZRAs), have long been widely used in the treatment of insomnia disorder and anxiety disorder. Although these medications offer the advantage of rapid symptom relief, advances in evidence-based medicine have shown that their long-term use may give rise to risks including dependence, tolerance, cognitive impairment, and falls. These effects are particularly pronounced in older adults, and have consequently attracted considerable attention from the international medical community and the public health field.

To help clinicians and healthcare teams stay abreast of the latest international trends, the Taiwan Food and Drug Administration, Ministry of Health and Welfare commissioned experts and scholars to collect and compile 23 key international guidelines from the United States, the United Kingdom, Canada, Australia, European countries, Singapore, and the World Health Organization (WHO). Taken together, the most recent recommendations across these jurisdictions consistently emphasize prioritizing non-pharmacological treatment, restricting BZRAs to short-term use, and actively promoting management strategies such as dose reduction and deprescribing.

It is our hope that this book will serve as a reference for healthcare professionals using BZRAs to treat insomnia disorder and anxiety disorder, supporting clinical decision-making and alignment with international practice, and thereby further enhancing the quality of patient care, medication safety, and quality of life.

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July, 2026

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Key Summary of International Guidelines: Recommendations on Prescribing of Benzodiazepines and Z-drugs for the Treatment of Insomnia and Anxiety

1. Introduction

Over the past several decades, benzodiazepines and Z-drugs—collectively referred to as benzodiazepine receptor agonists (BZRAs)—have been widely used for the treatment of insomnia and anxiety. However, as the global medical community has developed a deeper understanding of the risks associated with their long-term use, including physiological dependence, tolerance, cognitive impairment, falls, and complex sleep behaviors, international prescribing recommendations have undergone a marked paradigm shift. A review of recently updated clinical practice recommendations from the United States, the United Kingdom, Canada, Australia, European countries, Singapore, and the World Health Organization (WHO) shows that a high level of consensus has been reached regarding the prescribing and management of BZRAs. Health authorities and professional medical societies across these jurisdictions strongly urge that non-pharmacological treatment should be prioritized, short-term use should be strictly limited, and deprescribing and discontinuation should be actively promoted.

2.Summary of International Consensus

1.1. Establishing Non-Pharmacological and Alternative Medications as First-Line Treatment

Prescribing recommendations across countries consistently emphasize that BZRAs should not be used as the first-line routine medication for insomnia or anxiety disorders:

(1) Insomnia disorder: The first-line treatment should be cognitive behavioral therapy for insomnia (CBT-I) and good sleep hygiene education. Medications should be used only as short-term adjunctive therapy when functioning is severely impaired and non-pharmacological interventions have been ineffective.

(2) Anxiety disorder: The first-line treatment should be psychotherapy (e.g., cognitive behavioral therapy [CBT]) and antidepressants (e.g., selective serotonin reuptake inhibitors [SSRIs] and serotonin-norepinephrine reuptake inhibitors [SNRIs]). BZRAs should be limited to the transition period before antidepressants take effect, or for short-term relief of disabling acute anxiety.

1.2. Strict Limitation to Short-Term Use and the "Lowest Effective Dose" Principle

When initiation of BZRA therapy is necessary, prescribers should follow the principles below:

(1) Minimize treatment duration: The prescribed duration should be kept as short as possible, and it is strongly recommended not to exceed 2 to 4 weeks (including the tapering period). BZRAs should not be set as default long-term continuous repeat prescriptions.

(2) Minimize dosage: Treatment should begin with the lowest approved dose, with intermittent use on an as-needed (PRN) basis whenever possible, rather than routine daily dosing, in order to delay the development of tolerance.

1.3. Boxed Warning for Potentially Fatal Drug Interactions

BZRAs suppress the central nervous system(CNS) and respiratory function. Regulatory authorities in multiple countries (e.g., the U.S. FDA and the UK MHRA) have issued the most stringent warnings:

(1) Avoid concomitant use with opioids: Combined use produces synergistic depressant effects, which can substantially increase the risk of respiratory failure and death.

(2) Strictly avoid concomitant use with alcohol: Patients should be warned not to consume alcohol while taking these medications, as this may cause profound sedation and increase the risk of fatal overdose.

1.4. Prescribing Contraindications in Specific High-Risk Populations

For certain populations, the harms associated with BZRAs may far outweigh their potential benefits:

(1) Older adults (≥65 years): BZRAs are classified in multiple countries as potentially inappropriate medications for older adults at high risk (according to the Beers Criteria). Older adults have reduced drug clearance and are therefore highly susceptible to delirium, cognitive impairment, and gait instability, with a significantly increased risk of falls and hip fractures after use. If use is considered, the dose should be reduced by half, and an intermediate- to short-acting agent without active metabolites (e.g., lorazepam) should be selected.

(2) Other high-risk populations: In principle, BZRAs should be avoided in patients with severe obstructive sleep apnea (OSA), myasthenia gravis, pregnant women (due to the risk of neonatal withdrawal), and those with a history of substance use disorder (SUD).

1.5. Proactive Monitoring and Shared Decision-Making (SDM)

Preventing medication misuse and addiction is a key responsibility of the prescribing physician:

(1) Regular review and medical record documentation: Physicians should proactively review prescription monitoring programs (e.g., PDMPs / cloud-based medication records) to prevent duplicate prescriptions obtained across different institutions.

(2) Implementation of informed consent: At the time of initial prescribing, physicians must clearly discuss with the patient the medication's addictive potential, its possible impact on driving safety, and the expected goal that it is for short-term treatment only, and should document the communication in detail.

1.6. Safe Deprescribing Strategies for Dose Reduction and Discontinuation

Long-term BZRA use must not be discontinued abruptly, as this may precipitate potentially life-threatening withdrawal syndromes (e.g., seizures or delirium):

(1) Slow and gradual tapering: A personalized tapering plan should be developed based on the patient's duration of use and dosage, spanning several weeks, several months, or even up to one year (e.g., reducing the original dose by 5%–25% every 1–2 weeks).

(2) Medication switching strategy: For BZRAs with a short half-life and those that are difficult to split accurately for dose adjustment, clinicians may consider first converting to an equivalent dose of a long-acting agent (e.g., diazepam) before proceeding with gradual tapering.

(3) Psychological support interventions: During the discontinuation process, patients are prone to withdrawal-related or rebound anxiety/insomnia. Physicians should provide supportive care and, when appropriate, introduce CBT to help patients through the process.

3. Summary of Clinical Practice

1.1. Two to four weeks is the globally recognized "safety red line":

Nearly all national guidelines set the safe prescribing limit for BZRAs at 2 to 4 weeks. For insomnia, an even shorter duration is recommended (less than 2 weeks), and prescribing should follow an "as-needed (PRN) use only" principle.

1.2. There is no "one-size-fits-all" approach to tapering, but there are recommended tapering gradients:

(1) The longer the duration of use and the higher the dose, the slower the taper should be.

(2) A generally accepted safe tapering rate is to reduce the total dose by 5% ~ 25% every 1 ~ 2 weeks.

(3) Discontinuation strategy: When the dose has been reduced to a very low level (e.g., approximately equivalent to diazepam 1–2 mg), withdrawal symptoms are often most pronounced. At this stage, the tapering pace should be slowed further to one dose reduction every 2 to 4 weeks before complete discontinuation.

1.3. Use long half-life agents (e.g., diazepam) to support tapering and discontinuation: For patients at high risk of severe withdrawal, it is recommended to convert short-acting agents (e.g., alprazolam, lorazepam) to long-acting diazepam based on an equivalent dose table, and then use its more stable blood concentration profile to achieve smoother dose reduction and discontinuation; However, this method is not suitable for older adult.

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Overview of Prescribing Benzodiazepines in Clinical Practice

Prescribing Drugs of Dependence in General Practice, Part B: Benzodiazepines

Royal Australian College of General Practitioners (RACGP)

https://www.racgp.org.au/getattachment/1beeb924-cf7b-4de4-911e-f7dda3e3f6e9/Part-B.aspx

* Note: The content of this article is excerpted from the above reference.

1. Clinical pharmacology of benzodiazepines

Numerous benzodiazepines are available. They can be classified according to their main use, speed of onset, duration of action and drug half-life.

While benzodiazepines differ in their pharmacokinetics (absorption, distribution, metabolism, excretion), they all have similar pharmacodynamic properties and clinical actions.

1.1. Properties

Benzodiazepines have four basic properties that give rise to their clinical use:

- anxiolytic
- sedative/hypnotic
- anticonvulsant
- muscle relaxant.

Benzodiazepines can also produce anterograde amnesia. This effect is used periprocedurally.

These properties are the result of enhancement of activity of the major inhibitory neurotransmitter in the central nervous system (CNS), gamma-aminobutyric acid (GABA). Benzodiazepines bind to receptors on the GABA-A receptor complex

causing inhibitory effects throughout the brain, including drowsiness and cognitive impairment (cerebral cortex), dampening of emotions such as fear and anxiety (mesolimbic dopamine system), memory impairment and anticonvulsant actions (hippocampus), and impairment of balance, motor control, muscle tone and coordination (cerebellum and other motor areas). These effects are non-selective.

Newer Z drugs (eg zolpidem and zopiclone) enhance the activity of GABA by binding at the same location as benzodiazepines. While these drugs have similar actions to benzodiazepines, they are marketed for insomnia. High doses are required to produce the other actions such as decreased anxiety. There is evidence Z drugs, which are now the most commonly prescribed hypnotic agents, share similar risks to benzodiazepines.

1.2. Speed of onset

Benzodiazepines are rapidly absorbed orally. After ingestion, peak effects will occur within 30 minutes to 2 hours. The more fat-soluble drugs (eg diazepam) enter the CNS more rapidly.

1.3. Metabolism and duration of activity

Benzodiazepines vary greatly in the speed at which they are metabolised and several different mechanisms are involved. Depending on their metabolic structure, benzodiazepines are short, medium or long acting.

For the majority of benzodiazepines, the elimination half-life is significantly longer than the duration of clinical action. As they are rapidly redistributed into fatty tissue after absorption, the noticeable clinical effects wear off after a few hours. However, the drugs may continue to exert subtle effects and, with repeated dosing, accumulation within the fatty tissue occurs and a steady state of blood concentration can be reached in approximately five half-lives. Due to slow leaching from fatty tissue, benzodiazepines may be detected in urine tests weeks to months after cessation of benzodiazepine use.

Benzodiazepines are metabolised by the liver and excreted renally. Metabolism may be impaired in patients with liver and/or kidney disease. Lorazepam, oxazepam and temazepam are metabolized by glucuronidation and therefore do not produce active metabolites. These are rarely susceptible to medication interactions, although their sedative effects remain synergistic. Some other benzodiazepines undergo metabolism by the cytochrome P450 (CYP450) 3A4 hepatic enzyme system and many are weak inhibitors of the CYP enzymes. Therefore, these benzodiazepines may have significant interactions with other drugs that are metabolised by these enzyme pathways.

1.4. Tolerance

Tolerance to all drugs of dependence develops with repeated use. Steady state plasma concentrations of benzodiazepines and their metabolites are reached after about five elimination half-lives, usually a few days to 2 weeks after starting therapy. Within a few days of reaching a steady state of plasma concentration, patients may start to experience a loss of effect from benzodiazepines, due to a range of neuroadaptive and physiological mechanisms.

Tolerance to the different benzodiazepine effects develops at different speeds and to different degrees, and may never be complete. The degree of tolerance differs between patients:

- A high proportion of patients with epilepsy develop tolerance to the anticonvulsant effects within a few weeks. This is similar to patients with spasticity disorders and the muscular relaxant effects.
- Tolerance to the hypnotic effects is less clear. Some of the literature claims it develops rapidly, while other authors claim it is slower. The evidence is limited by the length of trials. Sleep studies have shown that tolerance develops to the hypnotic effects of some rapidly eliminated benzodiazepines (eg triazolam) by 2 weeks, whereas for others (eg midazolam) tolerance emerges slowly and minimally. Tolerance also appears to develop with the Z drugs, however to a low degree.

- Tolerance to the anxiolytic and amnesic effects of benzodiazepines probably does not occur at all. Although, there is some evidence that a slow (years) tolerance may develop.

Long-term use of benzodiazepines may produce chronic changes in benzodiazepine-receptor functioning, which are thought not to fully return to their pre-addicted state after withdrawal and abstinence.

There is a high degree of cross-tolerance between benzodiazepines and other sedative/hypnotic medications and alcohol.

The development of tolerance is associated with escalation in dose, binge dosing and is one of the criteria for dependence and SUD. However, it is unusual for patients to steadily increase their dosage, even with long-term use, as might be expected with the development of tolerance. Patients who are prescribed benzodiazepines for anxiety or sleep problems usually do not escalate their doses even over a lengthy period of use. However, high-dose benzodiazepine mono-dependence has been reported.

Tolerance also makes it difficult to calculate equivalence.

1.5. Equivalent dosages

Equivalent doses are primarily used when making a transfer between drugs. Comparative oral doses of benzodiazepines are described in various sources, such as the Therapeutic Guidelines. However, the clinical potency of different drugs varies among individuals and it is difficult to demonstrate equivalence with drugs having very different half-lives (refer to Table 1). Due to this and variations in metabolism among people, these equivalence tables should be used with caution.

Table 1. Summary of the speed of onset, half-life and equivalent dose

Generic name	Trade name	Speed of onset, time to peak concentration	Elimination half-life	Approximate equivalent dose to diazepam 5 mg*	Comments
Diazepam	Antenex, Ducene, Valium, Valpam	Rapid 30–90 minutes	Biphasic: rapid phase 3 hours; elimination half-life 20–48 hours	5 mg	Risk for accumulation because of long-acting metabolites (temazepam, desmethyldiazepam, oxazepam) Increased risk for abuse because of quick onse
Alprazolam	Alpraz, Kalma	Rapid–intermediate, 1 hour	6–25 hours	0.5 mg	Increased risk for abuse because of greater lipid solubility Clinically, non-medical users report onset of effects at 20 minutes and lasting up to 6 hours
Bromazepam	Lexotan	Rapid, 0.5–4 hours	20 hours	3 mg	
Clonazepam	Paxam, Rivotril	Intermediate, 2–3 hours	22–54 hours	0.25 mg†	Use caution in patients with liver disease
Flunitrazepam	Hypnodorm	Rapid, 1–2 hours	20–30 hours*		
Lorazepam	Ativan	Intermediate, 2 hours	12–16 hours	1.0 mg‡	Preferred for patients with liver impairment, as no active metabolites
Nitrazepam	Alodorm, Mogadon	Rapid, 2 hours	16–48 hours	5 mg	
Oxazepam	Alepam, Murelax, Serepax	Slow–intermediate, 2–3 hours	4–15 hours	15 mg	Preferred for patients with liver impairment, as no active metabolites

Temazepam	Euhypnos, Normison, Temaze, Temtabs	Intermediate, 30–60 minutes after tablets or 2 hours after capsules	5–15 hours	10 mg	Preferred for patients with liver impairment, as no active metabolites
Triazolam	Halcion	Rapid, 1–3 hours	Biphasic: rapid phase 2.5–3.5 hours; elimination half-life 6–9 hours	0.25 mg	Lacks active metabolites
Zolpidem	Stilnox	Rapid, 0.5–3 hours	2.5 hours	10 mg	
Zopiclone	Imovane	Rapid, 1.75 hours	5 hours	7.5 mg	

*A broad review of published equivalents shows inconsistent data. The widely varying half-lives and receptor binding characteristics means that exact e quivalence is difficult.

†There is a wide variety of reported equivalence between clonazepam and other benzodiazepines. ‡Lorazepam may be relatively more potent at higher doses.

1.6. Adverse effects of benzodiazepines

1.6.1. Adverse effects on mental health and functioning

While used commonly for mental illness, benzodiazepines are associated with a range of adverse effects on mental health and function.

Cognitive impairment

Cognitive impairment is a broad term that encompasses several symptoms of benzodiazepine induced CNS effects.

Acute administration may induce dose-related sedation, drowsiness, learning impairment, psychomotor slowing and anterograde amnesia.

Chronic cognitive effects are modified by tolerance to some, but not all of the acute effects. A range of cognitive and psychomotor effects may persist after withdrawal.

One aspect of psychomotor functioning that has received a lot of attention is driving ability. Benzodiazepines are associated with a 60–80% increase in the risk of traffic accidents, and taking alcohol and benzodiazepines together increases accident risk more than seven times.

Anxiety

Patients may experience new or worsened anxiety while taking benzodiazepines long term or after stopping long-term use (rebound anxiety).

Depression

Patients taking benzodiazepines may experience aggravated depression or depression that first appears during benzodiazepine use. Benzodiazepines may cause and aggravate depression, possibly by reducing the output of neurotransmitters such as serotonin and noradrenaline.

Paradoxical stimulation and disinhibition

Benzodiazepines may have a disinhibitory effect (especially at high doses), leading patients to behave out of character and potentially placing themselves in dangerous situations because of an impaired perception of inherent risk. Common scenarios involve high-risk sexual behaviour and reckless driving. So called 'benzo binges' have been associated with shoplifting and other crimes.

Patients may also experience paradoxical excitement with increased anxiety, insomnia, talkativeness, restlessness, mania, and occasionally rage and violent behaviour (known as the 'Rambo effect').

1.6.2. Dependence, withdrawal syndrome and problematic use

Dependence – A contemporary understanding

Despite its familiarity and ubiquitous use, the concept of dependence is complex. Historically, dependence has been defined in pharmacological terms. That is a state that develops during chronic drug treatment in which cessation elicits an abstinence reaction (withdrawal). This is time limited and reversible by renewed administration of the drug.

Editor's Note: Current international guidelines indicate that the vast majority of dependence associated with benzodiazepines (BZDs) is physiological (physical) dependence, which represents a normal physiological response to long-term medication use. The development of withdrawal syndrome likewise occurs when long-term or high-dose use is followed by abrupt discontinuation or rapid dose reduction.

Withdrawal syndrome

Benzodiazepine withdrawal syndrome is highly variable. It remains unclear why some long-term users can withdraw without difficulty, even after years of continuous use, while others undergo protracted agonies.

The symptoms of withdrawal usually appear within 2–3 half-lives of the benzodiazepines being withdrawn. They usually lessen and then disappear within a few weeks. Sudden withdrawal of benzodiazepines can be associated with seizures.

The mildest form of withdrawal is rebound. Rebound comprises of the original symptoms recurring transiently at a greater intensity. Discontinuation of benzodiazepines is frequently associated with rebound anxiety and insomnia. Withdrawal symptoms include irritability, paraesthesia, tinnitus, headaches, dizziness, poor memory, poor concentration, perceptual distortions, menstrual disturbances and sensory hypersensitivity. Withdrawal symptoms can usually be minimised by gradual reduction. There is evidence that some patients suffer protracted withdrawal symptoms that can continue for months to years after cessation. There is debate about whether these persistent symptoms are withdrawal reactions, or simply features of an underlying disorder or worsening of that condition, which is triggered by treatment withdrawal.

Short- and intermediate-acting benzodiazepines carry a greater risk of rebound and withdrawal than long-acting benzodiazepines. Withdrawal syndrome can appear while the patient is still taking medication. This may be because the patient avoids increasing the dose to cover increased tolerance, or the patient is taking short-acting formulations and experiencing withdrawal as blood levels drop.

Incidence of withdrawal symptoms

The occurrence of withdrawal syndrome is related to high dosage and long-term use.

2. Benzodiazepines are used for a broad range of conditions including:

- insomnia
- anxiety disorders
- alcohol withdrawal
- mania/hypomania
- epilepsy
- acute seizures
- arousal/agitation in the in-patient setting
- palliative care
- musculoskeletal disorders.

The following article discusses two of the most commonly treated indications: insomnia and anxiety disorders.

2.1. Insomnia

Key points

- Insomnia is a common problem seen in general practice. The understanding of chronic insomnia is still evolving.
- In acute insomnia, sleep often returns to normal once the precipitating factor has resolved.

- In chronic insomnia, treatment is focused on addressing underlying comorbid precipitants (where present), and psychological and behavioural management.
- Pharmacotherapy for acute and chronic insomnia may be necessary for severe or resistant cases of insomnia. The decision to prescribe should be on an individual basis and involve serious consideration of all risks and possible benefits.
- Benzodiazepines and Z drugs have been shown to be effective treatments and may be prescribed for short-term or intermittent use. Harm, such as dependence and adverse events, may occur with both drug groups.
- Dose reduction and cessation should be discussed with the patient on first prescription and commenced once sleep patterns return to normal.
- Pharmacological treatment should be accompanied by specific patient education and regular review.

2.1.1. Acute insomnia

Factors that can precipitate acute insomnia include:

- physiological – hyperarousal due to stress, being ‘on-call’, caring for a sick child/relative, being in a strange situation (eg in hospital)
- pharmacological – prescribed drugs (eg newly prescribed diuretic causing nocturia) and nonprescribed drugs
- physical – coughing, environment (eg noise, temperature)
- disruption of circadian rhythm (eg jet lag).

Treatment of acute insomnia

Treatment is focused on avoiding or withdrawing the precipitant, if possible. All patients should receive basic behavioural counselling on sleep hygiene and stimulus control.

Drug treatment may be indicated as an adjuvant to non-drug therapies for acute insomnia that is severe, disabling and causing distress. Benzodiazepines and Z drugs are the most effective drugs.

The short-term use of benzodiazepines as hypnotic agents should only be one aspect of general management, with a clear endpoint of drug cessation once sleep patterns return to normal.

2.1.2. Chronic insomnia

The causes of chronic insomnia are complex and the management of chronic insomnia starts with addressing any relevant, underlying problems that are present, such as:

- pharmacological – prescribed drugs (eg some antidepressants, withdrawal of sedatives) and non-prescribed drugs (eg caffeine, alcohol)
- physical (eg pain, respiratory and cardiovascular disorders, neurological disorders, movement disorders, restless leg syndrome and other sleep disorders)
- psychiatric disorders (eg depression, anxiety, dementia and substance misuse)
- disruption of circadian rhythm (eg shift work).

Non-drug interventions

First-line therapy for chronic insomnia should be non-drug interventions that are supported by evidence in achieving sustained improvements in sleep parameters. Interventions include:

- CBTs (eg stimulus control, sleep restriction therapy, relaxation techniques, cognitive therapy and sleep hygiene education)
- brief behavioural therapy (ie modification of waking behaviours that affect the physiological systems regulating sleep)
- exercise.

Psychological and behavioural treatments administered weekly over a 4-8-week period have shown robust and stable improvements in sleep continuity for up to 2 years. These therapies are now available online, which has vastly improved access.

Drug therapy

Pharmacological treatment should be accompanied by specific patient education, regular review and continued effort to employ the lowest effective maintenance dosage of medication, and to taper medication when conditions allow.

- Benzodiazepines – May have a place in the treatment of severe acute insomnia or treatment-resistant chronic insomnia. For patients with sleep onset insomnia, a short-acting medication is a reasonable choice for an initial trial of pharmacologic therapy. This may improve the insomnia with less residual somnolence the following morning. For patients with sleep maintenance insomnia, a longer-acting medication is preferable for an initial trial of pharmacological therapy.
- Z drugs – Have been shown to be effective in the treatment of insomnia in the short term. However, there is very limited evidence that they retain their efficacy during long-term treatment. Z drugs are associated with issues relating to adverse events, rebound insomnia, development of tolerance and SUD, and need to be carefully monitored in individual patients. Zolpidem's black box warning states, 'Zolpidem may be associated with potentially dangerous complex sleep-related behaviours which may include sleep walking, sleep driving and other bizarre behaviours. Zolpidem is not to be taken with alcohol. Caution is needed with other CNS depressant drugs. Limit use to four weeks maximum under close medical supervision'.

Psychological and behavioural treatments produce comparable outcomes to Z drugs during active treatment and have better durability beyond the active administration of treatment.

Prescription of zolpidem and zopiclone should be treated with the same precautions and patient management as benzodiazepines.

- Melatonin – An endogenous hormone associated with the control of circadian rhythms and sleep regulation. Melatonin levels may be reduced in middle-aged and elderly patients with insomnia. Supplementation with melatonin has been shown to improve limited aspects of sleep in 30–50% of patients over 55 years of age. Data from clinical trials are variable.

Some showed that some patients gain clinically significant improvements in quality of sleep and morning alertness with prolonged-release melatonin, but many patients in the clinical trials did not respond to treatment. Melatonin does not appear to be addictive or cause withdrawal effects when stopped. There are a lack of long-term study data.

At the time of writing, melatonin is available in Australia as a prolonged-release formulation for short-term treatment of primary insomnia, characterised by poor sleep quality in patients aged 55 years or older. The recommended dose is 2 mg orally at bedtime, and at present, there is insufficient evidence to support treatment beyond 3 weeks.

In a European campaign to reduce benzodiazepine and Z drug usage, the availability of prolonged-release melatonin was shown to positively contribute to success.

- Other prescription medications – Includes antipsychotics (eg quetiapine, olanzepine). Studies demonstrating the usefulness of these medications for either short- or long-term management of insomnia are lacking. Furthermore, these agents have significant risks and therefore, their use in the treatment of chronic insomnia (without a relevant comorbid condition) cannot be recommended. Numerous other medications have a sedating effect, but are not recommended for routine use in patients with insomnia. These include antidepressants, diphenhydramine and antipsychotics.
- Over-the-counter (OTC) medications – Such as antihistamines or antihistamine/analgesic type drugs, and herbal and nutritional substances (eg valerian) are not recommended in the treatment of chronic insomnia due to the relative lack of efficacy and safety data.

2.2. Anxiety disorders

Key points

- Anxiety disorders are common and exist as a spectrum of conditions that vary from mild to severe.

- Comprehensive clinical assessment is the first step in management. Effective management requires obtaining a diagnosis, and recognising that patients may not present with a single disorder (eg patients may experience generalised anxiety, panic disorder as well as depression).
- Where treatment is indicated:
  - First-line therapy for generalised anxiety disorder (GAD), panic disorder, and panic attacks should include CBT (due to its effectiveness at reducing the symptoms of anxiety in the short and long term.
  - SSRI and SNRI medications are effective across the range of anxiety disorders and generally suitable for first-line pharmacological treatment of anxiety.
  - Short-term benzodiazepines as occasional adjunctive therapy may be effective at reducing worsening of symptoms that can occur in the first days to weeks of initiating antidepressant medication, and therefore aid adherence
  - Benzodiazepine use in anxiety disorders is mostly limited to severe or treatment-resistant cases.
  - Patients who use two or more psychoactive drugs in combination (polydrug use) may be more vulnerable to major harms.

Editor's Note: Anxiety disorders include GAD, panic disorder, OCD, PTSD, phobias and SAD.

3. Duration of benzodiazepine therapy

Optimal duration of therapy

Guidelines and formularies typically give durations of 1–4 weeks for benzodiazepine therapy, depending on the indication. Short-term therapy is generally advised to reduce the risk of dependence and withdrawal, as well as other potential harm such as cognitive impairment. Short-term therapy does not reduce the risk of accidents or falls.

Dependence is recognised as a risk in some patients who receive treatment for longer than 1 month, and health professionals should be conscious of this when

considering the relative benefits and risks of treatment.

Lacking the means to determine the optimal duration of therapy, a rational approach is to allow the duration of treatment to be determined by a series of risk–benefit decisions and shared decision making, with periodic trials of tapering and discontinuing medication to determine whether continued therapy is indicated. This approach provides an 'exit strategy' and thereby addresses concerns that once started, hypnotic therapy could be unending.

Clinical discipline and accountable prescribing are essential when considering long-term benzodiazepine therapy.

Rationale for long-term benzodiazepine prescribing

Benzodiazepines are generally regarded by clinical practice guidelines as a short-term therapeutic option. Long-term use, beyond 4 weeks, is not generally advocated by clinical practice guidelines, hence long-term therapy should be should be uncommon and made with caution.

Prescribing benzodiazepines, like other aspects of clinical practice, should be based on thoughtful consideration of the likely risks and benefits, and the risks and benefits of alternative interventions. This decision should be made in conjunction with the patient and their carers, where appropriate. Benzodiazepines may be prescribed longer term where:

- patients do not respond to, or cannot tolerate, numerous first-line therapies
- use is intermittent
- specialists make a recommendation and are able to provide a rationale of therapy.

For some patients, benzodiazepine alternatives fail, have limited benefit, are unavailable or clinically inappropriate. If there is no history of drug dependence, positive indicative 'lifestyle' factors are present and a clinical decision for benzodiazepine treatment can be justified, then long-term therapy should not necessarily be regarded as a deviation from good clinical practice. Supervised

benzodiazepine treatment may remain an acceptable long-term therapeutic option for some patients.

Management of long-term benzodiazepine prescriptions

Many patients are able to safely take short courses of benzodiazepines, or to use them intermittently longer term, on a 'as required' basis and to stop them when no longer needed.

In a situation where the clinical decision is that the ongoing use of a benzodiazepine is the most appropriate management, this requires ongoing monitoring of health outcomes and continuing vigilance for potential hazards throughout treatment.

The responsible specialist or GP should clearly outline a prescribing plan that should be documented in the patients' notes or management plan.

The prescribing plan may include instructions that:

- regular prescription reviews take place
- no repeat prescriptions will be made without face-to-face contact
- all prescriptions will be made by one doctor within a single practice
- one pharmacy will dispense all medication.

Benzodiazepine prescriptions should be at the lowest effective dose and given intermittently, with regular reviews of the treatment plans and regular attempts at withdrawal.

At the time of benzodiazepine prescription renewal or medication review, GPs should continue to discuss the risks of long-term benzodiazepines and the benefits of discontinuation (eg cognition, mood, sleep and energy level) and advise the patient to reduce or discontinue the benzodiazepines if there are issues. GPs should document this communication.

Patients should be monitored closely for problematic use or any therapeutic dose dependence behaviour. Any escalation of dose or inappropriate use would lead to a

complete review of prescribing and attempted withdrawal of benzodiazepine, along with a review of alternative therapy.

Discontinuing after short-term use

For patients on less than 4 weeks of benzodiazepine therapy, it should be possible to stop medication without tapering. Caution should be exercised with patients who are at risk of seizures.

Discontinuing after longer term use – Withdrawal

Withdrawal is possible for most patients on longer term benzodiazepines, although the process of reduction may be difficult and lengthy. The withdrawal process is aided by a good therapeutic alliance between the GP and patient, with specialist support where needed. Discontinuation is usually beneficial as it is followed by improved psychomotor and cognitive functioning, particularly in the elderly. Up to 15% of patients who experience withdrawal will go on to have protracted symptoms lasting months to years.

Withdrawal strategies will vary with the type of dependence (therapeutic dose, prescribed high dose, recreational high dose or polydrug). Withdrawal symptoms (Table 2) are highly variable and each patient will need tailored withdrawal management that will also address any underlying problems. Withdrawal symptoms may appear in 1–2 days for agents with shorter half-lives, but may not appear until 3–7 days for agents with longer half-lives.

Table 2. Acute withdrawal symptoms

Anxiety symptoms		**Distorted perceptions**	**Major incidents**
Psychological	Physical		Mainly when high doses are stopped abruptly

● Anxiety ● Panic attacks ● Insomnia ● Poor memory ● Depression ● Paranoia ● Intrusive memories ● Cravings ● Nightmares ● Excitability ● Agoraphobia ● Social phobia ● Obsessions ● Rage, aggression ● Irritability	● Agitation ● Tremor ● Headache ● Weakness ● Dizziness ● Nausea ● Vomiting ● Diarrhoea ● Constipation ● Palpitations ● Rashes ● Tingling, numbness, altered sensation ● Fatigue ● Flu-like symptoms	● Hypersensitivity to sound, light, touch, taste ● Abnormal body sensation eg itching, pain, stiffness, blurred vision, paraesthesia, muscle twitching, tinnitus, burning sensations ● Feeling self or world to be abnormal (depersonalisation or derealisation)	● Fits (1–2% of patients) ● Delirium (rare) ● Transient hallucinations (visual, tactile, auditory) or illusions (rare) ● Psychosis (very rare)

General principles for the management of withdrawal of benzodiazepines

If dependence on benzodiazepines has become established, it is often difficult to treat and can become a long-term, distressing problem. All patients with dependence should be encouraged to discontinue the drug and offered a detoxification program at regular intervals. For some patients, discontinuation will be difficult, but the effort should be made. For other patients, a reduction in dose, rather than discontinuation, will be the first goal.

Evidence-based recommendations for general practice management of benzodiazepine withdrawal are difficult due to a lack of data. The following are general principles:

- Review the patients' prescription records and discuss the situation to those receiving long-term benzodiazepines.
- Send patients letters suggesting methods of tapering off benzodiazepines (this may be enough to motivate them to withdraw).
- Teach patients ways to deal with anxiety and insomnia (either as primary conditions or due to withdrawal).

- Acknowledge that withdrawing from benzodiazepines can be stressful.
- Encourage family and friends to provide encouragement and practical help during withdrawal.
- Refer patients to appropriate services (eg psychologist or support groups). Only refer to drug or alcohol dependence services if the service has shown specific interest in benzodiazepine dependence or the patient also has a drug or alcohol problem.
- Advise patients to make changes in lifestyle such as regular exercise.
- Advise patients to avoid alcohol.
- Advise patients to avoid mild stimulants (eg coffee and chocolate [theobromine]) as these can cause anxiety, panic and insomnia.
- Postpone advice on smoking cessation until after the benzodiazepine has been withdrawn.

Benzodiazepine reduction requires a team approach with regular communication between the prescriber and other practitioners involved in the patient's care (eg pharmacist, counsellor, psychiatrist, addiction services).

Editor's Note: International Trends

Benzodiazepines (BZDs) and Z-drugs have long been widely used in the treatment of anxiety disorders and insomnia disorder. However, with their widespread clinical use, the adverse consequences associated with long-term exposure—including dependence, tolerance, misuse, and serious outcomes such as falls and cognitive impairment—have emerged as major global public health concerns.

Over the past several decades, clinical guidelines have largely focused on how to prescribe these medications. In recent years, however, a clear paradigm shift has occurred at the international level. Health authorities and professional medical organizations worldwide have not only tightened prescribing restrictions but have also redirected attention toward systematic approaches to deprescribing, shared decision making, and safe withdrawal.

Reference: Joint Clinical Practice Guideline on Benzodiazepine Tapering: Considerations When Risks Outweigh Benefits. Journal of General Internal Medicine, 2025: 40(12), 2814–2859. https://doi.org/10.1007/s11606-025-09499-2

Judicious Prescribing of Benzodiazepines

The New York City Department of Health and Mental Hygiene
https://a860-gpp.nyc.gov/concern/nyc_government_publications/vt150j81t

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

INTRODUCTION

- Benzodiazepines increase the risk of fatal overdose when taken in combination with opioid analgesics, alcohol, or other central nervous system depressants.
- If benzodiazepines are indicated, prescribe the lowest effective dose for the shortest duration—no more than 2 to 4 weeks.*
- Avoid co-prescribing benzodiazepines and opioid analgesics because of the risk of fatal respiratory depression.

*The guidance in this document is not intended for end-of-life care.

BENZODIAZEPINES

- Benzodiazepines bind to GABA receptors and depress the central nervous system.
- They are prescribed for their sedative-hypnotic, antianxiety, muscle relaxant, and anticonvulsant effects.

BOX 1. MYTHS AND FACTS ABOUT BENZODIAZEPINES AND Z-DRUGS

Myth: Benzodiazepines are first-line treatment for anxiety.

Facts: Benzodiazepines

- May be used for 2 to 4 weeks to treat severe symptoms of anxiety disorders, ideally while waiting for the full effect of other treatment options (Boxes 2 and 3).
- Diminish in effectiveness beyond 4-6 weeks.

Myth: Benzodiazepines are first-line treatment for insomnia.

Facts: Benzodiazepines

- May provide short-term (1 to 2 weeks) symptomatic relief for severe insomnia while other treatment modalities are being implemented.
- May result in rebound insomnia once stopped.
- Do not appear to be effective for chronic insomnia or late-night insomnia, experienced more commonly by older adults.

Myth: Low-dose benzodiazepines are not addictive.

Facts:

- Benzodiazepine use can result in physical dependence at any dose with prolonged use.
- May be misused to prevent perceived or anticipated withdrawal rather than for their originally intended purpose.

Myth: Z-drugs (eg, zolpidem, zaleplon) are safer than benzodiazepines.

Facts: Z-drugs

- Bind to GABA receptors, similar to benzodiazepines.
- Are not recommended for long-term use.
- Offer no safety benefit compared with benzodiazepines, especially in older adults.
- Increase risk for falls in older adults.

BOX 2. NONBENZODIAZEPINE TREATMENTS FOR ANXIETY

Nonpharmacologic

- Cognitive behavioral therapy
- Relaxation techniques
- Yoga, meditation
- Exercise

Long-term pharmacologic

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs)

BOX 3. NONBENZODIAZEPINE TREATMENTS FOR INSOMNIA

Nonpharmacologic

- Cognitive behavioral therapy—considered first-line treatment18
- Good sleep hygiene
  - Maintaining a regular sleep schedule
  - Avoiding daytime napping
  - Developing a calming bedtime routine, which may include taking a bath or reading a book
  - Avoiding screen time before bed
  - Keeping your bedroom dark, quiet, and at a comfortable, cool temperature
  - Limiting alcohol, caffeine, and tobacco at night
- Regular exercise—except heavy exercise within several hours of bedtime
- Relaxation techniques

Pharmacologic

- Melatonin

TABLE 1. INTERACTIONS BETWEEN BENZODIAZEPINES AND SELECT COMMON MEDICATIONS

Interaction	Medication Class	Examples
Increased serum benzodiazepine levels (CYP450 inhibition)	Antifungals	Ketoconazole Itraconazole
	Macrolides	Clarithromycin Erythromycin
	SSRIs	Fluoxetine Paroxetine
	Histamine-2 blockers	Cimetidine
Increased sedative effects of benzodiazepines	Opioids	Oxycodone
	Antipsychotics	Chlorpromazine Clozapine
	Barbiturates	Phenobarbital Secobarbital
	Sedating antihistamines	Diphenhydramine Hydroxyzine

TABLE 2. COMMONLY USED BENZODIAZEPINES AND Z-DRUGS

Generic name	Brand name	Elimination half-life (h)
BZD		
Short-Acting		
Triazolam	Halcion®	1.5 to 5.5
Intermediate-Acting		
Alprazolam	Xanax®	11.2 (range: 6.3-26.9)
Clonazepam	Klonopin®	12 to 50
Lorazepam	Ativan®	10 to 20
Oxazepam	Serax®	8.2 (range: 5.7-10.9)
Temazepam	Restoril™	8.8 (range: 3.5-18.4)
Long-Acting		
Chlordiazepoxide	Librium®	24-48
Clorazepate	Tranxene®	48
Diazepam	Valium®	Up to 100
Flurazepam	Dalmane®	47-100
Z-Drugs		
Short-Acting		
Zaleplon	Sonata®	Approx. 1
Zolpidem	Ambien®	5-mg tablets: 2.6 (range: 1.4-4.5) 10-mg tablets: 2.5 (range: 1.4-3.8) 12.5-mg dose: 2.8 (range: 1.62-4.05)
Eszopiclone	Lunesta®	Approx. 6
Consult product prescribing information for detailed warnings, precautions, contraindications, and potential interactions.		

BOX 4. CHECKING THE PRESCRIPTION MONITORING PROGRAM

The New York State Prescription Monitoring Program (PMP) provides quick, confidential, 24/7 access to your patients' controlled substance prescription history.

1. Consult PMP to determine whether your patient recently filled a prescription for an opioid analgesic, benzodiazepine, or other controlled substance.

2. If the patient has recently filled multiple prescriptions written by different providers and/or filled at different pharmacies:

- Discuss your concerns with your patient, explaining the risk for overdose when benzodiazepines are used with other agents (especially opioid analgesics and other CNS depressants).
- Communicate and coordinate with your patient's other controlled substance prescribers.
- Avoid abruptly discontinuing benzodiazepines.
  - Withdrawal can be severe, causing hallucinations, seizures, and in rare cases has been life-threatening.
  - A taper schedule is strongly recommended and clinically appropriate versus refusing continuation of this medication.
- Consider that your patient might be misusing controlled substances and/or have a substance use disorder.
  - If needed, explain that effective treatments for substance use disorder are available, and treat the patient yourself or refer for treatment.
  - For opioid use disorder, discuss and arrange for medication-assisted treatment (eg, buprenorphine or methadone).

BOX 5. WHAT TO TELL PATIENTS ABOUT BENZODIAZEPINE TREATMENT

- You'll be taking this medicine for a short time—no more than 4 weeks. If your symptoms don't improve in a few weeks, we'll reevaluate the treatment plan.
- Get your prescriptions for benzodiazepines and other controlled substances only from me.
- Fill your prescription at only one pharmacy.
- Make sure to tell other providers that you're taking this medicine. Some other medications can have a serious interaction with this one.
- Keep the medication in a secure place, preferably locked.
- Do not share your medication with others.
- Take the medication exactly as directed.

- Dispose of the medicine safely. Mix it with an unpalatable substance like coffee grounds or kitty litter and place in a sealed container before discarding with your trash. Or find a medication disposal event near you.

- There are some risks when taking this medicine:
  - Overdose: Avoid alcohol, opioids, and sedatives; they increase risk of overdose. Some over-the-counter medicines, such as antihistamines, also increase risk.
  - Tolerance: When you need more medication to get the same effect. Do not increase the dose, even if you think the medicine has stopped working.
  - Physical dependence: If you develop physical dependence, stopping the drug may make you miss it or feel sick (withdrawal). You may get a fast heartbeat, insomnia, anxiety, shaky hands, nausea, have hallucinations, or just feel agitated.
  - Mood or behavior changes, including depression, anxiety, or irritability.
  - Substance use disorder: Some patients who become physically dependent on or misuse the medicine can develop a substance use disorder.
- Seek help right away if you think you may be developing tolerance or dependence or if you experience side effects—especially ones that are new or concern you.

BOX 6. PHYSICAL DEPENDENCE, WITHDRAWAL, SUBSTANCE USE DISORDER, AND MISUSE

Physical dependence

- Physiologic adaptation to a substance requiring the person to take more of the substance to achieve a certain effect.
- Can occur with the chronic use of many drugs—including many prescription drugs, even if taken as instructed.
- Causes drug-specific withdrawal symptoms if drug use is abruptly ceased.
- Benzodiazepine withdrawal syndrome symptoms include:
  - Autonomic hyperactivity (eg, sweating, tachycardia)
  - Hand tremor
  - Insomnia

- Nausea or vomiting
- Transient visual, tactile, or auditory hallucinations or illusions
- Psychomotor agitation
- Anxiety
- Grand mal seizures

Substance use disorder

- Maladaptive pattern of use leading to significant impairment or distress.

Benzodiazepine misuse

- Using someone else's benzodiazepines or using benzodiazepines in a manner other than prescribed.
- May or may not be associated with physical dependence.
- Signs may include pattern of early refills; prescription problems such as lost, spilled, or stolen medications; and escalating drug use in the absence of a physician's direction.

BOX 7. BENZODIAZEPINES IN OLDER ADULTS

- Benzodiazepine treatment in patients aged 65 and older can increase risk for:
  - falls and hip fractures
  - possible cognitive impairment
  - negative interactions with other medications
  - daytime fatigue
  - confusion and delirium
- Initiate treatment at one-half the standard adult starting dose.
- Monitor response to treatment and minimize dosage and/or frequency to avoid adverse effects.

In older adults, benzodiazepines should never be used as first-line treatment for insomnia, agitation, or delirium, and long-acting benzodiazepines should not be used for any indication.

BOX 8. BENZODIAZEPINES DURING PREGNANCY AND LACTATION

- Benzodiazepine use during pregnancy is associated with risks to the newborn:
  - respiratory depression
  - poor temperature regulation
  - hypotonicity
  - neonatal abstinence syndrome
- For patients planning a pregnancy, gradually discontinue benzodiazepine treatment and consider other options.
- If postpartum benzodiazepine treatment is being considered, explain that benzodiazepine metabolites can be found in breast milk.

SUMMARY

HOW TO PRESCRIBE BENZODIAZEPINES JUDICIOUSLY

- Provide appropriate first-line treatment for anxiety and insomnia.
- If benzodiazepines are clinically indicated:
  - fully assess your patient,
  - prescribe the lowest effective dose for the shortest duration—no more than 2 to 4 weeks,
  - talk to your patient about the benefits and risks of benzodiazepine treatment,
  - avoid co-prescribing with opioids or other CNS depressants because of the risk of fatal respiratory depression.

Benzodiazepine Prescribing Guidance

Colorado Consortium for Prescription Drug Abuse Prevention
https://corxconsortium.org/wp-content/uploads/Benzo-Prescribing.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Benzodiazepines (BZs) and Z-drugs are the most commonly prescribed medications in the benzodiazepine receptor agonist (BZRA) class. Today, there are 14 BZs and 3 Z-drugs that are FDA approved, with anxiety and insomnia being the primary approved conditions for prescribing.

Restraint on BZRA prescribing is urged as they may lose efficacy and/or cause worsening adverse reactions over time including physiologic dependence with disastrous consequences. Restraint on BZRA prescribing is urged. BZRA efficacy may wane overtime, especially when use is consistent. In a subset of patients, both during titration and/ or after cessation, BZs can cause disabling discontinuation syndromes that can last years. Repeated BZ cessation can cause central nervous system sensitization, a phenomenon known as kindling. BZs are also implicated in a third of opioid-related overdose death. While BZRAs do have some limited indications, they are often prescribed in the absence of adequate research and for far longer than the recommended time limitation of 2-4 weeks. Present day prescribing guidance is limited, contradictory and based on insufficient research that has not been adequately adjudicated for quality and bias.

The recommendations in this guidance are evidence-based and/or amplified by collective clinical experience. They are not comprehensive and should not replace clinical judgement informed by individual circumstances.

CLINICAL PRACTICE BZRA PRESCRIBING RECOMMENDATIONS

1) Listen carefully and respectfully to affected individuals as they are experts on their own lived experiences and often have a sophisticated understanding of therapeutic interventions including BZRAs
2) Fully assess patient concerns and medical conditions for which BZRAs might be prescribed
3) Establish the diagnosis, severity, and the need to treat
4) Screen for addiction-prone substance use risk by means of
   a) Personal and family history of substance use disorder and personal history of trauma
   b) Screening portion of *SBIRT (Screening Brief Intervention and Referral to Treatment) to help identify and then address current addiction-prone substance use
   c) Online review of prescription database to identify prescribed addiction-prone substances
   d) Definitive drug testing, if indicated based on clinical judgment

   ＊ Note：Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: comparison at intake and 6 months later. Drug Alcohol Depend. 2009;99(1-3):280-95.
5) 1st consider non-BZRA treatments:
   a) Non-medication approaches, notably Cognitive Behavioral Therapy (CBT, CBT-I)
   b) Non-BZRA medications
6) BZRAs should be avoided when contraindicated, ineffective, or of unproven or minimal benefit:
   a) In depression because any benefit is soon lost
   b) In post-traumatic stress disorder
   c) In obsessive compulsive disorder
   d) In individuals with a history of substance use disorder (e.g., alcohol) outside of treating withdrawal
   e) Pain conditions other than burning mouth syndrome and stiff person syndrome

7) Consider other contraindications to BZRA use:
    a) Prior adverse BZRA experiences
    b) Non-medical use of and/or addiction to BZRAs and/or other substances
    c) Drug-drug interactions with medications, notably respiratory depressants, opioids
    d) Significant cognitive, psychomotor, or respiratory problems
    e) Pregnancy and breastfeeding
8) Consider 1st line indications for BZRA therapy:
    a) Withdrawal from BZRAs and alcohol
    b) Status epilepticus
    c) Crisis anxiety without psychotic features
    d) Procedure anesthesia (analgoanesthesia)
    e) Pain conditions: burning mouth syndrome (clonazepam)
    f) Acute movement disorders, such as stiff person syndrome, catatonia, status dystonicus
    g) End of life palliative care
9) Consider 2nd line use of BZRA therapy for short-term use:
    a) Insomnia and anxiety disorder defined as >6 months, function limiting, anxiety level > actual threat
    b) Certain treatment-resistant, intractable seizure disorders (clobazam, clonazepam)
10) Provide information about BZRA use to the patient:
    a) Highlighting the boxed warnings required by the FDA in product labeling
    b) Describe BZRA risks, benefits, and alternatives (i.e., informed consent)
    c) Highlighting the risks of long-term use - BZRA physiologic dependence and withdrawal syndrome with rapid taper and/or discontinuation
    d) Make clear that adverse effects and loss of efficacy might not be evident during use
11) Provide reliable, useful resources to the patient:
    a) The Ashton Manual https://www.benzo.org.uk/manual/

b) The Benzodiazepine Information Coalition (patient-focused) https://www.benzoinfo.com/

c) The Alliance for Benzodiazepine Best Practices (prescriber-focused) https://benzoreform.org

12) Other qualifiers to prescribing BZRAs

a) Use only if the medical condition causes major functional limitations

b) Use only if delay in onset of action of alternative therapies place the patient in jeopardy

c) Ensure the balance of risks and benefits favors BZRA use before prescribing

d) Ensure decision-making is shared with fully informed patients who provide consent

13) If BZRA is prescribed

a) Prescribe BZRA initially for no more than 7 days at the anticipated lowest effective dosage

b) Simultaneously prescribe non-BZRA therapy. BZRAs should be thought of as a bridge awaiting the onset of benefit of another medication or non-medication therapy like CBT

c) Establish 1st follow-up within 7 days, ensuring availability for problems during the interval

14) On follow-up, assess progress addressing the target medical condition:

a) BZRA efficacy – re-prescribe only as necessary at the lowest effective dosage

b) Status of non-BZRA therapy ordered at the time BZRAs are 1st prescribed

c) Need for additional referrals

15) On follow-up, provide ongoing informed consent and identify and address any BZRA side effects:

a) Depression, anxiety, suicidality, cognitive, psychomotor, respiratory problems

b) Drug-drug interactions

c) Inter-dose withdrawal symptoms which evolve towards the end of the dosing interval or when BZs are frequently used as needed and can be easily misdiagnosed as underlying or new organic symptoms

d) Do not discount symptom reports as psychosomatic if they seem unusual or bizarre

e) Do not assume BZRA-related problems means BZRA addiction - this is very infrequent

16) Continue weekly follow-ups to address efficacy and adverse outcomes and provide informed consent

17) Limit duration of BZRA therapy to 4 weeks or less in the majority of circumstances

18) Do not abruptly discontinue BZRAs if used > 2 weeks: rather, taper off the medication

19) Thoughtful deprescribing is essential to best practice prescribing

Benzodiazepine Receptor Agonist Prescribing Information Link	**FDA-Approved Indications**	**FDA-Approved Duration Limitations**
Alprazolam Xanax	Anxiety disorder Short-term relief of anxiety symptoms	4-10w duration for panic disorder
Chlordiazepoxide Chlordiazepoxide	Anxiety disorder Short-term relief of anxiety symptoms Acute alcohol withdrawal Preoperative apprehension and anxiety	Long-term use, ie >4m, has not been assessed by systematic clinical studies
Clobazam Onfi	Adjunctive for seizures associated with Lennox-Gastaut syndrome	[No listed time frame]
Clonazepam Klonopin	Panic disorder + agoraphobia Specified treatment-resistant seizure disorders	Effectiveness in long-term use, ie >9w, has not been systematically studied in controlled clinical trials

Clorazepate Clorazepate	Anxiety disorder Short-term relief of anxiety symptoms Acute alcohol withdrawal Preoperative apprehension and anxiety	Long-term management of anxiety, ie >4m, has not been assessed by systematicclinical studies
Diazepam Valium	Anxiety disorder Short-term relief of anxiety symptoms Acute alcohol withdrawal Adjunctively in convulsive disorders Relief of specified skeletal muscle spasm, spasticity	Effectiveness in long-term use, ie >4m, has not been assessed by systematic clinical studies
Estazolam Estazolam	Short-term management of insomnia	There is evidence to support ability of estazolam to enhance duration, quality of sleep for intervals up to 12w
Flurazepam Dalmane	Treatment of insomnia	Effective for at least 28 consecutive nights of drug administration
Lorazepam Ativan	Anxiety disorders Short-term relief of anxiety symptoms Anxiety associated with depressive Sxs	Effectiveness in long-term use, ie >4m, has not been assessed by systematic clinical studies
Midazolam Midazolam	Procedural sedation, anxiolysis, amnesia	NA
Oxazepam Oxazepam	Anxiety disorders Short-term relief of anxiety symptoms Anxiety associated with depression Acute alcohol withdrawal	Effectiveness in long-term use, ie >4m, has not been assessed by systematic clinical studies
Quazepam Doral	Treatment of insomnia	Sustained effectiveness has been established in a sleep lab study of 28 nights duration

Temazepam Restoril	Short-term treatment of insomnia (generally 7-10d)	Clinical trials performed in support of efficacy were 2w in duration
Triazolam Halcion	Short-term treatment of insomnia (generally 7-10d)	Short-term - generally 7-10d

FDA requiring Boxed Warning Updated to Improve Safe Use of Benzodiazepine Drug Class

FDA Drug Safety Communication
Food and Drug Administration (09-23-2020).

https://www.fda.gov/media/142368/download?attachment

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

09-23-2020 FDA Drug Safety Communication

- **What safety concern is FDA announcing?**

✓ To address the serious risks of abuse, addiction, physical dependence, and withdrawal reactions, the U.S. Food and Drug Administration (FDA) is requiring the Boxed Warning be updated for all benzodiazepine medicines. Benzodiazepines are widely used to treat many conditions, including anxiety, insomnia, and seizures. The current prescribing information for benzodiazepines does not provide adequate warnings about these serious risks and harms associated with these medicines so they may be prescribed and used inappropriately. This increases these serious risks, especially when benzodiazepines are used with some other medicines and substances.

✓ Benzodiazepines can be an important treatment option for treating disorders for which these drugs are indicated. However, even when taken at recommended dosages, their use can lead to misuse, abuse, and addiction. Abuse and misuse can result in overdose or death, especially when benzodiazepines are combined with other medicines, such as opioid pain relievers, alcohol, or illicit drugs. Physical dependence can occur when benzodiazepines are taken steadily for several days to weeks, even as prescribed. Stopping them abruptly or reducing the dosage too quickly can result in withdrawal reactions, including seizures, which can be life-threatening.

- **What is FDA doing?**

✓ We are requiring the Boxed Warning, FDA's most prominent warning, be updated and adding other information to the prescribing information for all benzodiazepine medicines. This information will describe the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions consistently across all the medicines in the class. We are also requiring updates to the existing patient Medication Guides to help educate patients and caregivers about these risks.

✓ Other changes are also being required to several sections of the prescribing information, including to the Warnings and Precautions, Drug Abuse and Dependence, and Patient Counseling Information sections.

- **What are benzodiazepines and how can they help me?**

✓ Benzodiazepines are a class of medicines approved to treat generalized anxiety disorder, insomnia, seizures, social phobia, and panic disorder. Most benzodiazepines are recommended for periods of weeks or months to treat these disorders. However, the amount, frequency, and duration of treatment vary depending on the patient and the medical condition being treated. Benzodiazepines are also used as premedication before some medical procedures.

✓ Chlordiazepoxide was the first benzodiazepine approved in 1960, and FDA approved many subsequent medicines in this class in the 1960s and 1970s (see List of Benzodiazepines). These medicines differ in how long they take to start working and how long their effects last, but they all work to slow brain activity by binding to gamma-aminobutyric acid (GABA) receptors in the brain, which causes drowsiness or calming effects.

List of Benzodiazepines

Generic Name	Brand Name(s)
alprazolam	Xanax, Xanax XR
chlordiazepoxide HCl/clidinium bromide	Librax
chlordiazepoxide HCl	Librium

chlordiazepoxide HCl/amitriptyline HCl	Limbitrol, Limbitrol DS
clobazam	Onfi
clonazepam	Klonopin
clorazepate	Gen-Xene, Tranxene
diazepam	Diastat, Diastat Acudial, Valium, Valtoco
estazolam	No brand name currently marketed
flurazepam	No brand name currently marketed
lorazepam	Ativan
midazolam	Nayzilam, Seizalam
oxazepam	No brand name currently marketed
quazepam	Doral
temazepam	Restoril
triazolam	Halcion

- **What should health care professionals do?**

✓ When deciding whether the benefits of prescribing a benzodiazepine outweigh the risks, health care professionals should consider the patient's condition and the other medicines being taken, and assess the risk of abuse, misuse, and addiction. Particular caution should be taken when prescribing benzodiazepines with opioids and other medicines that depress the central nervous system (CNS), which has resulted in serious side effects, including severe respiratory depression and death. Advise patients to seek immediate medical attention if they experience symptoms, such as difficulty breathing.

✓ Limit the dosage and duration of each medicine to the minimum needed to achieve the desired clinical effect when prescribing benzodiazepines, alone or in combination with other medicines. Throughout therapy, monitor the patient for signs and symptoms of abuse, misuse, or addiction. If a substance use disorder is suspected, evaluate the patient and institute, or refer them for, early substance abuse treatment, as appropriate.

✓ To reduce the risk of acute withdrawal reactions, use a gradual taper to reduce the dosage or to discontinue benzodiazepines. No standard benzodiazepine tapering schedule is suitable for all patients; therefore, create a patient-specific plan to gradually reduce the dosage, and ensure ongoing monitoring and support

as needed to avoid serious withdrawal symptoms or worsening of the patient's medical condition.

✓ Take precautions when benzodiazepines are used in combination with opioid addiction medications. Careful medication management by health care professionals can reduce the increased risk of serious side effects.

- **What should patients, parents, and caregivers do?**

Always tell your health care professionals about all the prescription and over-the-counter (OTC) medicines you are taking or any other substances you are using, including alcohol. Take benzodiazepines and all medicines exactly as prescribed by your health care professional. To avoid serious problems, including withdrawal reactions, patients taking benzodiazepines should not suddenly stop taking them without first discussing with your health care professional a plan for slowly decreasing the dose and frequency. Contact your health care professional if you experience withdrawal symptoms or your medical condition worsens. Go to an emergency room or call 911 if you have trouble breathing or other serious side effects such as seizures.

- **What did FDA find?**

✓ We reviewed postmarketing databases, adverse event cases reported to FDA, and the published literature on abuse, misuse, addiction, dependence, and withdrawal associated with benzodiazepine use (see Data Summary). Our review found that benzodiazepines are widely prescribed in the U.S., often for long periods of time. They are also widely abused and misused, often together with alcohol, prescription opioids, and illicit drugs, which worsen the risks of serious problems. We also found that some patients have had serious withdrawal reactions after benzodiazepines were stopped suddenly or the dose was reduced too quickly. Some patients experienced withdrawal symptoms lasting many months.

✓ We previously communicated about the serious risks of combining benzodiazepines with opioid pain or cough medicines in August 2016, and cautioned about withholding medication for opioid use disorder from patients taking benzodiazepines or CNS depressants in September 2017.

- **What is my risk?**

All medicines have risks even when used correctly as prescribed. It is important to know that people respond differently to medicines depending on their health, the diseases they have, genetic factors, other medicines they are taking, and many other factors. As a result, we cannot determine how likely it is that someone will experience adverse side effects when taking benzodiazepines. Your health care professionals know you best, so talk to them if you have questions or concerns about risks of taking benzodiazepine medicines.

- **How do I report side effects from a benzodiazepine?**

To help FDA track safety issues with benzodiazepines, we urge patients and health care professionals to report side effects involving benzodiazepines or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box.

- **How can I get new safety information on medicines I'm prescribing or taking?**

You can sign up for email alerts about Drug Safety Communications on medicines or medical specialties of interest to you.

- **Facts about Benzodiazepines**

✓ Benzodiazepines are a class of medicines approved to treat generalized anxiety disorder, insomnia, seizures, social phobia, and panic disorder. They are also used as premedication before some medical procedures.

✓ Most benzodiazepines are recommended for use for weeks or months. However, the dose, frequency, and duration of treatment vary depending on the patient, the medicine being prescribed, and the medical condition it is being used to treat.

✓ Benzodiazepines work by binding to GABA receptors in the brain to slow brain activity, causing drowsy or calming effects.

✓ Common side effects of benzodiazepines include drowsiness, dizziness, weakness, and slowed breathing.

✓ Benzodiazepines are commonly prescribed medicines. In 2019, an estimated 92 million benzodiazepine prescriptions were dispensed from U.S. outpatient retail

and mail-order pharmacies, with alprazolam (38%) being the most common followed by clonazepam (24%) and lorazepam (20%).

- **Additional information for patients**

✓ FDA is requiring the Boxed Warning be updated for all benzodiazepine medicines to include warnings about the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions.

✓ Do not drink alcohol with benzodiazepines. Alcohol can increase the risk of serious and life-threatening side effects.

✓ Always inform all your health care professionals about all the medicines you are taking, including prescription and OTC medicines and other substances. It is helpful to keep a list of all your current medicines in your wallet or another location where it is easily retrieved. You can fill out and print a copy of My Medicine Record.

✓ Take benzodiazepines and all medicines exactly as your health care professional prescribes. Seek medical attention immediately by going to an emergency room or calling 911 if you experience serious side effects and have symptoms like trouble breathing.

✓ Most benzodiazepines are recommended for use for periods of weeks or months. However, the dose, frequency, formulation, and duration of treatment vary depending on the patient, the medical condition treated, and the medicine prescribed.

✓ Patients who have been taking a benzodiazepine for weeks or months should not suddenly stop taking your benzodiazepine without first discussing a plan for gradually getting off the medicine with your health care professional. Stopping benzodiazepines abruptly or reducing the dosage too quickly can result in serious withdrawal reactions, including seizures, which can be life-threatening.

✓ Even when the benzodiazepine dosage is decreased gradually, you may experience withdrawal symptoms, such as abnormal involuntary movements, anxiety, blurred vision, memory problems, irritability, insomnia, muscle pain and stiffness, panic attacks, and tremors.

✓ Contact your health care professional if you experience more severe withdrawal symptoms, such as:

- Catatonia (unable to speak, rigid body, repetitive and meaningless movements)
- Seizures
- Delirium tremens (shaking, shivering, irregular heartrate, sweating)
- Depression
- Hallucinations (seeing or hearing things that others do not see or hear)
- Thoughts about killing yourself or someone else
- Mania (euphoria, delusions, over activity)
- Psychosis (false beliefs)

✓ Treatments other than benzodiazepine medicines may be useful to manage some conditions, such as insomnia, stress and anxiety. Visit the National Center for Complementary and Integrative Health for resources, including Mind and Body Approaches for Stress and Anxiety: What the Science Says and Insomnia: Relaxation Techniques and Sleeping Habits.

✓ Benzodiazepine abuse occurs when the medicine is not taken as prescribed to treat a medical condition but is instead taken to produce a "high" or euphoric feeling or some other desired effect. Misuse occurs when the medication is not taken as prescribed to manage a medical condition (for example, taking more than the recommended dose or taking medicine prescribed for someone else).

✓ Physical dependence is the body's adaptation to repeated use of a drug, resulting in withdrawal reactions when the medicine is abruptly discontinued or the dose is significantly reduced. Dependence may also lead some individuals to continue using the medicine to avoid symptoms of withdrawal.

✓ It is important to lock up benzodiazepines and dispose of them properly to keep them from being taken accidentally by children or falling into the wrong hands.

✓ Read the patient Medication Guide every time you receive a prescription for a benzodiazepine because there may be new or important additional information about your medicine. The Medication Guide explains the important things you need to know about the medicine, including the side effects, what the medicine is used for, how to take and store it properly, and other things to watch out for when you are taking the medicine.

- ✓ To help FDA track safety issues with medicines, report side effects from benzodiazepines or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box.
- ✓ You can sign up for email alerts about Drug Safety Communications on medicines or medical specialties of interest to you.

- **Additional information for health care professionals**

- ✓ FDA is requiring the Boxed Warning be updated for all benzodiazepine medicines to include warnings about the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions.
- ✓ Before prescribing a benzodiazepine and throughout treatment, assess each patient's risk for abuse, misuse, and addiction. Standardized screening tools are available.
- ✓ Particular caution should be taken when prescribing benzodiazepines with opioids and other medicines that depress the CNS, which has resulted in serious side effects, including severe respiratory depression and death. Advise patients to seek immediate medical attention if they experience symptoms such as trouble breathing.
- ✓ Take precautions when benzodiazepines are used in combination with opioid addiction medications. Careful medication management by health care professionals can reduce the increased risk of serious side effects.
- ✓ Warn patients and caregivers about the risks of abuse, misuse, addiction, dependence, and withdrawal with benzodiazepines and the associated signs and symptoms. Also alert them of the serious risks of taking benzodiazepines with alcohol or other substances, including opioids.
- ✓ Use a gradual taper to discontinue benzodiazepines or reduce the dosage.
- ✓ There are no standard benzodiazepine tapering schedules suitable for all patients. A patient-specific plan should be used to taper the dosage of the benzodiazepine gradually.
- ✓ Most benzodiazepines are recommended for use for periods of weeks or months. However, the dose, frequency, formulation, and duration of treatment vary depending on the patient, the medical condition treated, and the medicine prescribed.

- ✓ If benzodiazepines indicated for very short-term use (i.e., 1 to 2 doses) are used inappropriately for long-term use, their abrupt discontinuation or rapid dosage reduction may precipitate acute withdrawal reactions, which can be life-threatening. Benzodiazepines approved for very short-term use include:
  - ➢ Diazepam injection (Diazepam)
  - ➢ Diazepam nasal spray (Valtoco)
  - ➢ Diazepam rectal gel (Diastat)
  - ➢ Midazolam nasal spray (Nayzilam)
  - ➢ Midazolam injection (Seizalam)
  - ➢ Lorazepam injection (Ativan)
- ✓ If a patient experiences withdrawal symptoms, it may be necessary to pause the taper for a period of time, or raise the benzodiazepine to the previous dosage and then proceed with a more gradual taper once stable.
- ✓ Frequent follow-up with patients receiving benzodiazepines is important. Reassess these patients regularly to manage their medical conditions and any withdrawal symptoms.
- ✓ Be prepared to address more severe or life-threatening reactions, including:
  - ➢ Catatonia
  - ➢ Seizures
  - ➢ Delirium tremens
  - ➢ Depression
  - ➢ Hallucinations
  - ➢ Homicidal thoughts
  - ➢ Mania
  - ➢ Psychosis
  - ➢ Suicidal ideation and behavior
- ✓ Protracted withdrawal syndrome persists beyond 4 to 6 weeks after initial benzodiazepine withdrawal. Symptoms may last weeks to as long as 12 months. These include:
  - ➢ Anxiety
  - ➢ Cognitive impairment

- Depression
- Insomnia
- Formication
- Motor symptoms (e.g., weakness, tremor, muscle twitches)
- Paresthesia
- Tinnitus

✓ Consider all therapeutic options for management of the patient's condition, and provide information about non-drug alternatives to help with stress, anxiety, insomnia, etc.

✓ Benzodiazepine abuse occurs when the medicine is not taken as prescribed to treat a medical condition, but instead taken to produce a euphoric effect or some other desired effect. Misuse occurs when the medication is not taken as prescribed to manage a medical condition (e.g., taking more than the recommended dose or taking medicine prescribed for someone else).

✓ Physical dependence is the body's adaptation to repeated use of a drug, resulting in withdrawal reactions when the medicine is abruptly discontinued or the dose is significantly reduced. Dependence may lead some individuals to continue using the medicine to avoid symptoms of withdrawal.

✓ Encourage patients to read the Medication Guide they receive with their benzodiazepine prescriptions because there may be new or important additional information about the medicine.

✓ To help FDA track safety issues with medicines, report adverse events involving benzodiazepines or other medicines to the FDA MedWatch program, using the information in the "Contact FDA".

✓ You can sign up for email alerts about Drug Safety Communications on medicines or medical specialties of interest to you.

Benzodiazepine and Z-drug Safety Guideline

Kaiser Permanente (2022)

https://wa.kaiserpermanente.org/static/pdf/public/guidelines/benzo-zdrug.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Expectations for Kaiser Foundation Health Plan of Washington Providers

Using protocols and standard documentation, Kaiser Foundation Health Plan of Washington aims to minimize practice variation in the management of patients on chronic benzodiazepine therapy to improve patient safety and increase both patient and provider satisfaction.

- Patients should not be prescribed benzodiazepines if currently taking any opioid.
- Benzodiazepines should not be combined with another benzodiazepine, Z-drug, or muscle relaxant.
- Patients treated with chronic benzodiazepines are risk-stratified to the highest appropriate category by the prescribing clinician and the risk level is documented.
- Patients prescribed chronic benzodiazepines shall have regular monitoring visits that:
  - ✓ Occur at a frequency based on the patient's risk stratification, and
  - ✓ Include standard components.
- Patients on chronic benzodiazepines shall receive all benzodiazepine prescriptions from one physician and one pharmacy whenever possible. Clinicians treating a patient on chronic benzodiazepines are expected to clarify and document—both among themselves and with the patient—which clinician holds primary prescribing responsibility.

Background

Benzodiazepines and Z-drugs (i.e., newer GABA receptor agonists, like zolpidem [Ambien]) are overprescribed, and many prescription treatment plans are not supported by scientific evidence or published guidelines. Despite warnings about the risks of long-term use of benzodiazepines, millions of prescriptions are still issued for benzodiazepines and Z-drugs each year. As a result, clinicians may encounter patients who have been prescribed benzodiazepines or Z-drugs on a long-term basis and are averse to discontinuing these treatments.

The purpose of this guideline is fivefold:

- To reduce inappropriate prescribing of benzodiazepines and Z-drugs,
- To clarify when short-term prescribing of benzodiazepines and Z-drugs may be indicated,
- To confirm that long-term use of benzodiazepines and Z-drugs is rarely, if ever, indicated,
- To aid primary care and mental health providers in identifying and managing patients on long-term benzodiazepines and Z-drugs, and
- To provide appropriate advice to providers for discontinuing benzodiazepine and Z-drug use.

This guideline is in alignment with the National Permanente Medical Group 2021 Practice Recommendations for Benzodiazepines & Non-Benzodiazepine Sedative-Hypnotics/Z drugs.

Target population

The recommendations in this guideline apply to patients who are:

- Already on prescribed long-term benzodiazepine or Z-drug therapy, or
- Being considered for initiation of short-term therapy with either drug class.

Exclusions

This guideline does not apply to:

- Patients who are using benzodiazepines illicitly. These patients may require treatment by an addiction specialist or chemical dependency treatment provider and should be referred to Mental Health and Wellness.

- Patients who are using benzodiazepines for treatment of alcohol withdrawal.
- Patients who are using benzodiazepines for treatment of seizure disorder.
- Patients receiving palliative, hospice, or other end-of-life care.
- Other situations for which benzodiazepines may be appropriate:
  - ✓ Urgent treatment of acute psychosis with agitation or acute mania
  - ✓ Single-dose treatment of phobias, such as flying phobia
  - ✓ Sedation for procedures
  - ✓ Spasticity treatment

About benzodiazepines and Z-drugs

Benzodiazepines are gamma-aminobutyric acid (GABA) receptor agonists that have hypnotic, anxiolytic, muscle relaxant, and anticonvulsant properties. Benzodiazepines are commonly divided into three groups according to how quickly they are eliminated from the body:

- Short-acting (half-life less than 12 hours), such as midazolam and triazolam.
- Intermediate-acting (half-life between 12 and 24 hours), such as alprazolam, lorazepam, and temazepam.
- Long-acting (half-life greater than 24 hours), such as diazepam, clonazepam, clorazepate, chlordiazepoxide, and flurazepam.

Z-drugs (e.g., zaleplon, zolpidem, and eszopiclone) were developed as alternatives to benzodiazepines.

- Like benzodiazepines, they are GABA receptor agonists, but because they have a different structure they produce fewer anxiolytic and anticonvulsant effects.
- Z-drugs are not“safer”than benzodiazepines, and patients on benzodiazepines should not be switched to Z-drugs to try to improve safety.

Both benzodiazepines and Z-drugs are considered a “high-risk medication in the elderly” and are listed on the American Geriatrics Society Beers Criteria list.

Chronic benzodiazepine use is daily or near-daily use of benzodiazepines for at least 90 days and often indefinitely, and is defined as a minimum 70-day supply of benzodiazepines dispensed in the previous 3 calendar months.

Chronic Z-drug use is daily or near-daily use of Z-drugs for at least 90 days and often indefinitely, and is defined as a minimum 70-day supply of Z-drugs dispensed in the previous 3 calendar months.

Prescribing

Except where noted, statements about benzodiazepines in this guideline also apply to Z-drugs.

Prescribing quantity limits

- The default in KP Health Connect for acute benzodiazepine (or Z-drug) prescribing limit is 7 tabs/caps.
- For benzodiazepine-naïve patients (≤ 7-day supply within last 180 days), the maximum supply is 15 tabs/caps or 14-day supply (whichever is the lesser amount). There is currently no equivalent limit for Z-drugs.
- Benzodiazepine and Z-drug prescriptions are limited to a 30-day supply.

In addition to prescribing quantity limits, the following Best Practice Alerts fire in Health Connect to alert providers when:

- A benzodiazepine (or Z-drug) is prescribed to a patient 65 years or older
- A second benzodiazepine prescription (or Z-drug) is ordered within 60 days (transition to chronic)
- A benzodiazepine (or Z-drug) is ordered when the patient is already taking an opioid
- A second benzodiazepine (or benzo + Z-drug) is ordered for a patient who is already taking a benzodiazepine

Prescribing considerations

Before initiating a course of benzodiazepine treatment, the following should be considered:

- Do not prescribe benzodiazepines to patients already taking opioids, as this is associated with increased risk of fatal overdose.
- Concurrent use of marijuana and benzodiazepines is not recommended.
- Explicitly advise the patient regarding the duration of treatment. Use of benzodiazepines beyond 2 weeks is not recommended.
- Use the lowest dose for the shortest time.
- Review with the patient the risks and side effects, including the risk of dependence. Keep in mind that some patients will have difficulty discontinuing the medication at the end of acute treatment.
- Discuss exit strategies, such as tapering and/or transition to alternative treatments.
- Discuss alternative treatments, which may include:
  - ✓ Antidepressant medications (e.g., SSRIs, SNRIs, tricyclic antidepressants)
  - ✓ Psychotherapy (e.g., cognitive behavioral therapy)
  - ✓ Serotonergic agents for anxiety (e.g., buspirone)
  - ✓ Anticonvulsant medications for restless leg syndrome (e.g., pramipexole, ropinirole, gabapentin)
- The patient and health care provider should agree on one provider to be the benzodiazepine prescriber for that patient. This designated prescriber should also be responsible for prescribing other medications with abuse potential, specifically central nervous system (CNS) stimulants and narcotics; otherwise the prescriber of benzodiazepines should closely coordinate care with those who are prescribing other controlled substance medications.

Note for patients aged 65 years and over

- If prescribing for patients who are frail or aged ≥ 65 years, consider initiating the medication at half the adult dose.

- Individuals aged ≥ 65 years are especially vulnerable to the adverse effects of hypnotic drugs, as metabolic capacities and rates decline with age. Patients in this age group are:
  - ✓ More susceptible to CNS depression and cognitive impairment, and may develop confusion states and ataxia, leading to falls and hip fractures.
  - ✓ At risk of drug interaction with other medications.
  - ✓ At risk of permanent cognitive impairment when using high doses of benzodiazepines (e.g., diazepam 30 mg or equivalent) on a regular basis.

Short-term use

In rare circumstances of acute, severe, and debilitating insomnia that is not responsive to behavioral treatment, a one-time supply of ≤ 15 pills zolpidem 5 mg at bedtime for a brief period while the patient's evidence-based behavioral insomnia treatment is being adjusted, with no refills, is recommended. Ensure recommendations in the KPWA Insomnia Guideline have been followed prior to consideration of higher-risk treatments.

- Physical dependence rapidly occurs within 2 weeks of continuous daily use.
- Avoid in patients taking opioids and other sedative-hypnotics or substances with sedative effects such as alcohol, due to an increased risk of respiratory depression.
- Avoid in patients aged 65 years and over, due to increased adverse effects including fall risks and cognitive impacts.

Long-term use

Benzodiazepines and Z-drugs are not recommended for long-term use (longer than 2 weeks), except in exceptional circumstances (e.g., for terminally ill patients). There is no evidence to support the long-term use of these drugs for insomnia or any mental health indication. There are concerns regarding their safety.

- Insomnia: The treatment period should not exceed 2 weeks, as sleep studies have shown that sleep patterns return to pre-treatment levels after only a few weeks of regular use.

- Anxiety: Continuing beyond 2 weeks will result in loss of effectiveness, development of tolerance or dependence, potential for withdrawal symptoms, persistent adverse effects, and interference with the effectiveness of definitive medications and counseling.

Contraindications

- Concurrent use of another benzodiazepine, Z-drug, muscle relaxant, or opioid
- Active or history of substance use disorder
- Pregnancy or risk of pregnancy
- Treatment with opioids for chronic pain or agonist therapy for opioid use disorder
- Medical and mental health problems that may be aggravated with benzodiazepines, such as fibromyalgia, chronic fatigue syndrome, depression, bipolar disorders (except for urgent sedation in acute mania), attention deficit hyperactivity disorder, kleptomania, and other impulse disorders
- Cardiopulmonary disorders such as asthma, sleep apnea, chronic obstructive pulmonary disease, and congestive heart failure, as benzodiazepines may worsen hypoxia and hypoventilation

Adverse effects of benzodiazepines

- There is an association between benzodiazepine use and dementia, increased rate of falls, and increased risk of hip fracture.
- Tolerance to anxiolytic effects, which may develop after a few weeks of use. (This does not apply to Z-drugs because they are not anxiolytic.)

Adverse effects of both benzodiazepines and Z-drugs

- Dependence: Potent benzodiazepines with short or intermediate half-lives (e.g., alprazolam, lorazepam) appear to carry the highest risk of causing problems with dependence. Psychological or physical dependence can develop over a few weeks or months and is more likely to develop with long-term use or high doses, and in patients with a history of anxiety problems.

- Tolerance to the hypnotic effects, which may develop after only a few days of regular use
- Daytime somnolence
- Dizziness
- Impaired driving performance leading to an increased risk of traffic accidents
- Depression and increased anxiety
- Slowness of mental processes and body movements
- Particularly high risk of overdose when combined with sedative drugs, such as opioids or alcohol
- Increased risk of mortality
- Increased risk of cognitive impairment and delirium
- Increased risk of falls and fractures, especially among older adults

As of September 2020, the FDA requires that all benzodiazepine prescriptions include a boxed warning that addresses the serious risks of abuse, addiction, physical dependence, and withdrawal reactions of benzodiazepine medicines. See https://www.fda.gov/media/142368/download for more information.

Management of patients on chronic benzodiazepines and Z-Drugs

All patients should be encouraged to discontinue chronic use of benzodiazepines and Z-drugs. Providers should create a treatment care plan to help patients with tapering and discontinuation.

- For most people in primary care settings even a minimal intervention, such as a letter with self-help information from the treating physician or a single brief consultation, can be effective in reducing or stopping benzodiazepine use.
- For patients who do not want to stop the drugs, discuss the benefits of stopping. Set the expectation of revisiting the topic at least annually, and more frequently when there are changes in the patient's care plan.

Tapering and discontinuation

Tapering considerations

Taper planning must be individualized based on the patient's clinical needs, indication for taper, and ability to comply with the care team's tapering instructions, and on the provider's clinical judgment.

- Determine initial step of taper and document rationale in medical record.
- Do not reverse a taper. A temporary pause in tapering may be indicated to mitigate side effects.
- Assess the patient's response to the initial dose reduction in the first 1 to 4 weeks.
- Assess the patient's underlying condition for which the drugs were originally prescribed; discuss alternative treatments as needed.
- Assess the patient for readiness/suitability to taper off benzodiazepines. Patients are considered suitable if they:
  - ✓ Are willing and committed, with adequate social support,
  - ✓ Have no previous history of complicated drug withdrawal, and
  - ✓ Do not have an indication for rapid discontinuation.

  If a taper is needed but the patient does not meet the criteria above, or if you have specific questions about tapering, consult Mind Phone or Pharmacy.
- Cognitive behavioral therapy is recommended to help the patient cope with rebound anxiety and to assist with the withdrawal process.
- Consider referral to a specialist for patients who:
  - ✓ Have a history of alcohol use disorder or other substance use disorders,
  - ✓ Have a concurrent severe medical or psychiatric disorder,
  - ✓ Are on a high dose,
  - ✓ Are taking stimulants or opioids concurrently, or
  - ✓ Have a history of drug withdrawal seizures.
- Reassess taper weekly to monthly based on patient's response, and prior to each subsequent dose reduction.

Z-drug recommendations

Considering the frequency at which the patient takes the medication, choose one of these options:

- Stop the Z-drug and start an alternative medication (such as melatonin, trazodone, doxepin, or mirtazapine).
- Taper the Z-drug by decreasing the number of days per week the patient takes the medication (for example: take 6 nights per week x 2 weeks, then 5 nights per week x 2 weeks, and so on).
- For chronic, long-term Z-drug use:

Table 2. Methods for tapering of chronic Z-drug therapy

Z-drug	Taper method
Zolpidem	● Reduce by ~25% of original dose each week or every other week ● If dose > 10 mg/day IR or 12.5 mg/day CR: slower rate of tapering in conjunction with CBT-I
Eszopiclone	● Reduce by ~25% of original dose (up to 1 mg) each week or every other week ● If dose > 3 mg/day: slower rate of tapering in conjunction with CBT-I
Zaleplon	● Reduce by ~25% of original dose each week or every other week ● If dose > 20 mg/day: slower rate of tapering in conjunction with CBT-I

Benzodiazepine tapering recommendations

The most effective strategy to manage benzodiazepine discontinuation and prevent adverse outcomes associated with severe withdrawal—such as severe seizures—is a gradual taper of benzodiazepines.

- If the patient is established on a long- or intermediate-acting benzodiazepine, taper the medication per Table 3 or see “Switching to a longer-acting benzodiazepine,
- If the patient is established on a short-acting benzodiazepine or one that doesn’t easily allow for small dose reductions, switch to diazepam (patients 64 or younger) or lorazepam (patients 65 and older) and gradually taper per Table 3 or “Switching to a longer-acting benzodiazepine,”.

Table 3. Clinical indications and methods for tapering of chronic benzodiazepine therapy	
Indication	**Taper method**
● Function is not improved ● Tolerance has developed with long-term prescription	SLOW 10% every 2–4 weeks
● Medication adverse effects indicate risks are greater than benefit ● Comorbidities increase risk of complication	MODERATE 10% every week
● Urine drug screen is consistent with substance abuse concerns, ● Significant risk of respiratory depression due to unstable clinical condition or recent overdose, or ● Patient's behavior suggests possible misuse or diversion of medication. Such behaviors might include: ✓ Selling prescription drugs ✓ Forging prescriptions ✓ Stealing or borrowing drugs ✓ Frequently losing prescriptions ✓ Aggressive demand for benzodiazepines ✓ Injecting oral/topical benzodiazepines ✓ Unsanctioned use of benzodiazepines ✓ Unsanctioned dose escalation ✓ Concurrent use of illicit drugs, including opioids ✓ Getting benzodiazepines from multiple prescribers ✓ Recurring emergency department visits ✓ Concurrent use of alcohol	RAPID 25% per week and/or Refer patient for chemical dependency or addiction counseling.

- A subset of patients will experience clinically significant withdrawal symptoms even with 10% dose reductions and/or gradual tapering. Consider switching these patients to a longer-acting benzodiazepine; see "Switching to a longer-acting benzodiazepine," (Table 4).

- Tapering should be guided by individual choice and severity of withdrawal symptoms. Drug discontinuation may take 3 months to a year or longer. Some people may be able to discontinue the drug in less time.
- Review the patient's progress frequently to detect and manage problems early and to provide advice and encouragement during and after tapering. Development of withdrawal symptoms can be quite variable and insidious during a taper. A high index of suspicion for withdrawal-related etiology should be held if new symptoms arise during a taper.
- If the first attempt is unsuccessful, consider switching to long-acting benzodiazepines in second attempt.
- If patient compliance is an issue, consider dispensing medication in 7- or 14-day increments.

Switching to a longer-acting benzodiazepine for tapering

Diazepam (patients aged 64 and under)

There is a lack of good-quality evidence on switching to diazepam, but it can be considered for some people because diazepam has a long half-life (20–80 hours) and thus has fewer fluctuations in plasma levels. It is also available in a variety of strengths and formulations, which facilitates step-wise dose substitutions from other benzodiazepines or Z-drugs and allows for small incremental reductions in dosage. Switching is best carried out gradually, usually in a step-wise fashion.

Switching to diazepam should be considered for individuals who are:

- Using short- to intermediate-acting benzodiazepines (e.g., alprazolam and lorazepam)
- Using preparations that do not easily allow for small reductions in dose (e.g., alprazolam or flurazepam)
- Experiencing difficulty or likely to experience difficulty withdrawing directly from temazepam or Z-drugs due to a high degree of dependency (associated with long duration of treatment, high doses, or history of anxiety problems)

Alprazolam (Xanax) note: Care should be taken not to taper alprazolam too rapidly or to switch to another benzodiazepine too abruptly, as withdrawal seizures are more prone to occur with alprazolam than with other benzodiazepines. If difficulty tapering the last 1–2 mg of alprazolam: taper more gradually (0.25 mg/week) or substitute diazepam gradually over 1 week and taper as usual.

Lorazepam (patients aged 65 and over)

Switching to diazepam in patients aged 65 and over is not recommended, as case reports suggest that it may be associated with delirium. For older adults, lorazepam, oxazepam, and temazepam are the safest options because they don't have metabolites that can accumulate. Of these, lorazepam is the best in terms of dosing options—available as 0.5, 1, and 2 mg tabs, and as 2 mg/mL oral solution.

How to make the switch (Table 4)

- Substitute diazepam or lorazepam for one dose of the current benzodiazepine at a time, usually starting with the evening or nighttime dose to avoid daytime sedation. Replace the other doses, one by one, at intervals of a few days or a week until the total approximate equivalent dose (Table 4) is reached before starting the reduction.
- For patients on diazepam, the long half-life can enable them to take a single dose at night or a twice-daily dose.
- For patients on lorazepam, twice-daily dosing is recommended.

Table 4. Approximate dose equivalent to 5 mg diazepam

Note: Data shown are approximate equal potencies relative to diazepam as there is considerable variation in dose equivalents depending on the source of information. The sources used in this table are Lexicomp and UpToDate. Patients should be monitored closely during the tapering process to prevent over- or under-dosing. These dosing conversions are intended to be used only in the tapering process, not for initiation of therapy.

	Trade name	Half-life (hours)	Dose equivalent to 5 mg diazepam
Alprazolam	Xanax	12–15	0.5 mg
Chlordiazepoxide	Librium	5–30	10 mg
Clonazepam	Klonopin	18–50	0.25–0.5 mg
Diazepam	Valium	20–80	5 mg
Lorazepam	Ativan	10–20	1 mg
Temazepam	Restoril	3.5–18.5	30 mg
Triazolam	Halcion	1.5–5.5	0.25 mg
Prescribe 5 mg or 2 mg diazepam tablets only. Starting dose should not exceed 40 mg. Consult with Mental Health and Wellness if considering a higher dose.			

Treatment of withdrawal symptoms (Table 5)

Acute signs and symptoms of withdrawal

Anxiety-related withdrawal symptoms are common, and include restlessness, agitation, tremors, dizziness, panic attacks, palpitations, shortness of breath, sweating, flushing, shakiness, difficulty swallowing, poor sleep, sensation of choking, and chest pain. There is a wide range of other, less common acute withdrawal symptoms, such as seizures, bowel/bladder problems, changes in appetite, tiredness, faintness, poor concentration, tinnitus and delirium.

Long-term signs and symptoms of withdrawal

Some withdrawal symptoms can persist and may take months or years to resolve, including anxiety, fatigue, depression, poor memory and cognition, motor symptoms (pain, weakness, muscle twitches, jerks, seizures), depersonalization, psychosis, paranoid delusions, rebound insomnia, and abnormal perception of movement.

Prevention and treatment of withdrawal symptoms

Table 5. Medications used to prevent or treat withdrawal symptoms during gradual taper from chronic benzodiazepines or Z-drugs

Symptom	Medication	Dosing
Seizure prevention	Carbamazepine	Start 200 mg twice daily, adjust dose weekly up to 400 mg twice daily. Continue for 2–4 weeks after stopping benzodiazepines and then taper anticonvulsant.
	Valproic acid or Divalproex sodium EC	Start 500 mg twice daily, adjust dose weekly up to 2,000 mg daily. Continue for 2–4 weeks after stopping benzodiazepines and then taper anticonvulsant.
Tachycardia, hypertension, tremors, sweats, anxiety, restlessness	Propranolol	10 mg three times daily as needed for 3 days
Hypertension, tremors, sweats, anxiety, restlessness	Clonidine	0.1 mg three times daily as needed for 3 days
Anxiety, restlessness	Gabapentin	100–300 mg every 6 hours as needed
Insomnia	Hydroxyzine or Diphenhydramine	25 mg every 6 hours as needed
	Gabapentin	100–300 mg daily before bed as needed
	Hydroxyzine or Diphenhydramine	25–50 mg daily before bed as needed
Nausea	Promethazine	25 mg every 6 hours as needed
	Metoclopramide	10 mg every 6 hours as needed
Dyspepsia	Calcium carbonate	500 mg 1–2 tabs every 8 hours as needed
	Mylanta, Milk of Magnesia	Follow package instructions.
Pain, fever	Acetaminophen	500 mg every 4 hours as needed, not to exceed 3,000 mg in 24 hours
	Ibuprofen	600 mg every 6 hours as needed

1	In patients with liver impairment, consider topiramate, gabapentin or levetiracetam. Check CBC and liver function tests at baseline.
2	Check CBC and liver function tests at baseline and every 3 months during treatment.
3	These are high-risk medications for the elderly. Please consider alternatives for patients aged 65 and older.
4	Patients with chronic insomnia or worsening anxiety during the taper often do better with cognitive behavioral therapy to address these symptoms during the taper. Refer these patients to Mental Health Access for this specific therapy.

Referral criteria

Consider consultation with Mental Health and Wellness for patients who have any of the following:

- A history of alcohol use disorder or other drug use disorders
- A concurrent severe psychiatric disorder
- Concurrent use of stimulants or opioids
- A history of drug withdrawal seizures
- Suicidal thoughts

1. Patient-related barriers and enablers for deprescribing BZD

Barriers

- Dependence on BZD to cope with everyday life and/or for a physical or psychological underlying condition
- Psychological factors and existing personality traits
- Comorbid dementia or Parkinson's disease and a history of hospitalization in the past 3 months
- Fear of a return of the insomnia or anxiety
- History of alcohol or drug use
- Lack of family or social support
- Older age
- Lack or inadequate awareness of harms and side effects of BZRA treatment, and lack of knowledge of other treatment options

- Generalized frustration towards the medical profession and disappointment about their treatment, mainly due to limited consultation in decision-making. Some patients described their prescriber as adopting "a one size fits all approach."
- Perceived issues with prescribers' tendency to overprescribe and their lack of sufficient knowledge about BZDs
- Unsympathetic primary care physicians providing insufficient support
- Inability to talk openly about their BZDs and feeling stigmatized by their prescribers, who show little effort to understand them. Some interpreted the prescriber attitude as being dismissive or even punitive.

Enablers

- The patient's willingness to stop BZRA treatment and return to natural sleep
- Knowing the harms associated with long-term use and experiencing impairing side effects
- Recognizing the need to change their beliefs and attitude towards their medication
- Knowledge about other effective strategies to address underlying issues
- Voicing their opinion and being actively involving in decision-making
- Receiving the prescription from their personal primary care provider versus another provider or prescriber
- Patient's trust of the provider. The most significant influences on trust were the prescriber having a genuine desire to understand the patient, being knowledgeable about BZDs, open communication, shared decision-making, and, to a lesser degree, duration of the relationship.

2. Physician- and/or prescriber-related barriers and enablers for deprescribing BZD

Barriers

- Lack of knowledge about BZDs and lack of monitoring
- Expected patient resistance towards deprescribing of BZRA
- Reluctance to deprescribe treatment from functioning patients
- Conception that BZRA does not harm
- Concern about withdrawal symptoms
- General attitude that BZRA should not be avoided, and continued use is necessary
- Unequal balance of power between nurses and physicians

Enablers

- Engaging patients in motivational interviewing before beginning the deprescribing process and giving them time to consider the benefits
- The physician's knowledge of and willingness to follow the guidelines' instructions that BZRA use is only for the short term
- Physician empathy, demonstrated compassion, and encouragement during tapering
- Satisfactory knowledge about BZDs, diligence in monitoring their use, and providing regular suggestions and encouragement
- Actively involving the patient in shared decision-making
- Flexibility, collaboration with other healthcare providers, and involving nurses in the patients´ medications and evaluation.

National Permanente Medical Group Practice Recommendations for Benzodiazepines & Non-Benzodiazepine Sedative-Hypnotics / Z-drugs (for Adults 18 and Over).

Kaiser Permanente. Last edited March 17, 2021.
https://wa-provider.kaiserpermanente.org/static/pdf/provider/resources/sedative-hypnotics.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Purpose

The purpose of these practice recommendations are:

- To reduce the number of patients who are at risk of becoming newly dependent, tolerant, or addicted to benzodiazepines (BZDs) and non-benzodiazepine sedative-hypnotics/"Z drugs" (nBZD-Zs).
- To safely monitor and taper as medically indicated patients who are already dependent on long-term, chronic BZDs or nBZD-Zs.
- To provide recommendations for limiting the use of BZDs and nBZD-Zs for treatment of anxiety, insomnia, and other disorders.
- To avoid prescription medication and/or substance combinations that place a patient at higher risk of morbidity and mortality.
- To address the use and monitoring of BZDs and nBZD-Zs for other indications and in special populations.

Key Points to Consider:

- These recommendations do not pertain to palliative care, hospice, or other end of life care treatment.

- These are PMG recommendations; however, all prescribers need to be aware of additional state and national laws and regulations involving BZDs or nBZD-Zs prescribing that may supersede these recommendations. For questions pertaining to specific jurisdictional requirements, please refer to your respective Regional compliance and/or legal resources.
- For any prescribing outside of these recommendations (which would also fall outside of the CDC recommendations), it is highly advised that the reason(s) be documented in the patient's medical record. Recommendations should not replace medical judgment and individual assessment of treatment risks and benefits.
- Our focus is to avoid the use of BZDs or nBZD-Zs by employing non-pharmacologic and alternative pharmacologic therapies first, and reserve BZDs and nBZD-Zs for only when necessary.
- Chronic daily BZDs or nBZD-Zs monotherapy should be avoided. For suspected fraud or diversion of controlled substances, contact your local Compliance Officer or Special Investigations Unit (SIU).

Focus Area 1: Avoid New Start BZDs

Recommendation 1

(1) Avoid BZD by employing non-pharmacologic and/or effective and safe pharmacologic options for anxiety related disorders, panic disorders, and insomnia.

(2) Non-pharmacologic options are effective and may include:

a. Provider education to patient on anxiety

b. Kaiser Permanente Educational Programs

c. CALM App (includes many calming music options, sleep stories, guided meditation selections for focus, relaxation, and sleep)

d. myStrength App

e. Exercise

f. Mindful Meditation

g. Consider reducing alcohol, caffeine and other substances that may increase anxiety

h. If provider feels appropriate, patient can be referred for counseling, such as Cognitive Behavioral Therapy (CBT).

(3) Patients with acute, severe anxiety should also be evaluated for depression and/or substance use disorder (SUD). Consider ordering a urine drug screen.

Recommendation 2

(1) For a patient that presents with moderate to severe anxiety or panic attacks, initially start a SSRI, SNRI, or buspirone.

Pharmacologic options may include:

- SSRIs such as escitalopram, citalopram, sertraline, fluoxetine
- SNRIs such as venlafaxine or duloxetine, or
- Serotonergic agent for anxiety, such as buspirone
- Propranolol and hydroxyzine can be considered in selected patients

(2) SSRI and SNRI: Monitor closely in elderly patients for risk of falls, bleeding, or hyponatremia.

(3) For Patients aged 65 years and over, avoid paroxetine, hydroxyzine, or TCAs.

(4) If provider feels appropriate, evaluate the need for referral to Behavioral Medicine, Psychiatry, Mental Health, and/or Addiction Medicine.

Additional Recommendations/Comments

(1) BZDs use may be considered for occasional, rare (intermittent/situational) anxiety such as for pre-MRI/CT scans, pre-procedure, or pre-chemotherapy, or single-event treatment of specific phobias, such as flying phobia.

(2) In the rare case that a BZD is needed, set the expectation that it will only be for a brief period and not for chronic use. Use of short-acting BZDs, such as alprazolam (Xanax®), is especially hazardous, as it may cause more rapid dependence with severe withdrawal symptoms.

(3) All BZDs can promote addictive behavior, delirium and agitation, risk for falls or injury, increased risk for dementia, and difficulty with tapering and discontinuing.

(4) If other therapies are not effective and BZDs are being considered, they are generally reserved for situational, time limited, severe anxiety symptoms where functioning is compromised.

(5) In rare circumstances, such as visible, acute, severe anxiety or debilitating panic attacks, consider:

- Use of propranolol and hydroxyzine in selected patients as a PRN.
- A one-time small supply of a concurrent BZD for a brief period at the time of initiation of treatment with SSRI or SNRI i.e., prescribe a small quantity, with the smallest quantity necessary, with a maximum of up to 15 tabs/caps or less of a low dose and rapidly taper off the BZD within the first one or two weeks.
- Avoid starting BZDs in patients who are concurrently using alcohol, any illicit drugs, Tetrahydrocannabinol (THC), any opioids, or other sedating drugs such as zolpidem (Ambien®).

Focus Area 2: For Patients Already Prescribed BZD and nBZDs-Zs
Recommendation 1

(1) BZDs and nBZD-Zs are not recommended for longterm use due to the risks of physical and psychological dependence, tolerance, potential for severe withdrawal symptoms, and persistent adverse side effects.

- Abruptly stopping BZDs can lead to seizures and death.

(2) Discuss significant risks of BZDs and nBZD-Zs and treatment options with patients to encourage them to taper BZDs and nBZD-Zs.

- Address patients on BZDs or nBZD-Zs and use tapering recommendations.
- Create a treatment care plan to help patients with tapering and discontinuation.
- For most patients in primary care settings even a minimal intervention, such as a letter with self-help information from the treating physician or a single brief consultation, can be effective in reducing or stopping BZD use. (KPWA)

Recommendation 2

(1) Tapering:

- Consider starting an SSRI or SNRI before taper and provide education on non-pharmacologic therapy interventions such as behavioral therapies and other available resources to help manage symptoms.

(2) Gradual Tapering General Guide:

- Provide anticipatory guidance on the possibility of transient rebound anxiety. This anxiety is usually temporary, and rarely a reason to stop the taper.
- Tapering schedules should be individualized. The duration of time the patient has been on BZDs can help determine the tapering plan depending upon risk of severe harm, patient's clinical need, and/or on a physician's clinical judgment.
- Taper 10% a week if the patient has been on BZDs for several months or less, or 10% every 2 to 4 weeks if the patient has been on BZDs longer.
  - ✓ Slower taper by 5% may be needed if patient has symptoms of rebound anxiety and/or insomnia especially when at <20% original dose.

  If you are having trouble tapering the BZD, consider contacting Psychiatry.

Additional Recommendations/Comments

(1) Consider consultation with an Addiction Medicine specialist if you believe the patient may have a Substance Use Disorder (not just physical dependence), especially if there is continued escalation of dose.

(2) Consider consultation with behavioral/mental health for patients who have any of the following:

- A concurrent significant psychiatric disorder
- History of Substance Use Disorder
- Concurrent use of prescription stimulants or opioids
- A history of drug withdrawal seizures
- Suicidal thoughts

(3) Along with gradual tapering, non-pharmacologic options are recommended. When developing gradual taper care plan also consider counseling, including cognitive behavioral therapy, if available. This can be part of the therapy plan, to help the patient cope with rebound anxiety, assist with the withdrawal process, and improve the likelihood of long-term successful discontinuation.

(4) Set the expectation of revisiting the topic at face-to-face visits, with a minimum expectation that this be discussed at least annually, possibly more frequently when there are changes in the patient's clinical situation.

- If clinical decision is to continue the chronic use of BZD, then strongly consider conducting regular checks with UDS (urine drug screen) a minimum of every 12 months.
- PDMP (prescription monitoring program) should be checked on an ongoing basis.

Focus Area 3: Acute Insomnia

Recommendation 1

Medication treatment for insomnia is not first line and less effective than first line behavioral treatment.

There is effective evidence-based treatment for insomnia, including:

- Provider education to patient on insomnia
  - ✓ Sleep Hygiene education
- Kaiser Permanente Educational Programs
- CALM App (includes many calming music options, sleep stories, guided meditation selections for focus, relaxation, and sleep)
- myStrength App
- Light therapy
- CBT-I App
- Exercise
- Mindful Meditation
- As applicable, reduce alcohol, caffeine and other substances that may increase insomnia, including prescription and non-prescription medication.

Recommendation 2

Additional adjunctive pharmacologic treatment can be considered if no response to behavioral treatment and may include:

30-60 minutes before sleep

- Patients under 65:
  - ✓ OTC Melatonin 3-6 mg HS PRN
  - ✓ Trazodone 25-150 mg HS PRN (if no cardiac or other contraindications, titrate slowly- see Focus Area 3, additional recommendations/ comments)
  - ✓ Doxepin 5-10 mg HS PRN, (Oral liquid, capsules, or tablets)
  - ✓ Mirtazapine 7.5-15 mg HS PRN
- Patients age 65 or older:
  - ✓ OTC Melatonin 3-6 mg HS PRN
  - ✓ OTC Acetaminophen ER 650 mg QHS
    - ■ Avoid Acetaminophen plus Diphenhydramine (Tylenol PM)
    - ■ Most beneficial in patients who may be having some aches and pains affecting their sleep
  - ✓ Trazodone 25-50mg HS PRN
  - ✓ Mirtazapine 7.5-15 mg HS PRN
  - ✓ Doxepin 5 mg HS PRN (oral liquid)

Additional Recommendations/Comments

Do not continue BZDs or nBZD-Zs insomnia medication continuously for longer than 2 weeks, not for chronic use.

- Set the expectation with the patient that the medication will not be prescribed for chronic use.

In rare circumstances of acute, severe, and debilitating insomnia, not responsive to behavioral treatment, a one-time small supply less than or equal to 15 pills of zolpidem 5 mg at bedtime for a brief period while the patient's evidence-based behavioral insomnia treatment is being adjusted, with no refills is recommended.

- Physical dependence rapidly occurs within 2 weeks of continuous daily use.
- Avoid in patients taking opioids and other sedative-hypnotics or substances with sedative effects such as alcohol, due to an increased risk of respiratory depression.
- Avoid in Patients aged 65 years and over, due to increased adverse effects including fall risks and cognitive impacts.

Focus Area 4: Chronic Insomnia

Recommendation 1

There is no indication for BZDs or nBZD-Zs for chronic insomnia. Patients presenting with chronic insomnia should not be treated with these drugs even for occasional prn use.

- Consider non-medication therapies and other medication alternatives (as mentioned in Focus Area 3: Acute Insomnia).
  - ✓ CBT-I Cognitive Behavioral therapy is the recommended primary treatment for chronic insomnia (continually assessing for improvement in insomnia and severity).
  - ✓ If CBT-I alone is inadequate, consider use of other medication (e.g. melatonin, trazodone).
- nBZD-Zs drug effectiveness commonly diminishes after 6 weeks of treatment.
- Also consider underlying conditions that may be causing the symptom of insomnia and address those root cause conditions or circumstances.
- For patients that are already taking BZD, do not abruptly stop, initiate a slow taper.
- Patients are at an increased risk of physical dependency and therefore are also at a higher risk of physical withdrawal when stopping therapy.

Recommendation 2

Tapering

- nBZD-Zs should be discontinued similarly to BZDs (as mentioned in Focus Areas 2: For Patients Already Prescribed BZD and nBZD-Zs, Recommendation #2)
- Alternatively, nBZD-Zs can be tapered by decreasing the number of days per week the patient takes a medication. For example, take 6 nights a week for 1-2 weeks, then 5 nights a week for 1-2 weeks and so on.
  - ✓ Tapering schedules should be individualized.

Additional Recommendations/Comments

For melatonin titration: start with 3 mg, escalate weekly if needed to 6 mg, max of 10 mg, at least 60-90 minutes before sleep.

- Use with caution in geriatric patients with dementia who exhibit irregular sleep-wake disorder due to detrimental effects on daytime mood functioning.

For Trazodone Titration: Consider low dose trazodone: start with 25 mg nightly (if no cardiac or other contradictions). Titrate slowly by 25 mg at night every 3-4 days if needed up to 150 mg nightly, 30 minutes before bedtime.
In the adults 65 years and older, titrate slower, with lower doses up to 100 mg/day due to the increased risk of orthostatic hypotension and possible falls.

Focus Area 5: BZDs and nBZD-Z-drugs Combination with Other Drugs that Affect the CNS

- BZDs should not be used in combination with any substance with sedative hypnotic effects, such as alcohol, illicit drugs, opioids, or other nBZD-Zs such as zolpidem (Ambien®) that may place a patient at higher risk of morbidity and mortality due to CNS and respiratory depression.
- Concurrent use of BZDs and stimulant drugs (whether prescription or illicit), can hide symptoms of benzodiazepine overdose, may increase the risk of overdose and may cause dysrhythmias and possible heart failure.
- Concurrent use of BZDs and Tetrahydrocannabinol (THC) may place a patient at higher risk of morbidity and mortality due to combined cognitive impacts.
- BZDs & Opioids:
  - ✓ Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. (FDA)
  - ✓ For established patients presenting on chronic BZD and/or nBZD-Zs, if the patient is also on an opioid, the combination is not recommended due to a 20% to 60% higher risk of respiratory depression/overdose. It is recommended that either the sedative-hypnotics or the opioid be tapered off.
  - ✓ While the patient is being slowly tapered off either medication, patient and/or caregiver education on the risks of overdose and the use of naloxone should be strongly considered and a prescription for naloxone nasal spray, (Narcan®),

should be offered due to the higher risk of respiratory depression/overdose when these drugs are combined.

Focus Area 6: Possible Alternative Uses of BZDs

Conditions where BZDs may be an appropriate treatment (although there may be more preferred treatment options with less risk and stronger level of evidence):

- Alcohol withdrawal
- Acute and chronic vertigo
- Specific phobias (e.g. fear of flying)
- Burning mouth syndrome
- Non-REM and REM Sleep Behavior Disorders
- Tourette's/Tic's
- Anticipatory chemotherapy induced nausea and vomiting
- Seizures
- Tinnitus

Other rare neurologic indications (e.g., Catatonia)

- Muscle spasticity syndromes

Refer to the prescribing information for the contraindications, warnings, and precautions.

Guidelines for the Use of Benzodiazepines in the State of New Mexico

The New Mexico Overdose Prevention and Pain Management Advisory Council

https://www.nmhealth.org/publication/view/guide/6327/

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Introduction

Benzodiazepines (BZD) are indicated for a variety of uses due to sedative, hypnotic, anxiolytic, anticonvulsant, muscle relaxant, and amnesic actions. BZD are indicated for alcohol withdrawal, seizures, anxiety disorders, panic, agitation, and insomnia. BZDs have been widely prescribed since the 1960s, and are known to be associated with physical dependence and addiction. The more recently created and related "Z" drugs (i.e. zolpidem, zaleplon and eszopiclone) are now in use for insomnia. BZDs are thought to be relatively safe, but not in combination with other drugs, such as opioids, in individuals with substance use disorders, or in the elderly. Despite the hazards and despite the lack of clinical evidence for certain indications or long-term use, they are widely and perhaps excessively prescribed.

It has become increasingly apparent that benzodiazepines play a significant role in overdoses. The risk of overdose death increases as a patient concurrently uses benzodiazepines with other CNS-depressants, particularly opioids and alcohol. A black box warning was added to prescribing information by the FDA in 2016, warning against the use of benzodiazepines with opioids, recommending using alternatives, but if used, to monitor for respiratory depression and to limit quantities. The Centers for Disease Control and Prevention (CDC) in their guidelines for opioid use recommends avoiding use of benzodiazepines with opioids.

This is occurring in the context of benzodiazepines being amongst the most widely prescribed psychotropic medications, including for long-term use (greater than 6 weeks of use), despite the risks and lack of treatment guidelines of clinical evidence of long-term efficacy. Alprazolam is the most widely prescribed psychotropic medication in the US, with 48 million prescriptions dispensed in 2013. Benzodiazepines are controlled substances that can cause both physical and psychological dependence, and can be abused. Discontinuing benzodiazepines can often be challenging, and require expert support.

As New Mexico as a state continues to work towards decreasing drug overdose deaths and encouraging the proper use of potentially dangerous medications, it was felt that offering recommendations on the proper use of benzodiazepines could aid in that effort and provide guidance for prescribers.

The goal of this document is to provide recommendations on the appropriate use of these drugs, including evidence-based clinical indications and duration of use, enhance understanding of the risk of these drugs especially in the context of combination therapy with other sedatives, and to provide advice on how to identify and manage aberrant use, including how to safely discontinue these medications when indicated.

Pharmacology of Benzodiazepines and Z-Drugs

Benzodiazepines enhance the action of gamma-aminobutyric acid (GABA) on GABA receptors causing anxiolytic and sedative effects. Different forms all have the same effect on these receptors, but differ in rate of absorption, speed in crossing the blood-brain barrier, rate of elimination and active and inactive metabolites. Based on these pharmacologic characteristics, BZDs are categorized by duration of activity, which influences frequency or dosing.

Commonly prescribed BZDs are divided as follows:

- Short-acting: alprazolam, midazolam and triazolam.
- Intermediate-acting: oxazepam, lorazepam, and temazepam.
- Long-acting: diazepam, clonazepam, clorazepate, chlordiazepoxide, and flurazepam.

For alcohol/sedative withdrawal, catatonia, acute mania, single-dose treatment of phobias, such as flying phobia, sedation for office procedures and seizures.

Z-drugs (e.g., zaleplon, zolpidem, and eszopiclone) also enhance GABA transmission but only affect a subunit of the receptor that influences sedation. These drugs therefore are used as sleep-inducing agents. Of note, these medications have risks and can be abused.

Prescribing Guidance for BZDs and Z-Drugs

The following is a description of recommendations derived from a variety of treatment guidelines concerning the use of BZDs. As with all guidelines, providers should rely on individual clinical judgment for individual patients.

Before Initiating BZD Therapy

1. Alternative, non-BZD, medications should in most cases be offered as first-line medication, for example:
    a. Antidepressant medications (e.g., SSRIs, SNRIs, tricyclic antidepressants)
    b. Psychotherapy (e.g., cognitive behavioral therapy, which can be highly effect and obviate the need for any medications)
    c. Serotonergic agents for anxiety (buspirone)
    d. Medications for restless legs (e.g., pramipexole, ropinirole, gabapentin)
    e. Adjunctive symptomatic medications (hydroxyzine, clonidine, propranolol)
2. The NM Prescription Monitoring Program (PMP) must be reviewed before writing a new prescription for a benzodiazepine if prescribed for more than 4 days, and then every three months for ongoing prescriptions. Refer to your healthcare licensing board for specific requirements regarding PMP utilization.
3. The provider will counsel the patient on the risks of these medications, such as sedation and dependence. Discuss strategy for taper as more that 6 weeks of therapy is rarely indicated. Ensure that the patient understands these risks.
4. As with opioid prescribing, providers should consider using treatment contracts and periodic urine toxicology tests.

5. All sedative medication should only be prescribed by only one provider, or, if a behavioral health provider is prescribing BZDs and a primary care provider is prescribing an opioid, there should be close coordination between the two providers. Encourage the patient to use one pharmacy.

Patients Aged 65 Years and Over

Both benzodiazepines and Z-drugs are considered "high-risk medications in the elderly" and are listed on the American Geriatrics Society Beers Criteria list, such that BZD and Z-drugs should be particularly avoided in the elderly.

Individuals aged 65 and older are especially vulnerable to the adverse effects of hypnotic drugs, as their metabolic rates decline with age. Patients in this age group are more susceptible to CNS depression and cognitive impairment, may develop confusion and ataxia leading to falls and hip fractures, are at risk of drug interaction with other medications, and may be at risk of permanent cognitive impairment when using high doses of benzodiazepines (e.g., diazepam 30 mg or equivalent) on a regular basis.

If thought to be absolutely necessary, half of normal doses should be considered, using benzodiazepines that do not need a fully functioning liver for metabolism (e.g., lorazepam, oxazepam or temazepam).

Evidenced-based Indications for Behavioral Disorders

Four behavioral health conditions/disorders have clinical evidence to support benzodiazepines use: Panic Disorder, Generalized Anxiety Disorder, Social Anxiety Disorder and insomnia, but only if used for short durations, usually less than 2-4 weeks, and as second-line treatments as psychotherapy or antidepressants, in particular serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), are generally recommended as first line. Some providers will co-prescribe a BZD with an SSRI, to allow for immediate relief while titrating the SSRI and awaiting it taking effect.

One practice guideline (NICE 2011) recommends using BZDs only as a short-term measure during crisis. The British National Formulary is quoted as advising that "benzodiazepines are indicated for the short term relief (2 to 4 weeks only) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, alone or in association with insomnia or short term psychosomatic, organic or psychotic illness".

There is no evidence or indication to use a BZD for Post-traumatic Stress Disorder, despite BZDs being commonly prescribed for PTSD. In fact, BZDs can increase the incidence of developing PTSD and interfere with effective treatment. Many treatment guidelines, including the Department of Defense, recommend against the use of BZDs in the treatment of PTSD. The frequent overlap of substance use disorders in individuals with PTSD create increased risk in the use of these drugs.

For insomnia, due to the development of tolerance, only short-term use of either a BZD or Z-drug is effective.

Long-term Use

Benzodiazepines and Z-drugs are not recommended for long-term use (longer than 6 weeks), apart from in exceptional circumstances (e.g., for terminally ill patients). There is no evidence to support the long-term use of these drugs for insomnia or any mental health indication. Physical dependence can occur with over 12 weeks of use, especially with higher doses and short-acting forms.

Multiple Benzodiazepine Concurrent Use

There is no clinical evidence nor treatment guideline that supports using more than one form of a benzodiazepine at a time.

Avoid Benzodiazepine or Use with Great Caution in the Following Situations

1. Active or history of substance abuse
2. Pregnancy or risk of pregnancy
3. Treatment with opioids for chronic pain or opioid use disorder.

4. Medical and mental health problems that may be aggravated with benzodiazepines, such as fibromyalgia, traumatic brain injury, developmental disability, chronic fatigue syndrome, somatization disorders, depression, bipolar disorders (except for urgent sedation in acute mania), attention deficit hyperactivity disorder, kleptomania, and other impulse disorders.
5. Chronic BZD therapy is not recommended in the treatment of Borderline Personality Disorder.
6. Cardiopulmonary disorders such as asthma, sleep apnea, chronic obstructive pulmonary disease, congestive heart failure, and other cardiopulmonary disorders, since benzodiazepines may worsen hypoxia and hypoventilation

Adverse Effects of Both Benzodiazepines and Z-drugs

1. Dependence: Potent BZDs with short or intermediate half-lives (e.g., alprazolam, lorazepam) appear to carry the highest risk of causing problems with dependence. Psychological or physical dependence can develop over a few weeks or months and is more likely to develop with long-term use or high doses, and in patients with a history of anxiety problems.
2. Tolerance to the hypnotic effects which may develop after only a few days of regular use.
3. Daytime somnolence and impaired driving (hence risk when driving or operating machinery).
4. Depression and increased anxiety
5. Slowness of mental processing and body movements (including increased risk of dementia and falls in elderly).
6. Increased risk of overdose when combined with sedative drugs, such as opioids or alcohol
7. Increased association between benzodiazepine use and overall mortality

Withdrawal Symptoms

Abrupt cessation of a BZD can cause altered CNS activity (tremor, seizures or delirium) particularly for physically dependent individuals on higher doses.

Common symptoms over time, even with a tapering dose, can include anxiety, restlessness, irritability, insomnia, agitation, muscle tension, weakness, aches and pains, blurred vision and racing heart. Less commonly withdrawal symptoms include nausea, sweating, runny nose, hypersensitivity to stimuli, and tremor. Rarely, with the elderly or with use of high- dose and/or high-potency BZDs, psychosis, seizures, hallucinations, paranoid delusions and tinnitus can occur. The duration of symptoms can be variable but usually last less than two weeks.

Again, offering a slow taper as tolerated by the patient can minimize these symptoms. While no medications offer full and consistent relief from BZD withdrawal symptoms, some medications may offer some comfort including, carbamazepine, propranolol, clonidine and analgesics. Education, support and psychotherapy during and after the taper is completed are very helpful, including helping patients not relapse on BZDs, say with another provider.

It may be helpful in more complex situations to refer patients to a psychiatric or addiction medicine specialist for assistance in managing both the discontinuation of the medication and treatment of any underlying behavioral health issues.

Use of BZDs and Z-drugs in Patients on Methadone or Buprenorphine for Treatment of Opioid Use Disorder

Patients with opioid use disorder frequently abuse BZDs to enhance the euphoria of opioids or attempt to alleviate withdrawal from opioids. Also, many patients are prescribed BZDs often inappropriately, in effort to treat anxiety symptoms or even the substance use disorder. Those with BZD use are at higher likelihood of continuing opioid abuse and failing to stay in methadone treatment.

While a less significant issue, BZDs in combination with buprenorphine have been associated with deaths due to respiratory depression, warranting caution when these drugs are combined.

Therefore, while BZD use (common in polysubstance dependence) should not prevent a patient with an opioid use disorder being offered methadone or buprenorphine treatment (FDA 2016), extreme caution should be used and the guidelines issued by the American Association for the Treatment of Opioid Dependence (2018) should followed.

Key points include regular checking of the PMP (also required by your healthcare licensing board), close communication between the treatment program and BZD and Z-drug prescribers, education on the risks, efforts to decrease and replace BZDs with safer treatments, development of safety plans and addressing BZD misuse when it occurs. Note – methadone dispensed from an Opioid Treatment Program (OTP) is not reported to the PMP; therefore, will not be discoverable on the patient's PMP report.

Management of Patients on Chronic Benzodiazepines and Z-Drugs

Essentially all treatment guidelines concerning the use of BZDs recommend their being used for no more than 6 weeks and some recommend as little as 4 weeks; it is recommended that an effort be made to decrease and discontinue BZD use after that period due to the significant risks of these drugs especially in older patients.

However, approaching the issue of discontinuing long-term BZDs usage should be done with care. Continuing a potentially harmful and/or ineffective treatment is not recommended but discontinuation should only be done after a careful assessment occurs and if at all possible, with the patient's agreement. To do so without patient engagement risks withdrawal symptoms, getting "fired" by the patient who then gets inadequate or no care, or the patient turning to illegal sources.

The Following is a Recommended Approach, Especially When a Provider "Inherits" a Patient on Long-term BZD Treatment

1. Conduct a proper assessment to include an accurate diagnosis as to the presence of a primary behavioral diagnosis versus a BZD-induced disorder. Review treatment history including if appropriate evidence-based first or second line treatments such as SSRI's or psychotherapies were tried.

2. Then assess effectiveness with a focus on functioning, not just degree of symptomatology. Many patients are on high dose BZDs yet still will not leave their house. Assessing the effectiveness of the treatment (in the absence of obvious harms) should be a critical determinate if the medication should be continued or not.
3. Assess harms from the medication. Is the medication being misused, used concurrently with illicit drugs or alcohol, causing actual or risk of drug-drug interactions (for example, with opioids), or causing cognitive impairment or falls?

If benefits clearly outweigh risks and discontinuing BZDs would appear to cause harm and decreased functioning, ongoing careful monitoring should occur to include patient education about risks, regular follow-up appointments, monitoring of the PMP and periodic urine toxicology testing. This should also occur if the provider is in the process of working with a patient who is neither being helped nor harmed by the medications but is in the process of being counselled around stopping the medications and trying alternative treatments. Note that in using toxicology testing, the provider should become familiar with the lab performing the toxicology screening to determine which BZDs are identified and be aware of false positives (e.g. sertraline can appear as a BZD in some screens) and false negatives.

Discontinuation

For patients that agree with discontinuing long-term BZD use, and for those who are resistant but are clearly at immediate risk, there are several approaches. Of note, many patients are fearful of cutting back and stopping BZDs. Many patients will benefit from repeated education, and perhaps counseling for support along the way. There are cognitive behavioral therapy manuals and therapists who can assist in this process.

Tapering BZDs

1. Based on assessment, attempt to have appropriate replacement treatment in place for any primary behavioral health diagnoses.
2. Provide as needed, or refer for, supportive psychotherapy during taper process.

3. Provide education and a clear plan for the taper.
4. Many studies and guidelines recommend reduction of 25% every 2-3 weeks, with if needed, a slower decrease (12.5%) for last two weeks.
5. Many patients benefit by being offered a "rescue" dose, one dose per day to carry with them to use at their discretion. This seems to provide re-assurance and a sense of control. Most tend not to use that medication.
6. For higher-potency/short-acting BZDs (e.g. alprazolam) a slower taper may be needed, perhaps as slow as 0.25 mg decrease in the daily dose per week. While lacking clear research support, many experts suggest switching to a lower-potency/long-acting BZD (clonazepam or diazepam) at an equivalent dose (see Table 1), and then tapering. It is suggested that this may attenuate the withdrawal symptoms and allow for a longer taper using smaller doses near the end point. Some practitioners have had success switching to the long-acting form of alprazolam (Xanax XR) to ease withdrawal.
7. Discontinuation of Z-drugs is less well studied than discontinuation of benzodiazepines, but given that they work similarly, the same approach for tapering benzodiazepines is recommended for tapering Z-drugs.

Table 1. Diazepam Milligram Equivalent (DME)

	Trade Name	**Half-life (hours)**	**Dose equivalent to 5 mg diazepam***
Benzodiazepines			
Alprazolam	Xanax	12–15	0.25–0.5 mg
Chlordiazepoxide	Librium	5–30	15 mg
Clonazepam	Klonopin	18–50	0.25–0.5 mg
Diazepam	Valium	20–80	5 mg
Lorazepam	Ativan	10–20	0.5–1 mg
Temazepam	Restoril	3.5–18.5	10 mg
Triazolam	Halcion	1.5–5.5	0.25 mg
Z-drugs			
Eszopiclone	Lunesta	6–9	2 mg
Zaleplon	Sonata	1	10 mg
Zolpidem	Ambien	1.4–4.5	10 mg
*Approximate equivalencies vary depending upon the resource referenced.			

Assessing Aberrant Drug-Related Behavior

BZDs are often misused, abused and diverted in particular by individuals prone to substance use disorders. Identifying those individuals can be a challenge, but the following behaviors provide clues that should raise suspicion and be explored with the patient.

1. Being more interested in BZDs (especially short-acting) than in other medications or in any other aspect of treatment.
2. Taking doses larger than those prescribed or increasing dosage without consulting the clinician.
3. Insisting that higher doses are needed.
4. Resisting urine drug screens or referrals to specialists and other aspects of treatment.
5. Resisting changes to non-BZD therapy.
6. Repeatedly losing medications or prescriptions, or seeking early refills.
7. Making multiple phone calls about prescriptions.
8. Attempting unscheduled visits, typically after office hours or when the clinician is unavailable.
9. Appearing sedated.
10. Misusing alcohol or using illicit drugs.
11. Showing deteriorating functioning and beginning to experience adverse consequences from medications (e.g., problems at home or on the job).
12. Injecting (having track marks) or snorting oral formulations.
13. Obtaining medications illegally (e.g. street dealers, family members, the Internet (unlicensed pharmacies), forged prescriptions).

A more precipitous taper may be indicated in situations when there is abuse of these medications due to the risk of harm. Any patient thought to be abusing their medication should be counseled and assessed for a substance use disorder and offered appropriate treatment.

In Summary

Benzodiazepines have a long history, and at one point were safer alternatives than the medications previously in use, such as barbiturates and meprobamate. While relatively safe, they are readily abused by patients prone to substance abuse and can be fatal when combined with other sedating substances such as opioids and alcohol. There are other significant risks, especially in the elderly. While this class of medications remain an important tool, other as effective and safer treatment options are available. When appropriate, BZDs should be considered as second-line medications for appropriate psychiatric disorders and used for a limited time period.

Safe Prescribing of Benzodiazepines for Acute Treatment of Anxiety and Insomnia

Prescribing Guidelines for Pennsylvania

https://www.overdosefreepa.org/wp-content/uploads/2016/10/Benzo-for-anxiety-and-insomnia-FINAL-002.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Summary

Anxiety is commonly encountered in clinical practice, either as an acute isolated symptom associated with major life events or comorbid with another condition, e.g., depression. Anxiety may also be the core symptom of a psychiatric disorder, including panic disorder, phobias and generalized anxiety disorder. The prevalence of anxiety disorders in the U.S. is approximately 4 percent.

Though benzodiazepines are effective in the short-term treatment of severe anxiety and panic disorders, evidence shows that continuing them beyond four to six weeks will likely result in loss of efficacy and the development of tolerance and dependence and, consequently, increase the risk of development of a benzodiazepine substance use disorder. The risk of dependence increases with dose and duration of therapy.

While anxiety disorders are amenable to short-term treatment with benzodiazepines, they are not first-line treatments for anxiety disorders and are not effective for the long-term treatment of these disorders. Rather, there are other much more effective treatment options, including evidence-based psychotherapies, e.g., cognitive behavioral therapy (CBT), other non-pharmacological interventions, and medication management using selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors, (SNRIs).

Similarly, insomnia, either as a symptom of another disorder, or as the core symptom of a sleep disorder, may have a lifetime prevalence as high as 40 percent. Benzodiazepines can be effective in the short-term treatment of severe insomnia, i.e., for one to two weeks, but there is no evidence supporting the long-term use of benzodiazepines for the treatment of insomnia.

Beyond acute situational insomnia, persistent insomnia is best treated by addressing the underlying cause, such as poor sleep hygiene, poorly controlled pain or depression.

These guidelines address the use of benzodiazepines for the treatment of anxiety and insomnia. They are intended to help health care providers improve patient outcomes when caring for these patients and to supplement, but not replace, the individual provider's clinical judgement.

Guidelines

1. Before initiating benzodiazepine therapy, perform a thorough medical history, including personal and family history of substance use disorder and a thorough assessment of physical health, with special attention to hepatic, renal and pulmonary disease. Practitioners should take particular note of patients with or at risk of sleep apnea, as the use of benzodiazepines in this patient population increases the risk of adverse events. Likewise, prescribers should obtain accurate information regarding other current medications, especially the use of other centrally-acting sedating medications, including opioids.

   The use of benzodiazepines with opioids at least doubles the risk of respiratory arrest and death and should be avoided. The U.S. Food and Drug Administration now requires black boxed warnings – the FDA's strongest warning – for concurrent use of prescription opioids and benzodiazepines. In the rare instance that patients require both an opioid prescription and a benzodiazepine prescription, they should be counseled about the risk of respiratory arrest and death and co-prescribed naloxone.
2. When there is a history of past substance use disorder, extreme caution should be exercised before prescribing benzodiazepines, given the increased potential for dependence or misuse.

a) For patients with suspected current substance use, benzodiazepines are usually contraindicated.

b) If benzodiazepines are prescribed to patients with past history of substance use disorder or active substance use disorder, prescribing should be associated with careful patient monitoring that includes documentation of treatment benefit and assessment for potential harm, including regular urine drug screens.

c) Providers should understand how to interpret the results of urine drug screens and have an established process for responding to abnormal results. This process should include a referral for evaluation and treatment of substance use disorder.

d) When a referral is made, the prescriber should conduct and document ongoing coordination of care with the addiction treatment provider.

3. When initiating benzodiazepine treatment, the prescriber should discuss and document the risks and potential benefits associated with treatment (including education about the risk of developing dependence and/or tolerance) and the intended duration of treatment.

4. Providers are encouraged to use formalized written treatment agreements or contracts, which both educate patients about the risks of benzodiazepines use and clarify the expectations of the patients.

   Expectations included in such contracts counsel patients that they should:

   a) Tell other providers that they are taking this medicine;

   b) Keep the medication in a secure place, preferably locked;

   c) Not share the medication with others; and

   d) Properly dispose of any medication no longer needed at a prescription take-back box.

5. Practitioners should access and document review of data available through the Prescription Drug Monitoring Program (PA PDMP AWARxE) database prior to the initial prescription and periodically during treatment. It is strongly recommended that practitioners check the database every time they write a prescription.

6. Evidence supports short-term benzodiazepine use as best practice. It is strongly recommended that the prescriptions provided to patients reflect and endorse this practice, i.e., a 10-day supply to relieve situational insomnia rather than 30 days with refills.
7. Intermediate to long-acting benzodiazepines, e.g., clonazepam (Klonopin®), are preferred in the short-term treatment of anxiety, whereas shorter acting agents, e.g., temazepam, are preferred to facilitate sleep. Low to moderate doses should suffice for most of the clinical situations commonly encountered.
8. When initiating benzodiazepine treatment to provide symptom relief in the early phase of treatment of depression or an anxiety disorder, it is essential to educate the patient about evidence-based, non-pharmacological treatments available for that disorder and to facilitate appropriate referrals, e.g., for cognitive behavioral therapy (CBT); or to simultaneously initiate the intended first-line treatment, e.g., SSRIs or SNRIs.
9. Caution should be used in prescribing benzodiazepines to address the insomnia and/or overwhelming emotions seen in acute grief, as they may suppress and prolong the grieving process. Sleep hygiene education is essential. Similarly, longer-term use of benzodiazepines to relieve acute anxiety reactions encountered in PTSD can interfere with the necessary exposure to and cognitive processing of the trauma that is essential for definitive and lasting symptom relief. Benzodiazepines should not be used for patients with PTSD due to their proven lack of efficacy.
10. Extreme caution should be used prescribing benzodiazepines for the elderly, due to the increased risk of adverse reactions such as confusion, ataxia and falls. If no alternative treatment is effective or available, dosing should be ultra-conservative, and intermediate-acting drugs such as lorazepam or oxazepam are recommended. Long acting drugs such as diazepam or chlordiazepoxide should be avoided.
11. Extreme caution should also be used during pregnancy or lactation and specialist consultation sought for pregnant or breast feeding patients taking benzodiazepines.
12. It is important to keep in mind that benzodiazepine use can worsen the course of several conditions, including 1) depression and impulse control disorders

on the behavioral health side; 2) hypoxia associated with asthma, sleep apnea, COPD, CHF and other cardiopulmonary disorders on the physical health side; and 3) fibromyalgia and chronic fatigue syndrome at the interface.

13. For some patients, e.g., those who are intolerant of/or non-responsive to alternative pharmacotherapy, long-term use of benzodiazepines may be clinically warranted. Carefully selected patients with anxiety disorders can be maintained on low dose regimens for years without adverse effects. Abrupt discontinuation of such regimens can lead to severe withdrawal symptoms.
    a) Patients receiving chronic benzodiazepines require regular periodic monitoring that includes a determination of whether the benefits of treatment continue to outweigh the risks and if a slow benzodiazepine taper is indicated.
    b) Providers should consider specialty input regarding the appropriateness for chronic use of benzodiazepines and for guidance when benzodiazepine medications need to be tapered and discontinued.
14. Practitioners must note the FDA's black box warning of benzodiazepine prescribing and opioid prescribing, including those receiving medication assisted treatment (MAT) for substance use disorder. While the co-prescription of benzodiazepines and methadone have become too common, with research indicating that at least one in three patient receiving methadone are also using benzodiazepines, patients treated with methadone or buprenorphine and benzodiazepine are at extreme risk of overdose.

Practitioners are urged to weigh the considerable evidence demonstrating the substantial risk of concomitant prescription of benzodiazepines and opioids -- whether for pain management or as medication assisted treatment of addiction -- before prescribing either agent in the presence of the other.

In the rare instance that, despite the black box warning, a patient is prescribed methadone or buprenorphine and a benzodiazepine, they should be counseled about the risk of at increased risk for respiratory arrest and death and co-prescribed naloxone.

Benzodiazepine	Onset of Action	Peak Onset (hours)	Half-life Parent (hours)	Half-life Metabolite (hours)	Comparative Oral Dose
Long acting					
Chlordiazepoxide (Librium®)	Int. (po)	2-4(po)	5-30	3-100	10mg
Diazepam (Valium ®)	Rapid (po, IV)	1(po)	20-50	3-100	5mg
Flurazepam (Dalmane®)	Rapid	0.5-2	Inactive	47-100	30mg
Intermediate acting					
Alprazolam (Xanax ®)	Int.	0.7-1.6	6-20	-	0.5mg
Clonazepam (Rivotril ®)	Int.	1-4	18-39	-	0.25mg
Lorazepam (Ativan ®)	Int. (po) Rapid (sl, IV	1-1.5 (po)	10-20	-	1mg
Oxazepam (Serax ®)	Slow	2-3	3-21	-	15mg
Temazepam (Restoril ®)	Slow	0.75-1.5	10-20	-	30mg
Short acting					
Midazolam (Versed ®)	Most rapid IV	0.5-1 (IV)	1-4	-	-
Triazolam (Halcion ®)	Int.	0.75-2	1.6-5.5	-	0.5mg

Po: per oral; sl: sublingual; IV: intravenous

Clinical Practice Guidelines: Prescribing and Monitoring of Benzodiazepines and Related Medications

Community Behavioral Health (CBH)

https://cbhphilly.org/wp-content/uploads/2022/10/CBH_CPG_Benzodiazepine_2025-06.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

INTRODUCTION

These guidelines aim to reduce unsafe prescribing of benzodiazepines. The first consideration should be limiting the initiation of benzodiazepines when more effective or safer options are readily available, given the high liability for these medications to complicate recovery from substance use disorders or lead to iatrogenic benzodiazepine dependence. Tapering and discontinuing these medications once dependence has formed is challenging for several reasons, including the potential for a dangerous withdrawal syndrome. Safe tapering and discontinuation may require transfer to a higher level of care, increased contact with the prescribing physician or care team, and other individualized interventions. Please refer to Appendix A for additional information related to tapering benzodiazepines.

These guidelines apply to benzodiazepines as well as benzodiazepine receptor agonists (e.g., zolpidem), barbiturates, and other controlled sedative-hypnotics.

1. GUIDELINE REGARDING MONOTHERAPY:

Benzodiazepines should not be initiated as monotherapy for the treatment of anxiety disorders.

While there is evidence that benzodiazepines can be used safely and effectively for the treatment of anxiety, evidence-based guidelines recommend their reservation as second-line agents. Other pharmacologic treatments, primarily Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) and Selective Serotonin Reuptake Inhibitors (SSRIs) have the benefit of a much stronger base of clinical trial evidence to support as first-line use and have significant safety advantages.

Benzodiazepines may be appropriate in the treatment of anxiety and depression for short-term use to achieve rapid symptom relief at the beginning of therapy, with subsequent tapering when the SNRI/SSRI takes effect. Nonpharmacologic treatments may also be considered as first-line treatments for multiple anxiety disorders; those focusing on cognitive-behavioral and exposure-based models have the strongest supporting evidence.

Exceptions

Treatment should be individualized to help support individuals' recovery goals, and there may be rare instances in which benzodiazepine monotherapy is appropriate (e.g., in cases of documented intolerance or poor response to first-line treatments for anxiety disorders). In these instances, the rationale for the medication regimen should be documented in the member's medical record.

2. GUIDELINE REGARDING INSOMNIA TREATMENT:

Benzodiazepines should not be used for the treatment of insomnia without appropriate evaluation and should not be used chronically.

Before the initiation of benzodiazepines or benzodiazepine receptor agonist medications, a thorough evaluation for underlying causes of secondary insomnia should be performed and documented.

This evaluation should screen for sleep-related breathing disorders (e.g., obstructive sleep apnea), sleep-related movement disorders (e.g., restless legs syndrome), adverse medication or caffeine effects, behavioral causes (e.g., poor sleep hygiene), and psychiatric syndromes known to cause insomnia. Individuals should also be screened for other contraindications discussed in these guidelines.

The first-line treatment for chronic insomnia is cognitive behavioral therapy (CBT).

When benzodiazepines or benzodiazepine receptor agonists are used for the treatment of insomnia, they should be used at the lowest possible effective dose and for the shortest duration. Continued prescriptions should not be given without evidence of continued need. Members should be educated about the risks of the medication, with emphasis on the member's individualized risk factors.

Exceptions

Some individuals may experience chronic insomnia that recurs with attempts to taper, beyond expectable and short-term rebound insomnia. In such cases, longer-term treatment may be acceptable, provided an appropriately documented rationale exists. Referral for sleep medicine evaluation or behavioral sleep therapy should also be considered.

3. GUIDELINE REGARDING PRESCRIBING TO THOSE WITH SUBSTANCE USE DISORDERS:

Benzodiazepines should not be prescribed to individuals with substance use disorders.

Individuals with current or past substance use disorders should rarely, if ever, be prescribed benzodiazepines. For such an evaluation, individual self-report cannot be the only source of information: a treatment history from CBH Member Services, collateral information from other providers, or urine drug screening (UDS) are acceptable objective assessment methods.

Exceptions

There may be cases where therapy with benzodiazepines is medically necessary despite substance use, such as prevention of withdrawal symptoms linked to alcohol or other hypnotics.

Thorough documentation of medical decision-making and the steps taken to protect the individual from harm is required. A plan to assess for abuse or diversion of medications in an ongoing fashion must also be documented. Urine drug screening is typically the most straightforward method. CBH recommends UDS monitoring occur upon initial benzodiazepine prescribing, and then periodically throughout

treatment for these individuals. Evidence of persistent or repeated substance use, medication diversion, or other aberrant medication-related behavior should be addressed via behavioral contract, medication tapering, referral to an alternate level of care, or medical director/administrative review.

4. GUIDELINE REGARDING PRESCRIBING TO THOSE WITH OPIOID PRESCRIPTIONS:

Benzodiazepines should not be prescribed to individuals enrolled in Medication-Assisted Therapy (MAT) for opioid use disorders or to individuals who are prescribed chronic opioid medications for pain.

Given the danger (discussed above) represented by the combination of benzodiazepines and opioids, such a combination is contraindicated.

Exceptions

Initiation of benzodiazepines for individuals receiving MAT or opioids must be accompanied by documentation that such prescribing adheres to all other parts of these guidelines, and a documented rationale establishing medical necessity. In these rare instances, risk may be mitigated by managing and prescribing medications by a single prescriber. If this is not possible, there should be ongoing collaboration between all involved prescribers. In cases where prescribing providers do not respond to collaboration requests, communication efforts should be clearly documented. In cases where the patient refuses consent to collaboration with the opioid prescriber, the benzodiazepine prescriber may proceed with a taper or discontinuation if the patient's safety is at risk. The patient should be informed that this is a potential outcome of refusing collaboration.

In some cases, individuals will be encountered who have been maintained on chronic opioids and chronic benzodiazepines. In such cases, a rapid discontinuation of either medication is neither practical nor safe. Continued treatment must be accompanied by documented collaboration between the providers of each medication and a documented plan to taper one or both medications (or

documentation of why this is not possible). Thorough documentation of medical decision-making and the steps taken to protect the individual from harm is required. This includes education on the risks of overdose and provision of naloxone education and prescription, as well as monitoring parameters such as urine drug screens. CBH recommends UDS monitoring occur upon initial benzodiazepine prescribing, and then periodically throughout treatment for these individuals.

5. GUIDELINE REGARDING SPECIAL POPULATIONS:

Benzodiazepines should generally not be prescribed to children and adolescents, pregnant/lactating individuals, or senior citizens.

Exceptions

There may be exceptional cases in which the prescription of benzodiazepines is deemed appropriate in the special populations mentioned above. In these cases, close consultation with other involved physicians (e.g., OB-GYN, pediatrician, etc.) is recommended. Treatment should be accompanied by a documented rationale for benzodiazepine use, individualized risk-benefit analysis, informed consent, safety monitoring mechanisms, and a tapering plan (or documentation of why this is not recommended or not possible).

Risks of benzodiazepine use in senior citizens include higher rates of falls, fractures, delirium, and increased risk of motor vehicle accidents. Benzodiazepines can also increase the risk of short-term cognitive impairment (memory, learning, attention), sedation, and drug-drug interactions.

6. GUIDELINE REGARDING PDMP REQUIREMENTS:

Benzodiazepines and other controlled substances will beprescribed per state requirements related to the Prescription Drug Monitoring Program (PDMP).

In 2014, the Pennsylvania State Legislature passed Act 191, expanding the state's prescription drug monitoring program to include monitoring all Schedule II–V controlled substances. Registration for the PDMP is required for all PA prescribers.

Beginning in August 2016, all prescribers have legal responsibilities related to the use of the PDMP.
Providers should stay current and ensure their practices comply with all PA PDMP requirements. Additional information is available on the PA DOH Prescription Drug Monitoring Program Prescriber Q&A.

APPENDIX A: TAPERING BENZODIAZEPINES

Key Points

- Benzodiazepines should not be stopped abruptly, particularly if they have been used chronically or at high doses, as there is a risk of dangerous withdrawal syndrome.
- Safe tapering and discontinuation may require transfer to a higher level of care, increased contact with the prescribing physician or care team, and other individualized interventions. Providers should assess the risk of benzodiazepine withdrawal to help determine the appropriate level of care. Factors to consider include, but are not limited to:
  - Presence of benzodiazepine or alcohol withdrawal symptoms
  - Dose, duration, and frequency of benzodiazepine use
  - Comorbid alcohol or other substance use
  - Prior episodes of withdrawal or withdrawal seizures
  - Presence of high-risk medical conditions (TBI, epilepsy, recent illness/ surgery, etc.)
  - Expected duration of the tapering process
- Gradual tapering of benzodiazepines is recommended.
- Members should be engaged in discussions about the rationale for medication adjustments (including potential harms of benzodiazepine use) and participate in the creation of tapering plans if possible.

- Tapering plans and progress should be reviewed and documented at every prescriber encounter.
- Tapering and discontinuing benzodiazepines should be an ongoing, individualized clinical process that may require repeated adjustments. Prescriber documentation should reflect these individualized clinical decisions.
- A team-based approach is recommended when tapering benzodiazepines.
- Benzodiazepine tapering is a critical time to coordinate care with other prescribers, particularly of controlled substances.
- Adequate use of PDMP is required. Pennsylvania PDMP must be queried every time a prescriber prescribes benzodiazepines.
- For members who continue to receive benzodiazepine prescriptions, the appropriateness and efficacy of the benzodiazepines should be evaluated at every prescriber encounter. Treatment should be accompanied by a clearly documented rationale for benzodiazepine use, individualized risk-benefit analysis, informed consent, safety monitoring mechanisms, and a tapering plan (or documentation of why this is not recommended or not possible).
- Other recommended interventions to assist with benzodiazepine tapering include cognitive behavioral therapy (CBT), self-help instructions, supportive therapies, educational interventions, and taper/discontinuation letters from clinicians.

Joint Clinical Practice Guideline on Benzodiazepine Tapering: Considerations when Benzodiazepine Risks Outweigh Benefits

American Society of Addiction Medicine (ASAM)

https://pmc.ncbi.nlm.nih.gov/articles/PMC12463801/

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Introduction

Purpose

The following medical and professional societies partnered to develop and disseminate this Joint Clinical Practice Guideline on Benzodiazepine Tapering (hereafter referred to as the Guideline):

- American Academy of Family Physicians (AAFP)
- American Academy of Neurology (AAN)
- American Academy of Physician Associates (AAPA)
- American College of Medical Toxicology (ACMT)
- American Association of Nurse Practitioners (AANP)
- American Association of Psychiatric Pharmacists (AAPP)
- American College of Obstetricians and Gynecologists (ACOG)
- American Geriatrics Society (AGS)
- American Psychiatric Association (APA)
- American Society of Addiction Medicine (ASAM)

This Guideline provides information on evidence-informed and consensus based strategies to help clinicians determine whether tapering benzodiazepine (BZD)

medications may be appropriate for a given patient and, if so, how to taper them. This Guideline applies to adult patients who have been taking BZDs regularly and may be at risk for physical dependence and withdrawal.

Scope of Guideline

This Guideline focuses on whether and how to taper BZD medications, exploring considerations for assessing risks and benefits of continued prescribing, partnering with patients, level of care considerations, and tapering strategies, including management of withdrawal symptoms. It pertains to patients who have been taking BZDs regularly and are at risk for physical dependence and withdrawal. This Guideline also addresses population specific considerations, including for patients co-prescribed BZDs and opioids, patients with SUD, patients with other psychiatric disorders, older adults, and pregnant and lactating patients.

Intended Use of the Joint Guideline on Benzodiazepine Tapering

This Guideline is:

- Primarily intended for clinicians who prescribe BZDs in diverse settings such as primary care, specialty care, EDs, and hospitals settings (Z-drugs are beyond the scope of this guideline)
- Applicable to patients aged 18 years and older who are taking BZDs regularly and may be at risk for physical dependence
- A clinical tool for supporting individualized, patient-centered care in BZD tapering
- Intended to promote flexible and patient-centered care and shared decision-making

This Guideline is NOT:

- Intended for clinicians who prescribe BZDs in palliative and end-of-life care settings

- Applicable to patients taking BZDs for a short time (eg, less than 2 weeks) or irregularly (eg, as needed)
- A replacement for clinical judgment or individualized, patient-centered care
- Intended to be applied as inflexible standards of care or lead to the rapid tapering or abrupt discontinuation of BZDs
- Intended to suggest a one-size-fits-all approach to BZD tapering
- A law, regulation, or policy that dictates clinical practice
- Focused exclusively on patients with SUDs

Considerations for Tapering Benzodiazepines

Determining Whether to Taper

Recommendations for Considerations for Tapering Benzodiazepines

1. Clinicians should ideally assess the risks and benefits of ongoing BZD prescribing at least every 3 months for each patient taking BZD medications (see Table 2 and Table 3; Clinical Consensus, Strong Recommendation).
    a. At a minimum, clinicians should assess the risks and benefits with each new BZD prescription or BZD prescription renewal (Clinical Consensus, Strong Recommendation).
    b. Clinicians should review the information in the relevant prescription drug monitoring programs (PDMP) as part of the risk–benefit assessment (Clinical Consensus, Strong Recommendation).
2. Clinicians should avoid abruptly discontinuing BZD medication in patients who are likely to be physically dependent on BZDs and at risk for BZD withdrawal (see Table 3; Low Certainty, Strong Recommendation).
    a. Tapering is indicated for patients who are likely to be physically dependent when the risks of BZD medication outweigh the benefits (Low Certainty, Strong Recommendation).
    b. Clinicians should consider discontinuation or a short taper for patients who are unlikely to be physically dependent when the risks of BZD medication outweigh the benefits (Clinical Consensus, Strong Recommendation).

3. If the BZD medication is discontinued without a taper in patients who are unlikely to be physically dependent, clinicians should counsel patients to report the emergence of withdrawal and/or rebound symptoms (Clinical Consensus, Strong Recommendation).
    a. If significant symptoms emerge, clinicians can consider using medications for symptom management or restarting the BZD medication and initiating a taper (Clinical Consensus, Conditional Recommendation).

Implementation Considerations

- When considering the risks and benefits of continued BZD prescribing, clinicians should screen patients for non-prescription use of BZDs and use of other substances that may interact with BZDs or impact the tapering process.
- When the risks of BZD medication outweigh the benefits, clinicians should initiate a conversation with patients about tapering (or discontinuation if patients are unlikely to be physically dependent). Clinicians should elicit information from patients about their expectations and concerns about the tapering process and discuss them. Clinicians should discuss alternatives for managing the underlying condition(s) for which the BZD was initially prescribed that may be more effective and carry less risk compared to BZDs (eg, selective serotonin reuptake inhibitors [SSRIs] and/or cognitive behavioral therapy [CBT] for anxiety disorders, cognitive behavioral therapy for insomnia [CBT-I] for primary insomnia).
- The goal of tapering may be discontinuing the BZD medication or reducing the BZD dose to the lowest effective dose where the risks no longer outweigh the benefits. Clinicians should reassess risks and benefits throughout the tapering process to inform decision-making.
- Although many patients who have been taking BZDs for a short period of time (eg, less than a month) are able to discontinue the medication without a taper, clinicians can consider a short taper. A short taper may be indicated if clinicians have concerns for clinically significant withdrawal (eg, due to the pharmacological properties of the BZD, patient age, comorbidities, other substance use, prior history of withdrawal) or patients express concerns about discontinuing the medication.

- Many healthcare systems may not be able to manage the volume of patients who would benefit from BZD tapering. As such, clinicians and healthcare systems may need to triage patients, prioritizing those at higher risk of harm related to continued BZD use.

Table 2. Potential Benefits and Risks of Continued BZD Use and BZD Tapering*

Potential Benefits	Potential Risks	
BZD Use	**BZD Use**	**BZD Taper**
• Effectiveness in managing a patient's mental and physical health condition(s) • Related functional improvements	• Oversedation, including consideration of use with other sedating medications, alcohol, or other drugs • Falls and related injuries	• Withdrawal symptoms, including severe or complicated withdrawal (eg, seizures, delirium) • Recurrence of the condition for which BZD were prescribed • Impacts on co-occurring mental and physical health conditions
• Quality of life improvements ‡	• Memory and cognitive impacts • Motor vehicle accidents • Medical safety concerns (eg, medication interactions) • Impacts on co-occurring mental and physical health conditions • Disrupted sleep patterns • Impacts on work and family responsibilities • Diversion • Substance use disorder • Overdose • Fetal harm • Suicidality	• Protracted withdrawal • Return to illicit BZD use • Transition to illicit BZD use ‡

* Clinicians should consider the likelihood of each benefit and risk for the individual patient.

Ⱨ Including use for end of life or palliative care.

ǂ Including risks associated with counterfeit BZDs from the illicit drug market, such as contamination with HPSOs (eg, fentanyl) and novel synthetic substances.

Table 3. Risk for Clinically Significant BZD Withdrawal*

Duration of BZD Use	Frequency of BZD Use	Total Daily BZD Dose	Risk for Clinically Significant Withdrawal†
Any	≤3 days per week	Any	Rare
<1 month	≥4 days per week	Any	Lower risk, but possible
1–3 months	≥4 days per week	Low‡	Lower risk, but possible
1–3 months	≥4 days per week	Moderate§ to high**	Yes, with greater risk with increasing dose and duration
≥3 months	≥4 days per week	Any	Yes, with greater risk with increasing dose and duration

* This table is based on clinical consensus of the CGC. It is intended to provide general guidance and should not replace clinical judgment.

† Many factors influence the risk of physical dependence and BZD withdrawal syndrome, including but not limited to age, co-occurring physical and mental health conditions, other substance use, and prior history of withdrawal.

** Half-lives are unknown for some novel synthetic benzodiazepines available in the illicit market.

‡ A low daily dose is estimated as 10 mg diazepam equivalents or less (eg, ≤0.5mg clonazepam, ≤2 mg lorazepam, ≤1 mg alprazolam). See Appendix H for BZD dose equivalents.

§ A moderate daily dose is estimated as 10–15 mg diazepam equivalents (eg, 0.5–1.5 mg clonazepam, 2–3 mg lorazepam, 1–2 mg alprazolam). See Appendix H for BZD dose equivalents.

** A high daily dose is estimated as more than 15 mg diazepam equivalents (eg, >1.5 mg clonazepam, >3 mg lorazepam, >2 mg alprazolam). See Appendix H for BZD dose equivalents.

Partnering with Patients

Recommendation for Partnering with Patients

4. Clinicians should develop the BZD tapering strategy in coordination with patients and their care partners in a shared decision-making process, whenever possible (Clinical Consensus, Strong Recommendation).

Implementation Considerations

- Clinicians can consider utilizing educational resources when developing BZD tapering strategies with patients.
- Clinicians can consider utilizing a motivational interviewing (MI) framework, which is patient-centered and seeks to involve patients in resolving ambivalence to change.

Level of Care Considerations

Recommendation for Level of Care Considerations

5. Although BZD tapering can typically be managed in outpatient settings, clinicians should consider inpatient care for BZD tapering when:
    a. Patient presentation indicates an imminent risk for significant harm related to continued use of the BZD medication (eg, medication interaction, overdose, accidents, falls, suicidality or other self-harm) that is unlikely to be rapidly mitigated by the initial dose reduction of the BZD taper (Clinical Consensus, Strong Recommendation)
    b. Patient symptoms and/or co-occurring physical or mental health conditions are anticipated to complicate BZD tapering in a way that cannot be safely managed in an outpatient setting (Clinical Consensus, Strong Recommendation)
    c. The patient is experiencing or imminently anticipated to experience severe or complicated BZD withdrawal (Clinical Consensus, Strong Recommendation)

Implementation Considerations

- Clinicians should use the risk–benefit assessment to inform decisions regarding level of care.
- Most patients who have developed physical dependence to BZDs can complete tapering in outpatient settings. Clinicians should consider inpatient tapering when imminent risks to patient safety cannot be mitigated rapidly with outpatient treatment.
- Clinicians should consider prior history of severe or complicated BZD or alcohol withdrawal when determining patients' current withdrawal risk.
- If the clinician cannot obtain authorization for inpatient care, they should consider whether attempting an outpatient taper or continuing the medication poses a greater risk.

Benzodiazepine Tapering Strategies

The Tapering Process

Recommendations for the Tapering Process

6. Clinicians should generally consider dose reductions of 5% to 10% when determining the initial pace of the BZD taper. The pace of the taper should typically not exceed 25% every 2 weeks (Clinical Consensus, Strong Recommendation).
7. Clinicians can consider transitioning patients without contraindications to a comparable dose of a longer-acting BZD medication for the taper (Clinical Consensus, Conditional Recommendation).
8. Clinicians should tailor tapering strategies to each individual patient and adjust the taper based on a patient's response (Clinical Consensus, Strong Recommendation).
9. Clinicians should evaluate patients undergoing tapering for signs and symptoms related to the BZD taper with each dose reduction (Clinical Consensus, Strong Recommendation).

Implementation Considerations

- Prior to beginning a taper, clinicians should conduct a thorough medication and health review, with particular attention to other psychoactive medications and conditions that may be impacted during the taper.
- Clinicians should design the overall tapering strategy to minimize harms, considering the risk of harm related to continued BZD use and the risk of harms related to tapering the BZD (eg, withdrawal symptoms, recurrence of symptoms for which the BZD was originally prescribed).
- Clinicians should consider the lower end of the dose reduction range (ie, 5%) for the first reduction to assess a patient's initial response, unless there are imminent safety concerns.
- For patients who are likely to have strong physical dependence (eg, those who have been taking a high dose for more than a year), clinicians should consider a slower taper.
    - For the first reduction, consider the lower end of the dose reduction range (eg, 5%).
    - For further reductions, clinicians should adjust based on patients' initial response, considering reduction of 5% to 10% every 6–8 weeks, or slower as appropriate.
- Clinicians can consider the higher end of the dose reduction range (ie, 10-25%) for patients who are unlikely to have significant physical dependence (ie, patients who have been taking a lower dose of BZD for a shorter period of time [eg, less than 3 months]) but for whom tapering is indicated.
- When developing tapering strategies, clinicians should consider patients' current BZD dose and half-life, frequency and duration of BZD use, co-occurring physical and mental health conditions, and responses to previous missed doses and any prior BZD tapering attempts. Clinicians should also consider patient concerns and anxiety around tapering.
- When patients are taking multiple doses of BZDs each day, clinicians should carefully consider which dose to reduce first. For example, first reducing earlier doses may be appropriate if insomnia is a greater concern, whereas first reducing later doses may be more appropriate if daytime anxiety is a greater concern.

- Tapering strategies, including dosing frequency, should account for the pharmacokinetic properties of the BZD to avoid sharp declines in BZD receptor occupancy.
- Clinicians should monitor patients for symptoms of withdrawal and recurrence with each dose reduction. Virtual or telephonic check-ins can be leveraged for this purpose.
- Clinicians should monitor patients for post-acute signs and symptoms of withdrawal for 2–4 weeks after full discontinuation of the BZD. Clinicians should manage any ongoing symptoms, as appropriate, and regularly monitor patients until symptoms are resolved. Telehealth, including audio only check-ins, may help facilitate monitoring.
- Clinicians should consider pausing or slowing the pace of the taper and/or making smaller dose reductions for patients experiencing significant symptoms related to the BZD taper.
- The BZD tapering process can be more difficult for patients as they approach the point of discontinuation. Clinicians should proactively consider smaller dose reductions and/or slowing the pace of dose reductions as the taper progresses.
- If patients are unable to tolerate further BZD dose reductions, clinicians can consider—in partnership with patients, their care partners, and other members of the care team— maintaining patients on the lower BZD dose with regular risk–benefit assessments consistent with Recommendation #1.
- In some limited instances when patients are experiencing intolerable symptoms, returning to the prior BZD dose and pausing the taper until symptoms stabilize may be appropriate.
- In limited instances when necessary for patient safety, inpatient and medically managed residential settings may use more rapid tapering strategies.

Table 4. Common Benzodiazepine Withdrawal Signs and Symptoms*

General	Affective	Cardiovascular	Gastrointestinal
● Elevated blood pressure ● Headaches ● Sweating, night sweats	● Anxiety, panic attacks ● Depression, dysphoria ● Irritability, agitation, aggression	● Chest pain ● Palpitations ● Tachycardia	● Abdominal cramps ● Diarrhea ● Nausea and vomiting
Neurological	**Neuromuscular**	**Neuropsychiatric**	**Sleep**
● Cognitive impairment (eg, poor memory, reduced concentration) ● Confusion, delirium† ● Perceptual disturbance ● Seizures† ● Sensory hypersensitivity (ie, to light, sound, taste, and smell) ● Tingling, numbness, altered sensation ● Tinnitus	● Coordination, balance problems ● Dysesthesia, kinetic disorders ● Muscle pain (eg, tension, weakness, spasms) ● Muscle twitches, jerks, and fasciculations ● Tremors	● Akathisia, restlessness ● Depersonalization, derealization ● Psychosis (eg, paranoia)† ● Suicidality and selfharm	● Hypersomnia ● Insomnia ● Nightmares

* Adapted from Soyka (2017), Baldwin (2022), Gold & Ward (2022), and The Maudsley Deprescribing Guidelines. This table does not represent a comprehensive list of withdrawal symptoms. See The Maudsley Deprescribing Guidelines and The Ashton Manual80 for a more comprehensive list.

† Typically associated with abrupt cessation of high doses of BZDs

Adjunctive Interventions During the Tapering Process

Recommendations for Adjunctive Interventions

10. Clinicians should offer patients undergoing BZD tapering behavioral interventions tailored to their underlying conditions (eg, CBT, CBT-I) or provide them with referrals to access these interventions (Low Certainty, Strong Recommendation).
11. Clinicians should first consider pausing or slowing the pace of the BZD taper when patients experience symptoms that significantly interfere with the taper (eg, sleep difficulty, anxiety), although clinicians can also consider use of adjunctive medications (Clinical Consensus, Conditional Recommendation).

Implementation Considerations

- Clinicians should educate patients on lifestyle factors that could support BZD tapering (eg, sleep hygiene, physical activity as appropriate to ability).
- Clinicians can consider other evidence-based approaches such as mindfulness-based interventions.
- Clinicians can consider referring patients to peer specialist services for support during the taper.

Management of Severe or Complicated Withdrawal Symptoms

Recommendations for Management of Severe or Complicated Withdrawal Symptoms

12. Clinicians should manage patients experiencing severe or complicated withdrawal in inpatient or residential medically managed settings (eg, residential withdrawal management program) with:
    a. Monitoring for signs and symptoms of BZD withdrawal, including regularly measuring vital signs and using structured assessment tools (Clinical Consensus, Strong Recommendation)
    b. Assessments for seizure risk and managed as appropriate (Clinical Consensus, Strong Recommendation)

13. Tapering with very long-acting agents such as phenobarbital:
    a. Can be considered for BZD withdrawal management in inpatient settings (Low Certainty, Strong Recommendation).
    b. Should only be conducted by or in consultation with clinicians experienced in the use of these agents for the purpose of BZD withdrawal management (Clinical Consensus, Strong Recommendation).
14. Clinicians should avoid rapid BZD reversal agents such as flumazenil for the purpose of BZD tapering due to risks for refractory seizure, cardiac dysrhythmias, and other adverse effects (Clinical Consensus, Strong Recommendation).
15. Clinicians should avoid general anesthetics such as propofol or ketamine for the purpose of BZD tapering (Clinical Consensus, Conditional Recommendation).

Implementation Considerations

- Tapering initiated in an inpatient or residential medically managed level of care may be continued in a less intensive level of care once it is safe to do so.
- When tapering with very long-acting agents, discharge planning should include an outpatient follow-up appointment, ideally within 7 days.
    - Clinicians should assess patients for ongoing signs or symptoms related to discontinuation of the BZD, including re-emergence of symptoms for which the BZD was originally prescribed.
    - Clinicians should consider medications and/or behavioral interventions to address ongoing signs or symptoms related to discontinuation of the BZD.

Population-Specific Considerations

Patients Co-prescribed Benzodiazepines and Opioids

Recommendations for Patients Co-prescribed Benzodiazepines and Opioids

16. Because all patients co-prescribed BZDs and opioids are at increased risk for respiratory depression, clinicians should assess the risks and benefits

of continued BZD prescribing with every related clinical encounter or prescription renewal and at least every 3 months (Clinical Consensus, Strong Recommendation).

17. Clinicians should offer to provide or prescribe opioid overdose reversal medication (eg, naloxone) for all patients co-prescribed BZDs and opioids (Clinical Consensus, Strong Recommendation).
18. Clinicians should consider additional strategies for mitigating risk, including using the lowest effective doses of BZD and opioid medications and optimizing non-opioid interventions (Clinical Consensus, Strong Recommendation).

Implementation Considerations

- Prior to initiating a BZD taper for patients who are co-prescribed BZDs and opioids, clinicians should seek to coordinate care with other clinicians who are prescribing BZDs or opioids to a given patient. This may entail obtaining releases or other agreements for clinicians to contact other prescribers and/or consulting the PDMP.
- Clinicians should conduct risk–benefit assessments more often when patients have additional risk factors for adverse events related to concurrent BZD and opioid use. Additional risk factors may include but are not limited to having an SUD, a bipolar disorder, or schizophrenia and/or taking fentanyl, morphine, or methadone.

Patients with Benzodiazepine and Other Substance Use Disorders

Recommendations for Patients with Benzodiazepine and Other Substance Use Disorders

19. Clinicians should consider more frequent assessments of the risks and benefits of continued use of BZDs for patients with co-occurring SUDs and/or other co-occurring addictions (eg, behavioral addictions) who have a prescription for BZD medication compared with the general guidance in Recommendation #1 (Clinical Consensus, Strong Recommendation).

20. When tapering BZD medication in patients with SUD, clinicians should manage the underlying SUD concurrently with the BZD taper (Clinical Consensus, Strong Recommendation).
21. Clinicians should not use BZD prescribing or tapering considerations as a reason to discontinue or disrupt a patient's medications for SUD treatment, including buprenorphine and methadone (Clinical Consensus, Strong Recommendation).
22. Following the taper, clinicians should continue to monitor and treat the underlying SUDs or refer patients to an appropriate level of care for continuing care (Clinical Consensus, Strong Recommendation).
23. Clinicians should offer patients harm reduction services or provide them with referrals to access these services.
    a. Clinicians should provide opioid overdose reversal medication (eg, naloxone) and related education (Clinical Consensus, Strong Recommendation).
    b. Clinicians can consider providing drug checking or other safe use supplies (eg, fentanyl test strips, xylazine test strips, sterile syringes) and related education (Clinical Consensus, Conditional Recommendation).

Implementation Considerations

- Clinicians should refer patients with SUD who are undergoing BZD tapering for SUD treatment in parallel with the BZD taper. Care should ideally be coordinated between the clinicians providing SUD treatment and managing the BZD taper, when applicable.
- Clinicians should consider using existing standards for level of care recommendations such as The ASAM Criteria when considering treatment setting for patients with SUD (Clinical Consensus, Strong Recommendation).
- Clinicians may consider conducting BZD tapers in residential or inpatient settings for patients with SUD who are unlikely to participate effectively in outpatient tapering.
- Tapering with phenobarbital should typically be conducted in acute care settings (ie, hospital or ED) or medically managed residential settings. However, for

patients with SUD, tapering with phenobarbital may also be conducted in outpatient settings with extended nurse monitoring by or in consultation with clinicians experienced in the use of these medications for BZD tapering.

- Clinicians can consider using toxicology testing to support risk–benefit assessments for patients with SUD if indicated based on clinical concern.

Patients with Co-occurring Psychiatric Disorders

Recommendations for Patients with Co-occurring Psychiatric Disorders

24. Clinicians should optimize evidence-based treatment for any psychiatric disorder prior to the taper or concurrently if clinically indicated (Clinical Consensus, Strong Recommendation).
25. Clinicians should strongly consider tapering BZD medication in patients with posttraumatic stress disorder (PTSD; Clinical Consensus, Strong Recommendation).
26. Clinicians should monitor sleep closely during BZD tapering in patients with mood or psychotic disorders, particularly for patients with bipolar disorder as sleep disturbance can trigger episodes of mania (Clinical Consensus, Strong Recommendation).
    a. If patients with a mood and/or psychotic disorder experiences significant sleep disturbance, clinicians should pause the taper until the symptoms resolve due to the risk for destabilization (Clinical Consensus, Strong Recommendation).

Implementation Considerations

- Clinicians should refer patients with psychiatric disorder who are undergoing BZD tapering for psychiatric treatment in parallel with the BZD taper. Care should ideally be coordinated between the clinicians providing psychiatric treatment and managing the BZD taper, when applicable.
- Clinicians should consider using existing standards for level of care recommendations such as the Level of Care Utilization System (LOCUS) when considering treatment setting for patients with psychiatric disorders.

- Clinicians can consider offering patients with psychiatric disorders behavioral interventions (eg, CBT-I with sleep hygiene education) or providing them with referrals to access these interventions.
- Clinicians can consider consulting with clinicians with psychiatric expertise when tapering BZDs in patients with co-occurring psychiatric disorders.

Older Adults

Recommendation for Older Adults

27. Clinicians should generally taper BZD medication in older adults unless there are compelling reasons for continuation (Clinical Consensus, Strong Recommendation).

Implementation Considerations

- In general, the CGC recommends tapering BZDs in older adults because the risks of continued use tend to be higher in this population. However, clinicians should still base decisions to taper BZD in older adults on a careful assessment of risks and benefits for each individual patient.
- The goal of tapering for older adults may be discontinuation of the BZD or reducing the BZD dose to the point where the risks no longer outweigh the benefits.
- Care should ideally be coordinated between the clinician managing the BZD taper and other clinicians managing conditions that may be impacted by BZD prescribing or the BZD taper.
- An estimated 2 million older adults in the US have been taking prescribed BZDs for more than 120 days. Many healthcare systems may not be able to manage the volume of older adult patients who would benefit from a BZD taper. As such, clinicians and healthcare systems may need to triage patients, prioritizing those at higher risk of harm related to continued BZD use.

Patients Who Are Pregnant and Lactating

Recommendations for Patients Who Are Pregnant and Lactating

28. Clinicians should weigh the risks and benefits for the maternal–fetal dyad when considering continued BZD prescribing or tapering for pregnant patients (Clinical Consensus, Strong Recommendation).
29. For infants who have been exposed to BZD in utero and are at risk for neonatal withdrawal symptoms, clinicians should:
    a. Encourage breastfeeding, which can reduce neonatal withdrawal symptoms (Clinical Consensus, Strong Recommendation)
    b. Communicate with the infant's healthcare provider (with parental consent) regarding exposure to BZDs (Clinical Consensus, Strong Recommendation)

Implementation Considerations

- Clinicians should monitor patients who are pregnant closely for psychiatric symptoms during the BZD taper, as these symptoms may evolve rapidly during the pregnancy and postpartum period due to shifts in metabolism that influence the effects of medications, including BZDs. Clinicians should address evolving psychiatric symptoms as clinically indicated.
- Care should ideally be coordinated between the clinician managing the BZD taper and the prenatal care provider.
- Clinicians can consider consulting with healthcare professionals who have expertise in reproductive psychiatry or providing patients with referrals to these specialists.

Appendix F. Pharmacokinetic Properties of Benzodiazepines

Table F.1 summarizes pharmacokinetic properties of BZD that are important to consider in determining relative risk for physical withdrawal and planning tapering strategies.

Table F.1. Pharmacokinetic Properties of Benzodiazepines

Benzodiazepine	Time to Peak Plasma Level (h; via oral)	Relative Lipid Solubility*	Onset of Action (min)**	Elimination Half-Life (h)†	Metabolism‡
Alprazolam	1–2 h (tablet or ODT) 5–11 h XR	Moderate	15–30	6–12	CYP3A4
Chlordiazepoxide	0.5–4 h	Moderate	15–30	5–10 36–200 (AM)	CYP3A4
Clonazepam	1–2 h	Low	15–30	18–50	CYP3A4
Clorazepate§	0.5–2 h	High	15		CYP2C19 CYP3A4
Diazepam	0.5–2 h	High	≤15	20–100 36–200 (AM)	CYP1A2 CYP2C9 CYP2C19 CYP3A4
Estazolam	2 h	Low	30–60	10–24	CYP3A4
Flurazepam	0.5–2 h	High	≤15	40–250 (AM)	CYP2C19 CYP3A4
Lorazepam	2–4 h	Moderate	15–30	10–20	Glucuronide conjugation
Oxazepam	2–4 h	Low	30–60	4–15	Glucuronide conjugation
Quazepam	2 h	High	15	39 73 (AM)	CYP2C9 CYP2C19 CYP3A4
Temazepam	2–3 h	Moderate	30–60	10–20	Glucuronide conjugation
Triazolam	1–2 h	Moderate	15–30	1.5–5	CYP3A4

AM: active metabolite; ODT: orally disintegrating tablet; XR: extended release

* Increased lipid solubility results in more rapid onset of CNS activity but can also result in rapid redistribution into adipose tissue resulting in a shorter duration of action even in agents with long elimination half-life (eg, diazepam)

**Rapid onset of action is associated with high lipid solubility and increased potential for misuse.

† Agents with moderate to high lipid solubility will have shorter duration of action with single or intermittent doses than suggested by the elimination half-life as these medications distribute rapidly into adipose tissue. With initial dosing, multiple daily doses may be needed to maintain effect. With chronic use and repeated dosing, accumulation is more likely to occur with these agents, especially those with long elimination half-lives (eg, diazepam).

‡ Agents metabolized via glucuronide conjugation do not have pharmacokinetic interactions and are considered to be safer in older adults and patients with hepatic impairment.

§ Hydrolized to nordiazepam in the stomach.

Appendix H. Benzodiazepine Dose Equivalents

Table H.1 summarizes approximate dose equivalents to inform decisions about transitioning from one BZD to another for the purpose of tapering.

Table H.1. Benzodiazepine Approximate Dose Equivalents to 10 mg Oral Diazepam†

Benzodiazepine	ATC Therapeutic Class	VA/DoD SUD CPG (2021)	Ashton Manual (2002)
Alprazolam	Anxiolytic	1	0.5
Chlordiazepoxide	Anxiolytic	25	25
Clonazepam	Antiepileptic	1	0.5
Clorazepate	Anxiolytic	15	15
Diazepam	Anxiolytic	10	10
Estazolam	Sedative–Hypnotic	1	1-2
Flurazepam	Sedative–Hypnotic	15	15-30

Lorazepam	Anxiolytic	2	1
Oxazepam	Anxiolytic	30	20
Quazepam	Sedative–Hypnotic	10	20
Temazepam	Sedative–Hypnotic	15	20
Triazolam	Sedative–Hypnotic	0.25	0.5

ATC: Anatomical Therapeutic Chemical classification system; CPG: clinical practice guideline; DoD: US Department of Defense; SUD: substance use disorder; VA: US Department of Veterans Affairs

† These doses are intended for guidance only. Clinical decisions on dose should be individualized based on the patient response.

Sources:

1. Department of Veterans Affiars, Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. 2021.
2. Ashton CH. Benzodiazepines: How They Work and How to Withdraw (The Ashton Manual). Institute of Neuroscience, Newcastle University; 2002.

Benzodiazepines and Z-hypnotics Guidance on Prescribing and Deprescribing for the Management of Insomnia and Anxiety Disorders in Adults

Nottinghamshire Area Prescribing Committee

https://www.nottsapc.nhs.uk/media/cdxg4b0o/benzodiazepine-and-z-hypnotic-prescribing-guidance-update.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

KEY MESSAGES

- Benzodiazepines and z-hypnotics are classed as medicines associated with dependence or withdrawal symptoms.
- Benzodiazepines are effective and indicated for the short-term treatment of anxiety that is severe, disabling, or causing the patient unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness.
- Z-hypnotics are effective for the short-term treatment of insomnia; when the insomnia is severe, disabling or causing the patient extreme distress.
- The long-term use of benzodiazepines and z-hypnotics for insomnia and anxiety are of limited benefit and have well documented harms including tolerance, dependence, risk of falls and cognitive impairment.
- Before prescribing a benzodiazepine or z-hypnotic, explain the risks and have an agreed plan with the individual including information about how to stop the medicine.
- Non-pharmacological treatments including sleep hygiene and psychological approaches should be continued alongside prescribing.

- Established long term use of benzodiazepines and z-hypnotics should be proactively reviewed. Use Should I stop my benzodiazepine or z-drug? patient decision aid to support review.

  https://www.nice.org.uk/guidance/ng215/resources/should-i-stop-my-benzodiazepine-or-zdrug-patient-decision-aid-summary-pdf-13072600333

NONPHARMACOLOGICAL MANAGEMENT OF ANXIETY

Optimise treatment for co-morbidities:

- Consider other triggers or factors associated with the anxiety (e.g. physical illness, other stressors, substance misuse).
- Review and optimise treatment for underlying mental health conditions such depression and panic disorder.

Psychological therapies:

- Low intensity psychological interventions (individual and facilitated self-help therapies) are recommended first line for the management of anxiety. See NHS information on self-help for anxiety and NHS information on self-help therapies.
- Consider a referral to NHS Nottingham and Nottinghamshire Talking Therapies. They offer various psychological interventions for the treatment of anxiety. The interventions on offer include therapist led digital interventions as well as face to face therapy for more complex cases. They accept GP and self-referral for people across Nottingham City and County.

  Website: www.notts-talk.co.uk

  Telephone: 0333 188 1060
- The step 4 psychology service provides psychological therapies for people who have mental health or psychological difficulties which are chronic and complex enough to be unsuitable for intervention with a lower step of care. They accept healthcare professional referral (including GPs) for people across Nottingham City, County North, and County South.

  Website: https://www.nottinghamshirehealthcare.nhs.uk/step-4-psychology-service/

Other medicines:

- Although NICE doesn't recommend propranolol in anxiety, propranolol is licensed for anxiety with symptoms such as palpitations, sweating and tremor. Propranolol is toxic in overdose and there is a potential under recognised risk of harm which prescribers should consider before making a decision to prescribe. Further information is available from the 2020 Health Services Safety Investigation Body report.

NONPHARMACOLOGICAL MANAGEMENT OF INSOMNIA

Sleep hygiene:

- Good sleep hygiene should be considered in all people with insomnia and should be continued alongside any hypnotic prescription.
- More information on insomnia is available from the Patient.info website, and for tips on sleep hygiene check the Mind website.
- Sleep diaries can be helpful for identifying sleeping patterns and lifestyle factors that may exacerbate or maintain insomnia. The diary should be kept for at least two weeks. Sleep diary templates are available on the The Sleep Charity website.

Optimising treatment for co-morbidities:

- Consider other triggers or factors associated with the insomnia (e.g., physical illness, other stressors, substance misuse).
- If there is an underlying physical health condition such as pain, respiratory or cardiac disease, sleep problems are likely to improve when the condition has been adequately treated.
- Optimise any other medicines the person is taking that may be causing insomnia.

Psychological therapies:

- Recommended first line for the treatment of chronic sleep problems. The benefits of psychological interventions for chronic insomnia often last well beyond the termination of active treatment.

- Patients with insomnia and co-existing mental health conditions should be considered for referral to NHS Nottingham and Nottinghamshire Talking Therapies with an initial aim to focus on sleep.

Other medicines:

- Always check whether the patient takes any other prescribed or over the counter medicines to aid sleep (these may interact with benzodiazepines and z-hypnotics to cause additive side effects, present an increased risk of overdose and potential for misuse when used concomitantly).
- Sedating antihistamines such as promethazine (Phenergan®, Sominex®) are only licensed for temporary sleeping difficulties (1-2 weeks) and are not appropriate for the management of chronic insomnia.
- Sedating antidepressants are not licensed for the treatment of insomnia and are not recommended to be prescribed unless treating an appropriate co-morbidity.
- Daridorexant is licensed for adults with insomnia characterized by symptoms presenting for at least 3 months and considerable impact on daytime functioning. It is recommended by NICE if cognitive behavioral therapy for insomnia (CBTi) has been tried, but not worked, or if CBTi is not available or unsuitable.

PRESCRIBING PRINCIPLES – PRIMARY CARE

- Reserve benzodiazepine and z-hypnotic prescribing for short courses to alleviate severe, disabling symptoms.
- If a prescription is required it should be limited to a short period (no longer than two weeks, preferably less than one week).
- Use the lowest effective dose for the shortest possible period.
- Inform the patient that further prescriptions for z-hypnotics and benzodiazepines will not usually be given, ensure the reasons for this are understood and document this in the patient's notes.
- Do not issue further prescriptions without seeing the patient.

- Switching from one z-hypnotic to another should only occur if a patient experiences adverse effects considered to be directly related to the specific agent.
- Patients who have not responded to one z-hypnotic should not be prescribed any of the others.
- Ensure discharge communication for benzodiazepine and z-hypnotic prescriptions is reviewed and action taken in a timely manner; new prescriptions not containing information on course duration/review should be queried with the discharging service.

RESCRIBING PRINCIPLES – SECONDARY CARE

On admission

- Determine whether the patient takes one or more of these medicines, regularly or intermittently for anxiety, insomnia, or both.
- Review the patient's use of benzodiazepines and z-hypnotics to decide whether their continued use is indicated. This may involve speaking to the patient or carer, checking their online records e.g., Summary Care Record (SCR), SystmOne, or speaking to their GP.
- Patients who have taken these medicines for longer than four weeks should not have this treatment stopped abruptly due to the risk of precipitating withdrawal symptoms, unless risks outweigh benefits e.g., the patient is severely intoxicated.
- Discontinuation should be planned and gradual over at least 4-6 weeks (longer in most cases).
- If there are concerns about the length of time a patient has been taking one of these medicines, this should be referred to in any correspondence to the usual prescriber (e.g., GP, Community Mental Health Team).

New prescriptions

- Ensure non-pharmacological interventions are continued (see Appendix one – Practical Sleep Hygiene for Hospital Inpatients).

- Reserve for short prescribing duration to alleviate severe, disabling symptoms.
- If a prescription is required, it should be limited to a short time period (up to 7 days initially) and then reviewed.
- Start with the lowest licensed dose.
- A review/stop date should be stated clearly on the prescription.
- Ensure repeated PRN (as required) doses are recognized and reviewed in planned ward rounds and multidisciplinary team meetings.
- Out of hours doctors should not be expected to make decisions about continuation or prescription for discharge.
- Nursing and pharmacy staff should check with the prescriber if a benzodiazepine or z-hypnotic continues to be administered/requested after the stated review period.
- Intermittent use of z-hypnotics (every 2nd/3rd night) can help prevent tolerance developing. Explain to the patient the limitations of sleeping tablets. On initiation, consider a verbal 'contract' with the patient to manage expectations.
- Ideally, z-hypnotics should not be given/taken before midnight (to give the patient an opportunity to get to sleep without them).
- See Appendix 2 for a comparison of different benzodiazepines and z-hypnotics.

Discharge (TTO) and temporary leave prescriptions

- Review and aim to reduce or stop short-term benzodiazepine or z-hypnotics prior to discharge.
- Carefully consider if PRN benzodiazepines or z-hypnotics are still necessary for periods of leave or on discharge.
- The decision to prescribe benzodiazepines or z-hypnotics for periods of leave or discharge should only be made by a senior clinician in the treating team.
- If prescribed, the exact quantity to be supplied should be stated based on recent and likely usage.
- The minimum possible quantity should always be prescribed.
- If patients are discharged back to primary care on z-hypnotics or benzodiazepines, then the discharge summary should clearly state the likely duration of treatment and when this should be reviewed and stopped by the GP.

- Pharmacy will aim to confirm with the prescriber all discharge prescriptions for benzodiazepines and z-hypnotics where it is known that the patient was not taking these medicines prior to their hospital admission.

Outpatient prescriptions

- Exceptionally, there may be occasions where patients with severely disabling symptoms are prescribed longer courses under the supervision of a Consultant Psychiatrist.
- All out-patient repeat prescriptions should be reviewed regularly by the prescribing team to assess continuing need.
- Ensure no more than one prescriber is supplying z-hypnotics or benzodiazepines.
- All those involved in a patient's care (e.g., carers, care coordinator, community pharmacists) can play a valuable role in identifying chronic use of these medicines and bringing this to the attention of the prescribing team.

DISCUSSION WITH THE PATIENT

- Reiterate benefits of stopping (tolerance reduces effectiveness, and continuing treatment may only serve to prevent withdrawal symptoms, risk of withdrawal increases with higher doses and length of use, avoid adverse effects, reduce risk of accidents, and minimize risk of interactions with alcohol/illicit substances/ other sedative medicines).
- Use Should I stop my benzodiazepine or z-drug? to support discussion.
- Explain the risks associated with the long-term use of benzodiazepines and z-hypnotics (cognitive impairment, anxiety, depression, reduced coping skills, emotional blunting and reduced social functioning).
- Explanation that withdrawal symptoms may occur following each reduction, but these symptoms tend to settle within a few days.
- It is not possible to estimate the severity of withdrawal; this will depend on several individual factors.
- Stress that benzodiazepines and z-hypnotics should not be stopped suddenly, and that the reduction will take time (months not weeks).

- Stress that abrupt withdrawal of benzodiazepines may produce confusion, toxic psychosis, convulsions, or a condition resembling delirium.
- Assess whether this is a suitable time for withdrawal (consider physical and mental health)
- Consider whether the withdrawal can be appropriately managed in primary care (is the patient committed and willing with adequate social support? Can they be reviewed regularly?
- Seek specialist advice if there is a history of alcohol or other drug dependence, concurrent severe physical or mental health disorder or a history of drug withdrawal seizures.

If the patient is engaged and willing to taper

- Decide whether the patient can withdraw their current medicine without switching to diazepam first.
- Agree a reduction schedule with the patient; they should guide adjustments, so they remain comfortable and feel in control of the withdrawal.
- When considering frequency of reductions consider your capacity for follow up and review.
- Patients may experience withdrawal symptoms for several days after reduction so weekly reductions may be too quick.
- Withdrawal can take 4 weeks to 1 year (or longer)
- If symptoms relapse consider maintaining current dose for 1-2 weeks, then taper at a slower rate
- The reduction becomes a larger proportion of the dose as the dose reduces. Patients may run into difficulty as they reach lower doses. Consider smaller dose reductions as the dose gets lower.
- If a person does not succeed on their first attempt, encourage them to try again.

What if the patient is not keen?

- Address any concerns the patient has.
- Show empathy; this can be a very sensitive topic.

- Explain that we now have better ways of working out how helpful medicines really are, and we know that a lot of things that we thought were helpful in the past have proved to be disappointing.
- Reassure that if a tapering trial does not work, we can think again.
- Allow time to reflect on information and arrange a further appointment if necessary.
- If, after reflection, the patient is still not keen then do not pressurize to stop and review again in 3 to 6 months.

WITHDRAWAL SYMPTOMS

- The risk of withdrawal symptoms increases with longer use, higher dosage and higher potency medicines.
- May mimic the original condition being treated.
- Benzodiazepines – sweating, insomnia, loss of appetite, palpitations, perceptual disturbances, tremor, anxiety, depression, panic attacks, headache and nausea
- A protracted withdrawal syndrome may occur in a minority of people (up to 15%); usually those who have taken benzodiazepines for many years.
- Established benzodiazepine dependence can be very difficult to treat. This may result in prolonged withdrawal symptoms and may even become a long-term state.
- Z-hypnotics – Rebound insomnia (with broken sleep and vivid dreams), impaired concentration, abdominal cramps, palpitations, perceptual disturbances, anxiety and depression.

Managing withdrawal symptoms

- Provide reassurance – with slow tapering many people experience few or no withdrawal symptoms.
- If withdrawal symptoms are present, they will disappear in a few months for most people.

- Advise patient not to compensate by increasing intake of alcohol/illicit substances/other sedatives.

Anxiety

- Consider slower or suspending withdrawal until symptoms become manageable.
- Consider nonpharmacological management.
- Adjunct medications should not be routinely prescribed (but may be considered)

Depression

- Consider suspending withdrawal until the depression resolves.
- Treat as per NICE NG2226

Insomnia

- See information above on sleep hygiene and psychological therapies.

Driving

- Department of Health driving legislation is available at https://www.gov.uk/drug-driving-law
- There are DVLA regulations around benzodiazepine use and driving (note that doses outside of BNF guidance constitutes persistent misuse or dependence for licensing purposes whether in a programme of withdrawal or not).
- Advise patients not to drive if they feel drowsy, dizzy, or unable to concentrate.
- Counsel patients about the risks of impaired reaction times and injury even if they feel well.
- Remind that it is an offence to drive with more than a specified amount of benzodiazepine in your body, whether driving is impaired or not.
- Advise patients to keep evidence they are taking a benzodiazepine in accordance with medical advice (e.g., medication box with pharmacy label, evidence of repeat prescription).
- The DVLA provides no advice for people taking z-hypnotics.

APPENDIX 1

Sleep hygiene in hospital

Sleep in hospital may be disrupted for a number of reasons:

- Disruption to normal sleep patterns (usual wake / sleep times).
- Proximity of other people.
- Noise (from other patients, staff, machines).
- Lighting – too dark during the during the day, too light at night.
- Worries (about diagnosis, care, treatment, concerns outside the hospital).
- Being in an unusual environment.
- Physical symptoms (such as pain, nausea or breathlessness).
- Being woken for medical or nursing care during the night.
- Some medication may affect sleep patterns.

Rest and sleep are an important part of recovery and healing. Studies have suggested that sleep loss in hospital is associated with worse health outcomes, including cardio-metabolic derangements and increased risk of delirium in older patients.

In an acute care setting some common strategies to prevent insomnia may be more challenging to implement, however a thoughtful approach may allow integration of some of these into routine care.

At night:

- Avoid medical or nursing intervention unless necessary. Consider amending timing of medicine administration, blood tests and observations if safe to do so.
- If possible try to avoid diuretics and CNS stimulant medicines at bedtime (including steroids, nicotine, decongestants, and medicines for ADHD or narcolepsy).
- Encourage avoidance of caffeine (ensure decaffeinated options are available on the ward)
- Encourage toileting before bedtime.
- Actively address pain (one study suggested toileting and pain are the biggest causes of insomnia reported by patients in the hospital setting)

- Ensure a comfortable temperature – encourage patients to remove or request blankets.
- Ensure your patient is comfortable – assist with positioning, wearing own nightclothes if suitable.
- Avoid turning on lights, ensure conversations are at low volume and away from patient areas where possible. Minimise unnecessary phone calls (staff and patients).
- Patients may wish to bring ear plugs or eye masks in to hospital.
- Encourage avoidance of screen time within 1 hour of bedtime.
- Encourage relaxation strategies. Offering a milky or non-caffeinated drink (avoiding large volumes of liquid at bedtime), soft music / spoken word (via headphones) and breathing techniques have all been shown to aid relaxation.

During the day:

- Encourage natural light (open blinds, curtains).
- Encourage gentle exercise if appropriate (eg sitting out, use of day room).
- Encourage avoidance of napping in the afternoon. If needed, naps are better taken earlier in the day and limited to 30 mins.

Hypnotics / sleeping tablets

New prescriptions of hypnotics for sleep alone should be avoided unless absolutely necessary, and only used for the shortest possible time.

There can be a useful short term window for hypnotics to encourage sleep / wake cycle if non-pharmacologic options are insufficient e.g. after surgery or in times of distress. Discuss this with your patient before prescribing and have a clear plan for stopping before discharge.

Remember:

- Sleeping tablets do not just affect our sleep – they can also affect day time alertness, memory and coordination; they may increase harm from falls and reduce engagement in rehabilitation (eg therapy interventions.)

- Although many people assume that sleep medication will help them to function adequately the next day, there is little scientific evidence to support this.
- Effects on memory may also be at night – patients may report more sustained sleep due to not remembering waking episodes the following day.

APPENDIX 2

Comparison of Benzodiazepines and Z-hypnotics

Medicine	**Usual adult dose for anxiety (per day)**	**Usual adult dose for insomnia (per day)**	**Approximate half-life (hours) ****	**Other information**
Diazepam	2mg three times a day, increased if necessary to 15mg – 30mg daily in divided doses*	Insomnia associated with anxiety: 5mg – 15mg once daily at bedtime*	20-100 hours (36-200 hours for active metabolite)	In frail or older people consider very low starting dose
Lorazepam	1-4mg daily in divided doses*	Insomnia associated with anxiety 1-2mg once daily at bedtime*	10-20 hours	In frail or older people consider very low starting dose
Nitrazepam	N/A	5mg – 10mg daily before bedtime	15-38 hours	Avoid use in the elderly. Non-formulary in Nottinghamshire
Temazepam	N/A	10mg – 20mg daily before bedtime*	8-22 hours	Schedule 3 controlled drug
Zopiclone	N/A	7.5mg daily before bedtime*	5-6 hours	Slower onset than zolpidem but longer duration of action
Zolpidem	N/A	10mg daily before bedtime*	2 hours	Potent and quick acting (usually works within 15 minutes)

*For debilitated patients or older patients lower doses (e.g. half adult doses) are recommended. See the BNF or medication's Summary of Product Characteristics (SPC) for further information.

**Half-life does vary between patients and can be longer in certain patient groups (e.g. renal impairment, older patients).

Benzodiazepine / Z-drug Policy

NHS Clifton Court Medical Practice

https://www.cliftoncourtmedicalpractice.nhs.uk/policies/benzodiazepine-z-drug-policy/

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

INTRODUCTION

A controlled substance is generally a drug or chemical whose manufacture, possession, or use is regulated by the government because of the potential for abuse or addiction. Such drugs include those classified as narcotics, stimulants, depressants, hallucinogens, and cannabis.

A list of the most commonly encountered controlled drugs can be found at: https://www.gov.uk/government/publications/controlled-drugs-list–2

Some patients require strong, potentially addictive medication to help manage their condition(s). Of concern are 'drugs of dependence' (e.g. opioid medications, benzodiazepines and Z-drugs), particularly when these are prescribed on an on-going basis.

Due to increasing reports of abuse of prescription drugs and patient behavioural problems, Clifton Court Medical Practice has established a policy to ensure adequate treatment, while reducing the risk of problems with drug prescriptions.

GENERAL PRACTICE STANDARDS

- If the decision to prescribe is taken after a shared discussion of goals, plans, risks and benefits, patients may be required to confirm consent in writing.

- Patients may be asked to complete a withdrawal programme and sign a withdrawal contract which details our practice's expectations when prescribing drugs of dependence. This agreement details the patients' responsibilities as a patient taking a drug of dependence; any prescriptions issues; advice on taking medications; how we will monitor care; and the standards of behaviour that are expected.
- Patients may need to acknowledge that their care requirements may be complex, and that referral for on-going care for all or part of their healthcare may be required. It is our practice policy that patient care is matched with the level of complexity.
- Patients should be reminded that we have a zero tolerance on issues relating to staff abuse.

Sedative prescription requests for fear of flying

The surgery has a practice policy that we do not issue sedative prescriptions, such as diazepam, chlordiazepoxide or zopiclone to alleviate symptoms that patients may experience relating to a fear of flying.

This decision has been made by all of our GP partners; our main reasons are listed below:

- The use of any sedating drug causes longer reaction times and slower thinking which during a flight may put the patient and or other passengers at significant risk of not being able to act in a manner which could save life in the event of an emergency.
- The use of any CNS depressant has the potential to increase the risk of Deep Vein Thrombosis (DVT).
- For some countries it is illegal to import these drugs.
- National guidelines advise that medication should not be used for mild and self-limiting mental health disorders and/or phobias.
- Use of these medications increases the risks of falls and accidents.

What to discuss with the patient when considering use of a benzodiazepine or Z-drug

Ensure the patient is aware that the medication is for short-term use alongside self-care.

Ensure patients are aware of the risks of treatment including Central Nervous System (CNS) depressant effects, including 'hangover' effects, unsteadiness, reduced alertness and impaired memory, tolerance, dependence, and withdrawal.

The long-term use of benzodiazepines or Z-drugs is associated with a number of health conditions and an increased risk of death:

- Over-sedation from long-term use can increase the risk of falls and accidents on the road and in the home.
- Poisoning from overdose may contribute to increased mortality risk.
- Long-term use of benzodiazepines or Z-drugs (usually more than 4 weeks) may be associated with:
  - Tolerance — a higher dose is required to obtain the initial effect.
  - Dependence — the person feels they need the medication to carry out day-to-day activities, and/or withdrawal symptoms occur upon stopping or dose reduction.
- Other effects of long-term use of benzodiazepines include:
  - Cognitive effects, anxiety, agoraphobia, emotional blunting, reduced coping skills, and amnesia.
  - Reduced social functioning due to effects on memory, reduced ability to remember new people, appointments etc.
  - Depression, either for the first time, or aggravation of pre-exisiting depression with possible precipitation of suicidal tendencies.
- Older people are more vulnerable to the CNS depressant effects of benzodiazepines, possibly leading to confusion, night wandering, amnesia, ataxia, and hangover effects. Impaired cognitive function and memory may be wrongly diagnosed as dementia. In the UK, it has been estimated that older adults receive 80% of all prescriptions written for benzodiazepine hypnotics.

- Provide advice related to driving whilst taking the medication
- Warn of potential serious adverse effects if alcohol and other sedative substances are used with the medication.

Benzodiazepine/Z-drug Policy – Issuing Prescriptions

- All new benzodiazepines and Z-drugs will be issued as acute prescriptions.
- Wherever possible, patients will see the same Prescriber for review of the initial prescription.
- Where benzodiazepines and Z-drugs are initiated by an external provider the Practice will only take over prescribing once a written request has been received. GPs are under no obligation to prescribe on the advice or recommendation of an external provider and are reminded that they take on prescribing responsibility if they choose to prescribe. Where the GP chooses to accept this, the remainder of this policy applies, especially with regard to duration and review.
- Where patients are discharged from hospital on Benzodiazepines or Z Drugs the Practice should not automatically add these to the patients' medications. Patients should be reviewed by the GP prior to any further issue.
- All patients will be reviewed within 2- 4 weeks of initiation of a benzodiazepine/ Z-drugs prescription.
- Patients on long-term benzodiazepines/Z-drugs will be reviewed every 6 months.
- All benzodiazepines and Z-drugs will be issued on prescriptions with a maximum duration of 1 month.
- All benzodiazepines and Z-drugs prescriptions will include full directions wherever possible and use of PRN or MDU directions will be avoided.

Practice procedure for lost/stolen Controlled Drug Prescriptions

- The loss or theft of a controlled drug prescription must be recorded in the patients' medical record and a READ code added to enable the Practice to monitor/audit.
- If the prescription is stolen, the patient or the Practice must report the incident to the police and obtain a crime number.
- The loss or theft of a controlled drug or prescription must be reported to the CD

Accountable Officer via cdreporting.co.uk

- If Practices need to send out an alert regarding lost or stolen prescriptions, this can be done by sending an alert template to: EnglandCASalerts@nhs.net.
- The Practice must review the patient's records when considering if it is appropriate to re-issue a prescription. Notes should be assessed to identify if there is a pattern of regularly requesting additional prescriptions. Practices may consider reviewing ordering patterns for immediate family and household members when considering patterns of behaviour. If a pattern is identified this could indicate an underlying problem such as abuse, diversion or a safeguarding issue, report via cdreporting.co.uk and refer as appropriate.
- The patient should be invited in for review and the appropriate steps taken.
- Practices may issue a small supply of medication to cover the period until the patient attends.

At the review, Practices should review the appropriateness of the current prescription and steps that can be taken to support the patient such as:

- Reducing and withdrawing medication.
- Reducing script duration e.g. weekly prescriptions.
- Discussion about future action should there be further issues.
- Working with the community pharmacy e.g., if prescriptions are being stolen could the pharmacy collect prescriptions on the patient's behalf, use of EPS.

Existing patients with a regular prescription for Benzodiazepines or Z Drugs.

- Patients registered at the Practice who are already receiving regular prescriptions for Benzo's and Z Drugs will be systematically reviewed.
- The pharmacist or GP will identify and audit patients who require review and make appropriate recommendations which may include a reduction to stop regime.
- The Practice will support the Patient to reduce and stop Benzo and Z drug medication by following the recommendations, the timely issue of prescriptions as per the reduction plan and adhering to the Practice Policy.
- Where a patients' circumstances are such that a reduction regime would cause

undue distress or anxiety at the given time, they will be informed that further attempts will be made to reduce and stop at 6 monthly intervals.

- For any patients who repeatedly fail to engage in a reduction plan without appropriate clinical reason, the GP may cease to prescribe, after taking appropriate specialist advice.

Summary of relevant NICE Guidance

Medicines Optimisation Key Therapeutic Topic – Hypnotics (KTT6)

- Only use hypnotics if insomnia is severe, using the lowest dose that controls symptoms for the shortest period of time.

Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia (TA77)

- Z-drugs and the shorter-acting benzodiazepine hypnotics should only be considered for severe insomnia interfering with normal daily life.
- They should be prescribed for short periods of time only, in strict accordance with their licensed indications.
- There is no compelling evidence to distinguish between zolpidem, zopiclone or the shorter-acting benzodiazepine hypnotics.
- Patients who have not responded to one of these hypnotic drugs should not be prescribed any of the others (switching from one of these hypnotics to another should only occur if a patient experiences adverse effects considered to be directly related to a specific agent).

NICE CKS Insomnia

If a hypnotic is required for insomnia the recommended choices are:

- Non-benzodiazepines (the 'z-drugs') – zopiclone, zolpidem, and zaleplon (all are short acting).
- Short-acting benzodiazepines – temazepam, loprazolam, lormetazepam.
- Diazepam is not generally recommended, but it can be useful if insomnia is associated with daytime anxiety,prescribe 5 – 15 mg at bedtime.
- Use the lowest effective dose for the shortest period possible.

- Treatment should not continue for longer than 2 weeks.
- Sedative drugs other than hypnotics (such as antidepressants, antihistamines, choral hydrate, clomethiazole, and barbiturates) are not recommended for the management of insomnia. Expert opinion from reviews suggests that there is insufficient evidence to support their use, and that the potential for adverse effects is significant.

Generalised anxiety disorder and panic disorder in adults: management (CG113)

- Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short-term measure during crises. Benzodiazepines are associated with a less good outcome in the long term.
- Benzodiazepines should not be prescribed for the treatment of individuals with panic disorder.

NICE CKS Anxiety

If a benzodiazepine is required for anxiety the recommended choice is diazepam:

- For anxiety, prescribe 2 mg three times a day.
- If needed, the dose can be increased to 15–30 mg daily in 3 divided doses (half the dose should be prescribed in elderly or debilitated people).
- Caution in the elderly, due to the increased risk of falls — the manufacturer advises halving the recommended doses.
- Prescribe the lowest possible dose for the shortest period of time and review the patient regularly.
- Treatment should not exceed 2–4 weeks.

Depression in adults: recognition and management (CG90) and Depression in adults with a chronic physical health problem: recognition and management (CG91)

- Benzodiazepines are only to be considered as an option if a person with depression prescribed an SSRI develops the side effects of anxiety, agitation and/or insomnia early in antidepressant treatment and symptoms are problematic.
- In this case short-term concomitant treatment with a benzodiazepine is one of

several options that can be considered.

- If a benzodiazepine is prescribed this should be for no longer than 2 weeks in order to prevent the development of dependence.
- Benzodiazepines should not be used in people with chronic symptoms of anxiety.
- Benzodiazepines should be used with caution in patients at risk of falls

Social anxiety disorder: recognition, assessment and treatment (CG159)

- Do not routinely offer benzodiazepines to treat social anxiety disorder in adults.

Obsessive-compulsive disorder and body dysmorphic disorder: treatment (CG 31)

- Anxiolytics should not normally be used to treat OCD or BDD without comorbidity except cautiously for short periods to counter the early activation of SSRIs.

Post-traumatic stress disorder (NG116)

- Do not offer drug treatments, including benzodiazepines, to prevent PTSD in adults
- Antenatal and postnatal mental health: clinical management and service guidance (CG192)
- Do not offer benzodiazepines to women in pregnancy and the postnatal period except for the short-term treatment of severe anxiety and agitation.
- Consider gradually stopping benzodiazepines in women who are planning a pregnancy, pregnant or considering breastfeeding.

NICE CKS BPSD

- If challenging behaviour requires urgent treatment (when the person is a danger to themselves or others) and underlying causes (such as discomfort, thirst, or the need for the toilet) have been addressed, advise moving the person to a safe, low-stimulation environment (such as a quiet room) away from others and use of verbal and non-verbal de-escalation techniques (such as active listening,

effective verbal responding, pictures, and symbols).

- If these measures fail, seek advice from an elderly care psychiatrist, the challenging behaviour team, or an elderly care physician.
- Depending on the specific situation, short-term (off-label) use of drugs for behavioural control (such as haloperidol or lorazepam) may be suggested.
- Lorazepam (off-label) for the treatment of challenging behaviour associated with dementia should only be used on the advice of a specialist who should specify dose and duration of treatment.
- Short-term treatment with lorazepam (off-label use) may be suggested for immediate management of violence, aggression, or extreme agitation in people with dementia when non-pharmacological measures have failed and the person poses a risk to themselves or others. The aim of the treatment is to calm the person and reduce agitation or aggression, not to sedate.
- Treatment should start at the lowest possible dose (500 microgram) orally and be titrated slowly in increments, if necessary, to a maximum of 1 mg daily (2 mg daily in exceptional circumstances). One-to-one care of the person should be available while the dose is titrated in a controlled and safe manner.
- The person should be reviewed regularly, and lorazepam discontinued as soon as possible.

Medicines Associated With Dependence or Withdrawal Symptoms: Safe Prescribing and Withdrawal Management for Adults

National Institute for Health and Care Excellence (NICE)

https://www.nice.org.uk/guidance/ng215/resources/medicines-associated-with-dependence-or-withdrawal-symptoms-safe-prescribing-and-withdrawal-management-for-adults-pdf-66143776880581

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Overview

This guideline covers general principles for prescribing and managing withdrawal from opioids, benzodiazepines, gabapentinoids, Z-drugs and antidepressants in primary and secondary care.

It does not cover gabapentinoids prescribed for epilepsy, nor opioids prescribed for acute or cancer pain, or at the end of life, nor management of illicit drug dependence.

Who is it for?

- Healthcare professionals
- Commissioners of NHS and local authority services
- People using services, their families and carers, and the public

This guideline was commissioned by NICE and developed at the National Guideline Centre, which is hosted by the Royal College of Physicians.

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Supporting people taking a dependence-forming medicine or antidepressant

1.1.1

Aim to foster collaborative, trusting and supportive relationships with people considering taking, and at all stages of prescribing and withdrawal management of, an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant. Follow the recommendations in the NICE guideline on patient experience in adult NHS services, particularly those relating to:

- continuity of care and relationships
- enabling patients to actively participate in their care
- tailoring healthcare services to each person.

1.1.2

Ask people whether they would like to have support during appointments from a family member, carer, advocate or other person close to them.

1.2 Making decisions about prescribing and taking a dependence-forming medicine or antidepressant

1.2.1

Before starting or continuing treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, ensure that all suitable management options, including non-pharmacological approaches and watchful waiting, have been discussed with and offered to the person.

1.2.2

When making decisions about prescribing medicines, determine whether there are any factors that might increase the person's risk of developing problems associated with dependence, but do not withhold the medicine solely on the basis of one of

these factors. Explain and discuss the risk with the person. Factors that might increase risk include:

- a comorbid mental health diagnosis
- a history of drug or alcohol misuse
- not having a clear, defined diagnosis to support the prescription
- taking an opioid together with a benzodiazepine.

1.2.3

During the first discussion about prescribing, give the person information and advice (in their preferred format) to help them balance the potential benefit of the medicine and other treatment options with the risk of long-term consequences.

1.2.4

Recognise and acknowledge that decisions about medicines can be difficult for a person who is in distress.

1.2.5

Acknowledge that these decisions are also difficult for the prescriber particularly when supporting a person who is distressed, and in the presence of risk factors for developing problems associated with dependence, and that additional time may be required to consider options and consult with colleagues.

1.2.6

Consider delaying prescribing if the person needs more time to think about their options or the prescriber needs to consult with other members of the healthcare team. If prescribing is delayed, ensure that a follow-up appointment is arranged.

1.2.7

If a prescriber thinks that a medicine is not in the person's best interests but a shared decision about starting or continuing a medicine cannot be reached with the person, the prescriber should:

- not prescribe a medicine if they believe it is not in the person's best interests
- explain the reasons for their decision to the person

- document all discussions carefully and give a copy to the person
- offer the person a second opinion.

1.2.8

For people who find it difficult to communicate their symptoms, for example people with a learning disability or cognitive impairment:

- explore a range of methods to understand the person's symptoms, including discussion with family members, carers or an advocate if appropriate
- make necessary reasonable adjustments, for example increasing the appointment length, using short clear sentences or alternative methods of communication and visual aids during consultations, to help the person understand their options for treatment and the associated risks and benefits of each, and to express their view
- ensure that family members or carers are aware of the properties of any medicine prescribed, if appropriate.

  For more information, see the NICE guidelines on shared decision making, care and support of people growing older with learning disabilities and dementia.

1.2.9

Ensure that people with a learning disability or mental health problem have had a full assessment before prescribing a dependence-forming medicine or antidepressant, to ensure that they do not have other unmet needs and that prescribing is the appropriate option. Consider involving the relevant specialist teams.

1.2.10

Prescribers must understand and take into account the principles set out in the Mental Capacity Act 2005 when working with individuals who may lack capacity to make decisions.

1.2.11

Prescribers should use the Royal Pharmaceutical Society's Competency framework for all prescribers to support safe and effective prescribing and improve prescribing practice.

1.3 Starting a dependence-forming medicine or antidepressant

Information and support for people starting a medicine

1.3.1

Before starting treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, give the person verbal and written information (in their preferred format) about the medicine. Ensure that the information is evidence-based and understandable by the person. Explain to the person:

- the potential side effects of the medicine, whether these are likely to be temporary or permanent and whether they might improve or worsen over time
- any additional implications of taking the medicine if the person is pregnant or planning pregnancy
- what the options might be if the medicine does not work
- how difficult it might be to stop the medicine later and how that might be managed
- that missing doses may lead to symptoms of withdrawal
- how to store medicines safely.

1.3.2

Before starting treatment with an opioid, benzodiazepine, gabapentinoid or Z-drug, explain and discuss with the person:

- that dependence is an expected effect of these medicines and is not a reason in itself to avoid the medicine
- the potential for developing problems associated with dependence
- the symptoms that suggest the development of problems associated with dependence and, if appropriate, the importance of making family members, carers or other people close to them aware of these symptoms.

1.3.3

Before starting treatment with an antidepressant or gabapentinoid, explain and discuss with the person:

- that any beneficial effect of the medicine may occur slowly, and they might experience side effects before noticing any benefit
- that many side effects are likely to ease over time.

1.3.4

Consider supplementing verbal and written information with details of peer support networks or online forums suitable for the person.

Management planning

1.3.5

Discuss and agree a management plan with the person. Document the plan in the person's medical record and give them a copy in their preferred format. Include:

- what the medicine has been prescribed for, the intended outcomes of treatment and how these might be assessed
- the starting dose and intervals between dose adjustments or titrations
- who to contact if problems occur
- information about how long the medicine will take to work and how long they might be taking it for
- the duration of each prescription that will be issued
- the risks of taking more than the prescribed dose
- the symptoms and signs of an overdose and what they should do if this happens
- the plans for reviewing the medicine (including where and by whom this will be done) and the date of their next review.

1.3.6

Think about a strategy for regular reviews and include these in the management plan. Use regular reviews to:

- ensure that the benefits of the medicine continue to outweigh the potential harms
- check whether the dose needs to be adjusted and, if so, how to do this safely.

Prescribing strategies

1.3.7

Take steps to reduce the risk of developing problems associated with dependence, for example starting at a low dose, and consider avoiding modified-release opioids. Explain the importance of these steps to the person.

1.3.8

Discuss with the person the range of doses likely to be safe and effective. Start with a low dose and agree frequent, regular reviews to ensure that timely adjustments can be made to test effectiveness, safety and acceptability and to find the lowest effective dose. Once an effective dose has been established, avoid automatically increasing the dose if the response is not sustained.

1.3.9

If the person's individual circumstances or the setting (for example, a secure setting) mean that usual prescribing practices are not suitable, adjust the prescription to ensure that:

- the medicine can be administered safely as part of the setting's routine
- the medicine does not pose a risk to the person or to others living in that setting.

1.3.10

The duration of each individual prescription:

- should reflect the management plan (see recommendation 1.3.5)
- should comply with best practice in controlled drugs prescribing
- must comply with relevant legislation.

Working with other healthcare professionals

1.3.11

When starting a prescription suggested by another healthcare professional, taking over a person's care, or deciding whether to continue a prescription made by another healthcare professional:

- take the same level of care you would take if you were starting the prescription
- follow the section on supporting people taking a dependence-forming medicine or antidepressant to help establish the new relationship
- ensure that you have sufficient knowledge of the person's health and preferences to determine whether continued prescribing is in their best interests or whether careful withdrawal (in discussion with the person) would be more beneficial for them.

1.3.12

Healthcare professionals in secondary care who recommend a dependence-forming medicine or antidepressant to be started or continued in primary care should explain to the person that:

- the medicine will be prescribed by their primary care team
- the primary care team will need to review the medicine
- if the primary care team declines to prescribe the medicine, or wishes to delay it, the secondary and primary care teams will discuss the medicine and involve the person in these discussions, explaining the reasons for any delay
- the secondary care team might not continue to manage and provide the medicine if this is agreed after discussions.

1.3.13

When transferring responsibility for prescribing from secondary to primary care, ensure that all relevant healthcare professionals have access to the management plan in the person's medical record.

1.3.14

If possible, ensure that 1 person has overall responsibility for a prescription. If the initial prescriber is unable to review the medicine, ensure there are arrangements for review by another healthcare professional and that effective communication, including sharing the person's records and management plan as needed, is in place to support this.

1.4 Reviewing a dependence-forming medicine or antidepressant

Frequency of reviews

1.4.1

Offer regular reviews (by phone, video or face to face) to people taking an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant. Base the frequency of reviews on:

- the person's preferences and circumstances
- the type of medicine they are taking and the dose
- factors that might indicate a need for frequent reviews, for example if:
  - ✓ the person has additional care needs (such as people with a learning disability or cognitive impairment)
  - ✓ the person is taking the medicine for the first time
  - ✓ there are potential adverse effects or problems associated with dependence
  - ✓ the medicine is being used outside its licensed indications
  - ✓ there is potential for misuse of the medicine.

1.4.2

Consider increasing the frequency of reviews during dose adjustment. Take into account the person's clinical and support needs when agreeing review frequency.

1.4.3

Offer extra, unscheduled reviews when needed, for example if the person:

- reports adverse effects from the medicine
- becomes pregnant or is planning pregnancy
- has a change in their physical or mental health condition, or social circumstances
- starts taking medicines from a different prescriber
- requests a change in dose.

1.4.4

For guidance on reviewing medicines, see the section on medication review in the NICE guideline on medicines optimisation and the section on reviewing medicines in the NICE guideline on medicines adherence.

Content of reviews

1.4.5

During the review, discuss with the person the benefits and risks of continuing the current dose, adjusting the dose or stopping the medicine. Base decisions on this discussion, taking into account, for example:

- the benefits or harms the person is experiencing from continuing the medicine
- any signs that the person is developing problems associated with dependence (such as running out of a medicine early, making frequent requests for dose increases or reporting loss of efficacy of a medicine that was previously working well)
- the person's preferences.

1.4.6

Agree and update the management plan with the person after each review, and give them a copy (see recommendation 1.3.5). Check that they know who to contact if they have problems or concerns.

1.5 Withdrawing a dependence-forming medicine or antidepressant

Making shared decisions about withdrawing medicines

1.5.1

Discuss withdrawing an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant with the person if:

- it is no longer benefiting the person
- problems associated with dependence have developed
- the condition for which the medicine was prescribed has resolved
- the harms of the medicine outweigh the benefits

- the person wants to stop taking the medicine.

1.5.2

Explain the benefits the person can expect from reducing the medicine and aim to reach agreement using a shared decision-making approach. Allow enough time to explore the person's circumstances and preferences.

1.5.3

Understand that the person might be reluctant or anxious about discussing problems associated with dependence. Reassure them that dependence is an expected effect of these medicines and that problems associated with dependence sometimes develop. Be sensitive to the use of terminology that may apportion blame to the person or be perceived adversely.

1.5.4

Acknowledge and discuss with the person any differences between their views and your own about the risks and benefits of the medicine.

1.5.5

Be prepared for queries about prescribing decisions made previously. Explain that our understanding of the balance of risks and benefits of a medicine can change over time. If sufficient clinical detail is available, discuss the possibility that past prescribing was done in the person's best interests using the knowledge available at the time.

1.5.6

Do not stop a medicine abruptly (complete cessation with immediate effect) unless there are exceptional medical circumstances, such as the occurrence of serious side effects (for example, upper gastrointestinal bleeding from an antidepressant, respiratory depression from an opioid or severe ataxia from a gabapentinoid). In these circumstances, consider:

- scheduling more frequent reviews
- short-term use of medicines to treat the physical symptoms of withdrawal (for example, abdominal cramps and diarrhoea during withdrawal of an opioid).

1.5.7

When planning withdrawal from an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, take into account:

- the urgency of the withdrawal, for example gradual withdrawal of a medicine that is no longer effective or necessary, or more rapid withdrawal of a medicine that is causing significant harm (the speed of rapid withdrawal depends on the type of medicine and the person's circumstances, see recommendation 1.5.6)
- whether the initial goal should be complete withdrawal or, for people who find complete withdrawal too difficult, whether dose reduction with ongoing review is a more realistic initial aim
- which medicine to reduce first, if the person will be withdrawing from more than 1 medicine
- factors that might increase the person's risk of problems during withdrawal, including:
  - ✓ long duration of medicine use
  - ✓ high dose of medicine
  - ✓ history of withdrawal symptoms
  - ✓ history of problems associated with dependence
  - ✓ taking an antidepressant with a short half-life
- any concurrent medicines and how these might affect the person's response to withdrawal
- factors that might influence the timing of the start of the dose reduction, such as the person's circumstances and available support.

Information and support for people withdrawing from a medicine

1.5.8

Before starting withdrawal:

- give the person information about the process of withdrawal that is tailored to their situation and the medicine they are taking
- explain how the withdrawal will be carried out
- consider providing details of sources of peer support, national and local support groups for people who are withdrawing from a medicine.

1.5.9

Discuss withdrawal symptoms with the person and tell them about the support that is available. When discussing withdrawal symptoms, explain that:

- withdrawal can be difficult, and may take several months or more
- support will be available throughout the withdrawal process
- withdrawal symptoms do not affect everyone, and it is not possible to predict who will be affected
- withdrawal symptoms vary widely in type and severity, can affect both physical and mental health, may occur at any time during withdrawal or be delayed in onset and can change over time or persist over a prolonged period
- some people may experience withdrawal symptoms that can be difficult to distinguish from a re-emergence of their original symptoms or a new disorder, and it is important to discuss these with a healthcare professional if they occur (see recommendation 1.5.17).

Dose reduction

1.5.10

When agreeing a dose reduction schedule with the person:

- explain the risk of abrupt discontinuation and that the rate of safe withdrawal varies between people and can vary over time for the same person

- balance the risk of adverse events from continued exposure to the medicine with minimising the risk of withdrawal symptoms by slow dose reduction and withdrawal
- ensure that the planned rate of reduction is acceptable to the person
- explain that although withdrawal symptoms are to be expected, the reduction schedule can be modified to allow intolerable withdrawal symptoms to improve before making the next reduction
- consider giving the person additional control over the process of dose reduction (for example, by issuing their usual daily dose in a form that allows them to reduce the amount in small decrements at a pace of their choosing, rather than issuing successive prescriptions for reduced daily doses)
- agree regular intervals for reviewing and adjusting the reduction schedule as needed
- ensure the person knows who to contact if problems occur.

1.5.11

If the person is withdrawing from an opioid, benzodiazepine, Z-drug or antidepressant, suggest a slow, stepwise rate of reduction proportionate to the existing dose, so that decrements become smaller as the dose is lowered, unless clinical risk is such that rapid withdrawal is needed (see recommendation 1.5.6).

1.5.12

If the person is withdrawing from a gabapentinoid, reduce the dose by a fixed amount at each decrement, unless clinical risk is such that rapid withdrawal is needed (see recommendation 1.5.6).

1.5.13

If the person is withdrawing from a benzodiazepine with a short half-life, consider switching to a benzodiazepine with a longer half-life.

1.5.14

If using a published withdrawal schedule, apply it flexibly to accommodate the person's preferences, changes to their circumstances and the response to dose reductions.

1.5.15

During withdrawal, offer continued management of the underlying condition for which the medicine was prescribed, if needed.

1.5.16

Ensure the plan for dose reduction or withdrawal is clearly recorded in the overall management plan.

Identifying and managing withdrawal symptoms

1.5.17

Be aware that it can be difficult to distinguish between the re-emergence of underlying conditions and the emergence of withdrawal symptoms. The following may indicate withdrawal symptoms rather than symptoms of an underlying condition:

- rapid or early onset of symptoms after a dose reduction or cessation of the medicine
- symptoms of the underlying illness that the person reports as qualitatively different or more intense than before
- new symptoms that the person has not experienced before.

1.5.18

Follow recommendation 1.2.8 for people who find it difficult to communicate their symptoms, for example people with a learning disability or cognitive impairment.

1.5.19

Use clinical judgement to determine the need for further investigation to rule out new pathology.

1.5.20

If distressing symptoms occur or worsen after a dose reduction:

- determine whether they are withdrawal symptoms or a re-emergence of symptoms that were relieved by the medicine
- if the symptoms are new, think about delaying the next dose reduction, trying a smaller dose reduction or reverting to the previous dose.

Interventions to support withdrawal

1.5.21

Do not treat withdrawal symptoms with another medicine that is associated with dependence or withdrawal symptoms.

1.5.22

Do not offer sodium valproate or buspirone to aid withdrawal from a benzodiazepine.

1.5.23

Consider group cognitive behavioural therapy (CBT) when withdrawing from a benzodiazepine. Discuss the timing of referral for CBT with the person.

Strategies if withdrawal cannot be agreed or is unsuccessful

1.5.24

Follow recommendation 1.2.7 if a shared decision to withdraw cannot be reached and continuing the current prescription is not in the person's best interests. Be aware that medicines associated with dependence and withdrawal symptoms should not be stopped abruptly in most cases (see recommendation 1.5.6) and need to be reduced in line with the section on withdrawing medicines.

1.5.25

If continued use of the medicine may be particularly harmful for the person or others (for example, in a secure setting) and a dose reduction, or a more rapid reduction than the person wishes, is the safest option, consider:

- scheduling more frequent reviews
- short-term use of medicines to treat the physical symptoms of withdrawal (for example, abdominal cramps and diarrhoea during withdrawal of an opioid).

1.5.26

If dose reduction has been unsuccessful (for example because of intolerable withdrawal symptoms or a change in the person's physical, mental or social circumstances) and the current prescription needs to be continued:

- aim to stop any further escalation in dose
- make a plan to attempt dose reduction again at a later date
- clearly record the advice given to the person about the potential harms of continuing the medicine, and the reasons for continuing without a reduction, in the management plan.

Quality Prescribing for Benzodiazepines and Z-drugs. A Guide for Improvement 2024-2027

The Scottish Government (2024).

https://www.gov.scot/binaries/content/documents/govscot/publications/advice-and-guidance/2024/08/quality-prescribing-benzodiazepines-z-drugs-guide-improvement-2024-2027/documents/quality-prescribing-benzodiazepines-z-drugs-guide-improvement-2024-2027/quality-prescribing-benzodiazepines-z-drugs-guide-improvement-2024-2027/govscot%3Adocument/quality-prescribing-benzodiazepines-z-drugs-guide-improvement-2024-2027.pdf

Note: 1. The content of this article is excerpted from the above reference.
2. The arrangement of the content in this article follows the original sources.

Summary of recommendations

- People prescribed benzodiazepines or z-drugs (B-Z) are encouraged to initiate discussions regarding the appropriateness of treatment, including recommended duration and need for continuation, reduction or discontinuation of B-Z.
- In the short-term (e.g. less than two weeks) B-Z can provide some benefits for insomnia, and some anxiety disorders.
- B-Z use is associated with tolerance, dependence and avoidable medicine related harms.
- Studies have reported a higher risk of mortality associated with B-Z use in a range of populations e.g. people with schizophrenia.
- B-Z are associated with an increased incidence of depressive symptoms.
- B-Z may limit the efficacy of psychological therapies such as Cognitive Behavioural Therapy (CBT) due to their negative effects on cognitive function.
- B-Z use is associated with the use of selective serotonin re-uptake inhibitors (SSRIs), and higher SSRI doses for the treatment of depression.

Healthcare professionals should:

- Consider non-pharmacological options, including psychosocial or psychological interventions where appropriate.

- Recognise that the use of benzodiazepines is not recommended for the management of muscle spasm associated with acute low back pain or in the treatment of sciatica.
- Collaboratively develop a clear management plan with the individual, or carers where appropriate.
- Limit treatment duration to, for example, less than two weeks on an 'as required' basis when prescribed for the short-term treatment of insomnia or anxiety disorders.
- Record the indication for B-Z in clinical records.
- Consider the 'benzo-burden' – the total benzodiazepine-type medicine load prescribed per day. Benzodiazepines, z-drugs and gabapentinoids provide synergistic effects such as sedation and respiratory depression.
- Only prescribe B-Z and opioids together if there is no alternative and closely monitor individuals for signs of respiratory depression.
- Proactively review the need for B-Z when individuals are stable and well, to minimise avoidable medicine related harms and optimise care.
- Prescribe multiples of 2mg tablets as the preferred choice where diazepam treatment is required.
- Utilise the 7-Steps review process to ensure person-centred reviews.
- Apply a multidisciplinary whole system approach, including reception staff, pharmacy teams, practice nurses and GPs, to identify people for review.
- Use different strategies for reducing and stopping B-Z, depending on the individual's preferences and needs.
- Use clinical systems such as the Scottish Therapeutics Utility (STU) available within all GP practices in Scotland to help identify individuals for review.

NHS Boards and Health and Social Care Partnerships (HSCPs) should:

- Consider the prescribing advice within this guide to plan, resource and drive quality improvement and prescribing initiatives.

- Consider and engage a whole system approach to delivering quality improvements in prescribing.
- Recognise the significant influence of secondary care in prescribing behaviour.
- Ensure primary and secondary care are informed about the guide, to support continuity of care and the overall goals of reviewing and minimising inappropriate prescribing.
- Nominate local leads/champions to support implementation of the guidance.
- Work with third sector and services to develop and support the capacity for selfmanagement and access to non-pharmacological treatment options.
- Work with hospitals to review B-Z before discharge, to discontinue therapy or communicate a reduction plan for any B-Z prescriptions started in hospital.
- Support care homes to ensure any B-Z prescribed have an appropriate indication and are prescribed at the lowest therapeutic dose to achieve the desired effect and reduce risk of harm.
- Enable general practice clusters and local prescribing support teams to improve the quality of prescribing, through promotion and use of local and national measures, datasets and tools.
- Implement and use this guidance to improve care, clinical outcomes and minimise avoidable medicine-related harm from B-Z.

Medication Review: 7-Steps to Appropriate Prescribing and Polypharmacy

WHAT MATTERS?

RIGHT MEDICINE?

UNNECESSARY MEDICINE

EFFECTIVE MEDICINE?

HARMFUL MEDICINE

SUSTAINABILITY

AGREE AND SHARE MEDICINE PLAN

The 7-Steps medication review	
Steps	Person specific issues to Address
1. **Aims**： What matters to the individual about their condition(s)?	● Ensure a person-centred approach ● Consider non-pharmacological options where appropriate ● Consider if vulnerable or at risk of dependency
2. **Need**： Identify essential drug therapy	● Benzodiazepines and z-drugs used for anxiety or insomnia are not regarded as essential. They are only indicated for a maximum of two to four weeks ● If prescribed for long-term use consider potential of withdrawal reaction and provide support for reduction and stopping
3. Does the individual take unnecessary drug therapy?	● Not indicated for long-term use ● Consider the potential for harm
4. **Effectiveness**： Are therapeutic objectives being achieved?	● Can treatment be supported with non-pharmacological or psychological therapies where appropriate (such as sleep hygiene, CBT/cCBT resources)? ● Are alternative medicines more suitable for longer term management?
5. **Safety**： Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	● Consider risk of ADRs such as drowsiness, falls, memory impairment ● If treatment has been taken for long periods of time gradually taper to avoid withdrawal reactions. Abrupt cessation may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremors ● Consider if vulnerable or at risk of dependency
6. **Sustainability**： Is drug therapy cost-effective and environmentally sustainable?	● Check that all medicines are formulary choices ● Advise to only order what is needed, do not stockpile medicines ● Advise not to dispose of in household rubbish or in water waste. Promote safe disposal of medicines via community pharmacy

7. **Personcentredness**： Is the person willing and able to take drug therapy as intended?	Agreed plan ● Consider alternatives to prescribing where appropriate ● If the benzodiazepine or z-drug is to be stopped/ reduced then consider and agree reduction schedule with individual and set achievable goals ● Ensure awareness of potential for dependence or withdrawal effects, when to seek help and what actions to take ● Utilise available self help resources (e.g. NHS inform)

The majority of B-Z are prescribed by general practitioners (GPs) in primary care, however some of these prescriptions are initiated and continued on the advice of neurologists, psychiatrists and other specialists, and may result in deliberate or inadvertent long-term use.

For a very small minority of people long-term (≥8weeks) B-Z use may be considered appropriate, for example, in Parkinson's disease or epilepsy For the vast majority, long-term use of B-Z raises the risk of harm and runs contrary to current clinical guidelines and drug licensing, as B-Z are licensed for a maximum of four weeks duration.

B-Z use is associated with tolerance, dependence and avoidable drug-related harms.

These harms include but are not limited to:

- cognitive dysfunction (confusion, impaired concentration, memory impairment, impaired ability to drive and increased accidents)
- falls, and associated increased risk of hip fractures
- depressive symptoms
- paradoxical effects i.e. disinhibition, anxiety and impulsivity.

More recently studies have reported increased mortality associated with B-Z use in a range of populations.

In the short-term (e.g. less than two weeks) B-Z can provide some benefits for insomnia, and some anxiety disorders. However, they are associated with reducing the effectiveness of psychological therapies and worsening depressive symptoms, causing cognitive dysfunction which may prolong symptoms and slow recovery.

The use of benzodiazepines is not recommended for the management of muscle spasm associated with acute low back pain. Benzodiazepines should also not be used in the treatment of sciatica. It is acknowledged that they are used as muscle relaxants in other causes, such as managing muscle spasm pain in palliative care.

List 1: Benefits to reviewing benzodiazepines or z-drugs therapy

- Allows assessment of appropriateness and effectiveness of prescribing
- Allows reduction of inappropriate prescribing e.g. long-term
- Minimises risk of avoidable adverse harms associated with their use:
  - ✓ depression
  - ✓ emotional blunting
  - ✓ memory loss
  - ✓ paradoxical effects: anxiety, insomnia, aggression, etc.
  - ✓ falls and hip fractures
  - ✓ road traffic accidents
  - ✓ addiction and dependence
  - ✓ increased mortality risks
- An opportunity to consider more effective methods for treating symptoms

List 2: Groups of people that receive B-Z who could be prioritised for a proactive medicines review

- People recently discharged from hospital on new B-Z
- People receiving long-term (≥8 weeks) treatment
- Older adults (≥65 years)

- ✓ Care home residents
- ✓ People with dementia and/or receiving other medicines that may cause cognitive dysfunction e.g. anticholinergic medicines
- ✓ People receiving polypharmacy
- ✓ Higher risk of falls

- People receiving B-Z and opioids e.g. oxycodone, morphine, tramadol etc.
- People receiving other psychotropic medicines e.g. antidepressants, antipsychotics, gabapentinoids etc.
- People receiving high dose B-Z combinations: >30mg per day diazepam equivalent
- People receiving diazepam 10mg tablets – 'blues'
- People who report/present with street/non-prescribed B-Z use

People receiving long-term treatment (≥8weeks)

B-Z are only licensed for 28 days maximum use. Most studies are for short-term use (e.g. 7-14 days or less) and guidelines only recommend their use for management of short-term crises.

A very small minority of people may be considered appropriate for longer-term (≥8weeks) treatment e.g., some people with Parkinson's disease or multiple sclerosis, or as part of harm reduction strategies. However, long-term use is inappropriate for the large majority of people.

Older adults or frail people: avoidable adverse drug events/harms and polypharmacy

Older adults and frail people are more susceptible to the adverse effects and harms of B-Z: cognitive dysfunction (i.e. confusion, impaired concentration, memory impairment, impaired ability to drive and increased accidents); falls, and associated increased risk of hip fractures; depressive symptoms; and paradoxical effects i.e. disinhibition, anxiety and impulsivity.

They may also experience liver impairment or reduced kidney function which can reduce B-Z excretion, increasing the risk of adverse effects. Proactively reviewing, reducing and stopping B-Z will help to reduce avoidable B-Z-related harms.

People receiving combination treatment

Prescribers should consider the 'benzo-burden' – the total benzodiazepine-type medicine load prescribed per day – as benzodiazepines, z-drugs and gabapentinoids provide synergistic effects such as sedation and respiratory depression. All may interact with the individual's conditions to cause more adverse effects and avoidable drug-related harms e.g. increased breathlessness, fatigue, respiratory depression, which can be potentially fatal.

Opioids

The effects of B-Z and the 'benzo-burden' can be further exacerbated by the addition of a range of opioids, and even reduce the protective ceiling effects of buprenorphine. In line with the Medicines and Healthcare products Regulatory Agency advice, only prescribe B-Z and opioids together if there is no alternative and closely monitor individuals for signs of respiratory depression.

Non-prescribed B-Z

People who report street/non-prescribed B-Z use, often within the context of polysubstance use, are arguably at greatest risk of combination effects. To respond to what is recognised as a public health crisis, recent guidance, including key principles of care, are outlined in the Scottish Drug Deaths Taskforce and Public Health Scotland's Medication Assisted Treatment (MAT) standards informed response for benzodiazepine harm reduction.

Antidepressants

B-Z use is associated with the use of selective serotonin re-uptake inhibitors (SSRIs), and the use of higher SSRI doses for the treatment of depression. In part this may be due to higher SSRI doses causing more avoidable adverse effects such as anxiety, agitation and insomnia. However, B-Z are also associated with an increased

incidence of depressive symptoms. Therefore, person-centred review and reducing B-Z using the 7-Steps process may help to optimise care and recovery.

Antipsychotics

B-Z use is associated with a higher mortality risk for people with schizophrenia. Although some have argued that B-Z provide antipsychotic sparing effects, this is not supported by current evidence.

Psychological therapies

B-Z may limit the efficacy of psychological therapies such as CBT due to negative effects on cognitive function; impairing memory function and amnesia.

High dose combination B-Z use

As highlighted above the use of more than one B-Z will increase the 'benzo-burden' and provide synergistic effects which may lead to avoidable adverse effects and harms. Minimising the use of such combinations and high doses of B-Z will help to minimise adverse drug effects, see Reduction schedules. It is important to consider if benzodiazepines are being bought alongside those that are being prescribed.

Diazepam 10mg tablets

Historically these have enabled people to take higher doses with fewer tablets and have been desirable for those using substances illicitly. Due in part to these issues, where diazepam is required, multiples of 2mg tablets should be prescribed as the preferred choice.

Potential exclusions and cautions

It has already been acknowledged that a small minority of individuals may require long-term treatment. However, it would be good practice to routinely review ongoing need, e.g. as part of their routine annual medicines review.

It may be appropriate to consider excluding some people from proactive B-Z reduction reviews for example, in palliative care, people under the care of drug

treatment services or those with intractable epilepsy. However, closer working with specialist services may in some cases support the appropriate use and reduction of B-Z, such as linking with community mental health teams to minimise B-Z use in people with schizophrenia, where there is an association with increased mortality risk. For those presenting at greatest risk of harm from street B-Z use, both psychosocial and prescribing interventions may support harm reduction and establish stability with regular monitoring and review.

List 3: Clinical presentation of discontinuation/withdrawal symptoms

Acute symptoms - most commonly anxiety

- Panic attacks, agoraphobia
- Insomnia, nightmares
- Depression
- Poor memory, loss of concentration
- Tremor, sweating, palpitations

Acute symptoms - others specific to B-Z

- Perceptual distortions, depersonalization
- Tingling and loss of sensation, formication (a feeling of ants crawling all over the skin)
- Sensory hypersensitivity
- Muscle twitches and fasciculations (flickering or writhing muscles)
- Hallucinations (visual and auditory - rare and usually with rapid withdrawal from high doses)
- Psychotic symptoms, confusion, convulsions (rare and usually with rapid withdrawal from high doses)

Protracted symptoms - may affect up to 15% of people

- Anxiety - gradually recedes over a year
- Depression - may be a few months
- Insomnia - gradually recedes over 6-12 months
- Sensory symptoms - gradually recedes but may be a year and occasionally several years
- Motor symptoms - gradually recedes but may be a year and occasionally several years
- Poor memory and cognition - gradually recedes but may be a year and occasionally several years
- GI symptoms - gradually recedes but may be a year and occasionally several years

Adapted from the Ashton Manual and Maudsley Prescribing guidelines.

Switching to diazepam

Diazepam is a longer acting B-Z. If alternative benzodiazepines are being taken, converting to the equivalent diazepam dose allows for smaller dose reductions steps, due to the range of licensed preparations available. Diazepam's longer acting effects are less likely to be associated with withdrawal effects; especially for people receiving short acting B-Z and/or experiencing high levels of dependency.

Therefore this is the preferred method for gradual reduction.

Some individuals however may want to reduce by continuing their current B-Z. While this may be possible with nitrazepam and temazepam, due to a range of licensed preparations being available, it may be more challenging with other B-Z due to the range of tablet doses available. As a result the size of the dose reduction steps may be large - increasing the potential risk of withdrawal effects. Where individuals decide to reduce using their current B-Z, the risk-benefits should be discussed and closer follow up may be required.

Approximate dose equivalents and switching considerations:

- Due to individual variability and differing half-lives (Table 2) this means that these are approximate dose equivalents, not exact equivalence.
- Variability between individuals may be due to a range of effects e.g. liver impairment reducing/slowing drug excretion, which can increase B-Z half-lives and increase the risk of accumulation and drug effects.
- Dose equivalents can never be exact and should be interpreted considering your clinical knowledge and the individual's needs. Older adults and frail people may experience next day sedation due to the long half-life of diazepam.
- Drug interactions and drug-disease interactions should be considered.
- Dose equivalents vary between authors, they are based on clinical experience but may vary between individuals.

Table: Approximate equivalent doses

Drug	Approximate equivalent dose	Half-life (hours) (active metabolite)
Diazepam	**5mg**	**20 – 100 (36 – 200)**
Chlordiazepoxide	**12.5mg**	**5 – 30 (36 – 200)**
Clobazam*	**10mg**	**12-60**
Clonazepam*	**0.25mg (250mcg)**	**18 – 50**
Loprazolam	**0.5mg (500mcg) -1mg**	**6 – 12**
Lorazepam	**0.5mg (500mcg)**	**10 – 20**
Lormetazepam	**0.5mg (500mcg) -1mg**	**10 – 12**
Oxazepam	**10mg**	**4 – 15**
Nitrazepam	**5mg**	**15 – 38**
Temazepam	**10mg**	**8 – 22**
Zolpidem	**10mg**	**2**
Zopiclone	**7.5mg**	**5 – 6**

* Clobazam and clonazepam may be prescribed for intractable epilepsy, caution if considering reducing dose

Appendix 5. Patient information leaflet

Background

Benzodiazepines and z-drugs, also known as sedatives, anxiolytics and sleeping tablets, have limited therapeutic effects, and are known to cause a range of avoidable adverse drug effects and harms. Dependence (both physical and psychological) and tolerance (loss of effect) can develop quickly within weeks of starting them. Therefore, when they are needed, they should only be prescribed for a short course (e.g. maximum of seven days). However, some individuals may have received longer courses of treatment which may lead to difficulty withdrawing the drug after taking it regularly for more than a few weeks. It also exposes individuals to avoidable drug-related harms which can be reduced by reviewing, reducing and stopping treatment where appropriate.

What is the purpose of the benzodiazepines and z-drugs quality prescribing guide?

It is intended to:

- Empower and help people who receive benzodiazepines and/or z-drugs, and prescribers to review these medicines to ensure the best treatment for the individual.
- Improve the support available from the healthcare system for individuals experiencing dependence on, or withdrawal from, prescribed medicines.
- Help prescribers identify individuals who may benefit from a benzodiazepine and/or zdrug review and support routine medicines reviews.
- Provide a range of options, where appropriate, for individuals that have completed their course of benzodiazepines and/or z-drug treatment and are appropriate to reduce and stop their benzodiazepine and/or z-drug.

Do I need to have my benzodiazepines and z-drug reviewed?

- Yes, as benzodiazepines and z-drugs:
  - Have limited effects for reducing anxiety, insomnia and muscles spasms.
  - Are known to be associated with a range of avoidable adverse effects and harms:

- depression and low mood
- memory loss and dementia
- falls and hip fractures
- increase in road traffic accidents
- paradoxical effects: insomnia, anxiety, irritability, etc.
- addiction

- Having medicines reviewed regularly creates an opportunity to discuss if a medicine needs to continue and consider effective non-medicine treatments and lifestyle changes that may help.

Do I need to stop my benzodiazepines and z-drug?

- It may be appropriate for some individuals to stop, but not for others.
- Continuing treatment maybe appropriate because there are more benefits to continuing than risks of stopping treatment e.g. epilepsy, Parkinson's disease.
- Reducing and/or stopping may be necessary to reduce the risk of avoidable adverse effects and harms e.g. falls, confusion, sedation, etc.

How should I stop my benzodiazepines and z-drugs?

If you are ready to stop your benzodiazepines and z-drugs:

- Arrange a review with your general practice doctor, pharmacist or nurse.
- Discuss stopping your medicine and agree if this is appropriate.
- If appropriate to stop, then plan and agree the best way to do this for you considering the options outlined in the benzodiazepines and z-drug quality prescribing guide.

Benzodiazepine and Z-drug Prescribing: Resource Pack 2021

Great Manchester Medicines Management Group

https://gmmmg.nhs.uk/wp-content/uploads/2021/08/Benzodiazepine-and-Z-drug-Resource-Pack-GMMMG-FINAL-v1-0-for-GMMMG-website.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Foreword

1. This document brings together a number of resources clinicians can use to support the appropriate use and review of benzodiazepines and Z-drugs.
2. Risks associated with the long-term use of benzodiazepine and Z-drug hypnotic drugs have been well recognised for many years.
3. These risks include falls, accidents, cognitive impairment, dependence, withdrawal symptoms and an increased risk of dementia and are increased in the elderly.
4. Benzodiazepines and Z-drugs should not routinely be prescribed and where they are used, the lowest dose that controls symptoms should be prescribed for the shortest period of time.
5. Recent data suggests similar safety concerns with melatonin and there is a risk some Prescribers see melatonin as a “safer option” to benzodiazepines and Z-drugs.
6. Melatonin MR (Circadin) is licensed as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in people aged 55 years or over, for a maximum duration of 13 weeks treatment. GMMMG have advised melatonin is not recommended for the routine treatment of primary insomnia characterized by poor quality sleep in patients who are aged 55 years or over.

7. Melatonin MR (Slenyto) is licensed for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient. GMMMG have classified use of melatonin in ADHD as amber and the relevant shared care protocol should be followed.
8. The British National Formulary (BNF) advises that Prescribers have three main responsibilities when prescribing drugs likely to cause dependence or misuse:
   - To avoid creating dependence by introducing drugs to patients without sufficient reason.
   - To see that the patient does not gradually increase the dose of a drug, given for good medical reasons, to the point where dependence becomes more likely.
   - To avoid being used as an unwitting source of supply for addicts and being vigilant to methods for obtaining medicines.
9. The information and supporting resources within this document will support GP Practices deliver the recommendations included within the PHE report on drugs of dependence.

NICE Guidance

10. NICE does not recommend the routine use of benzodiazepines and Z-drugs in any guidance.
11. Where use of these drugs is included in NICE guidance it is for specific situations only, severe symptoms and always for short term use.

Practice resources

Appendix 1: Summary of NICE guidance

Self-Care

12. Sleep hygiene aims to make people more aware of behavioural, environmental, and temporal factors that may be detrimental or beneficial to sleep.
13. Regular exercise may have a beneficial effect on both the quality and quantity of sleep and has been shown to improve anxiety symptoms.

14. Relaxation techniques can help people to control their anxiety and there are various relaxation techniques that can be used to calm the mind and reduce the muscle tension anxiety can cause.
15. NHS Mental health and wellbeing offers practical advice, interactive tools, videos and audio guides to help people feel mentally and emotionally better: https://www.nhs.uk/conditions/stress-anxiety-depression/
16. The Royal College of Psychiatrists website contains useful information for patients on a number of conditions including:

    Insomnia:

    https://www.rcpsych.ac.uk/mental-health/problems-disorders/sleeping-well?searchTerms=sleeping%20well

    Anxiety:

    https://www.rcpsych.ac.uk/mental-health/problems-disorders/anxiety-panic-and-phobias

    Practice Resources

    Appendix 2: The Good Sleep Guide

    Appendix 3: The Good Relaxation Guide

    Appendix 4: Relaxation Exercises

Initiating Benzodiazepines and Z-drugs

17. Establish current sleep/anxiety patterns with the help of sleep/anxiety diaries.
18. Manage any underlying conditions.
19. Ensure referral into appropriate services.
20. Provide relevant self-care advice.
21. Only use benzodiazepines and Z-drugs when symptoms are severe and alongside non-drug options (see appendix 1 for summary of NICE guidance).
22. Avoid hypnotic medication in older people and women who are pregnant or breastfeeding.
23. Prescribe in accordance with GMMMG formulary, using the lowest effective dose for the shortest period possible ensuring an appropriate quantity is issued:
    - Insomnia – 2 weeks maximum
    - Anxiety – 2-4 weeks only

24. Benzodiazepine doses in the elderly and the frail should be much lower than the usual adult dose; often about half the adult dose and a short-acting benzodiazepine may be preferred.
25. Benzodiazepine doses should be reduced in impaired liver or kidney function.
26. Ensure patients are aware of the risks of treatment, including effect on driving, interaction with alcohol and interaction with opioid pain killers or other sedative drugs.
27. Inform the patient that further prescriptions for hypnotics will not usually be given, ensure that the reasons for this are understood, and document this in the medical record.
28. Prescribe small quantities and do not issue further prescriptions without consultation.
29. If there has been no response to the first hypnotic, do not prescribe another.
30. Issue the prescription as an acute item. Do not add benzodiazepines and Z-drugs to repeat prescriptions.

Practice Resources

Appendix 2: The Good Sleep Guide

Appendix 3: The Good Relaxation Guide

Appendix 4: Relaxation Exercises

Appendix 7: What to discuss with the patient when considering use of a Benzodiazepine or Z-drug

Appendix 10: Patient Information Leaflet – Sleeping Tablets

Appendix 11: Patient Information Leaflet – Benzodiazepines for Anxiety

Managing Patient Expectation

31. Where new patients are prescribed benzodiazepines and Z-drugs ensure the patient is aware that the medication is for short-term use only and that self-care advice should also be followed.
    - Insomnia – 2 weeks maximum
    - Anxiety – 2-4 weeks only

32. When new patients join the Practice, who are already prescribed these drugs ensure they are aware of any Practice policies in place.

Practice Resources

Appendix 12: Benzodiazepines and Z-drug Policy

Responsibility for Prescribing

33. Where practical, the patient should receive prescriptions from a single prescriber.
34. If the patient needs a prescription from someone other than the usual prescriber, documentation should be clear and accurate to support consistency of safe care.

Practice Resources

Appendix 12: Benzodiazepines and Z-drug Policy

Repeat Prescribing

35. In general, benzodiazepines and Z-drugs should not be added to the repeat prescribing system but should be generated as acute prescriptions.

Practice Resources

Appendix 12: Benzodiazepines and Z-drug Policy

Greater Manchester Formulary

	First choice	**Second choice**
Insomnia	Zopiclone	Zolpidem Temazepam
Anxiety	Diazepam	N/A

Practice Resources

Appendix 14: Benzodiazepine and Z-drug approximate equivalent doses to diazepam 5mg and duration of action

Stopping Benzodiazepines and Z-drugs in Primary Care

36. 'Almost anyone who really wants to come off can come off benzodiazepines'.

38. Withdrawal should be gradual (dose tapering, such as 5-10% reduction every 1-2 weeks, or an eighth of the dose fortnightly, with a slower reduction at lower doses), and titrated according to the severity of withdrawal symptoms.
39. Discuss with the person the potential complications of long-term benzodiazepine or Z-drug use and the benefits of stopping and enquire about their willingness to withdraw from the drug.
40. Assess whether this is a suitable time to stop taking the drugs.
    - The chances of success are improved when a person's physical and psychological health and personal circumstances are stable.
    - Symptoms of depression. Withdrawing these drugs can worsen symptoms of clinical depression. The priority is to manage depression first, before attempting drug withdrawal.
    - Symptoms of anxiety. Withdrawing treatment when significant symptoms of anxiety are present is likely to make symptoms worse and is therefore unlikely to succeed. However, when symptoms are reasonably well controlled and stable it may be possible to attempt careful drug withdrawal.
    - Symptoms of long-term insomnia. If insomnia is severe, consider addressing this with non-drug treatments prior to starting withdrawal of a benzodiazepine or Z-drug.
    - Any medical problems and whether these are well controlled and stable. If problems are causing significant distress, consider managing these first, prior to starting withdrawal of benzodiazepines or Z-drugs.
    - Consider whether the withdrawal of the benzodiazepine or Z-drug can be appropriately managed in primary care.
41. There are two approaches:
    a. slow dose reduction of the person's current benzodiazepine or Z-drug
    b. switching to an approximately equivalent dose of diazepam and then tapering down (seek specialist advice for patients with hepatic dysfunction and see CKS advice for more details about when switching to diazepam should be considered)
42. Agree and document the agreed tapering schedule and the outcomes of tapering e.g. stopping benzodiazepine or Z-drug completely; for patient on high doses reducing the dose to an agreed level may be appropriate.

43. Tapering can be paused but should not be reversed except in exceptional circumstances.
44. As the taper progresses, the reduction becomes a larger proportion of the dose that the patient is taking. This is why patients may run into difficulty as they reach lower doses. Consider smaller dose reductions as the dose becomes lower but warn the person not to be tempted to prolong the drug withdrawal to an extremely slow rate towards the end (such as reducing by 250 microgram diazepam each month). Advise the person to consider stopping completely when they reach an appropriate low dose (such as diazepam 1 mg daily).
45. Ensure the patient is aware of the arrangements for monitoring and available support during dose tapering.
46. Provide resources such as patient information leaflets in addition to information about local and national support groups.
47. Advise the person against taking extra tablets in times of stress and compensating for benzodiazepines or Z-drugs by increasing the intake of alcohol or other drugs (prescription, non-prescription, or illicit drugs) or smoking.
48. Consider seeking specialist advice, or referral to an appropriate specialist for people with:
    - A history of alcohol or other drug use or dependence - be aware that heavy users of alcohol may use it as a substitute for the drug being withdrawn.
    - Concurrent, severe medical or psychiatric disorder or personality disorder.
    - A history of drug withdrawal seizures - these generally occur in people who suddenly stop high doses of the drugs. Slow tapering is recommended for these individuals.

Practice Resources

Appendix 7: What to discuss with the patient when considering use of a benzodiazepine or Z-drug

Appendix 14: Benzodiazepine and Z-drug approximate equivalent doses to diazepam 5mg and duration of action

Appendix 16: Patient Information Leaflet – Stopping your medicines: Benzodiazepines and Z-drugs

Appendix 17: Suggested withdrawal for long-term Benzodiazepines and Z-drugs

What If the Patient isn't Keen?

49. General Medical Council (GMC) guidance is that doctors have to act in the patient's best interests.
50. In many people who are concerned about stopping treatment despite explanation and reassurance, persuading them to try a small reduction in dose may help them realise that their concerns are unfounded. In some cases, it may be necessary to suggest review at a later date.
51. On rare occasions, it may be necessary to reduce a benzodiazepine or Z-drug prescription against the patient's wishes e.g. a high-risk patient.
52. An enforced wean should only be considered if all attempts to engage the patient have failed and following a multi-disciplinary team (MDT) discussion. Where possible specialist services e.g. addiction services should be contacted for advice.
53. Document your reasons for embarking on an enforced wean and on your attempts to gain patient agreement.
54. If you have been unable to gain the patient's agreement to reduce their benzodiazepine or Z-drug and an enforced wean is necessary, a suggested strategy is:
    - Pick a reduction dose.
    - Inform the patient that you will reduce their prescription by that amount every month. They can decide at what point during the month they wish to reduce their intake but need to be ready for the lower dose when they collect their next prescription.
    - Make sure you implement the dose reductions.
55. You will need to ensure that the patient is not inadvertently prescribed benzodiazepines or Z-drugs by colleagues. This requires good communication within the Practice, with locum services and, if necessary, out of hours and emergency services.

Practice Resources

Appendix 7: What to discuss with the patient when considering use of a benzodiazepine or Z-drug

Appendix 14: Benzodiazepine and Z-drug approximate equivalent doses to diazepam 5mg and duration of action

Appendix 16: Patient Information Leaflet – Stopping your medicines: Benzodiazepines and Z-drugs

Appendix 17: Suggested withdrawal for long-term Benzodiazepines and Z-drugs

Withdrawal Symptoms

56. Withdrawal symptoms occur if benzodiazepines and Z-drugs are stopped or reduced abruptly and so doses should be gradually reduced.

57. The benzodiazepine withdrawal syndrome may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine but may occur within a day in the case of a short-acting one. It is characterised by insomnia, anxiety, loss of appetite and of body weight, tremor, perspiration, tinnitus, and perceptual disturbances. These symptoms may mimic the original anxiety disorder. Abrupt withdrawal may produce confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens.

58. Z-drug withdrawal symptoms include insomnia/sleep disturbance, anxiety, depression, impaired concentration, abdominal cramps, palpitations, and perceptual disturbances (such as hypersensitivity to physical, visual and auditory stimuli).

59. Nearly all the acute symptoms of withdrawal are those of anxiety. Some of the withdrawal symptoms may be similar to the original complaint but do not indicate its return.

60. With slow tapering, many people experience few or no withdrawal symptoms. If withdrawal symptoms are present, some users will have lost all their symptoms by the end of the drug withdrawal schedule. For most people, symptoms will disappear within a few months. Only a very small number of people will suffer from protracted withdrawal symptoms which will gradually improve over a year or longer.

61. The risk of withdrawal symptoms increases with longer use, higher dosage, and higher potency.

Practice Resources

Appendix 17: Suggested withdrawal for long-term Benzodiazepines and Z-drugs

Practice Strategies for Reduction of Long-Term Benzodiazepine and Z-drug Prescribing

62. Practices should audit their prescribing to identify patients suitable for withdrawal and to assess compliance with Practice policies and procedures.
63. There is evidence that sending educational letters/leaflets to patients explaining the problems associated with long term benzodiazepine and Z-drug use and encouraging them to gradually step down, is a successful intervention, even in patients who have previously been advised (or attempted) to reduce.
64. It is recommended that practices send an educational letter to all suitable patients, possibly on annual basis.
65. Practices could work with Care Homes by trialling PRN use of these drugs rather than regular use.
66. Deprescribing.org has produced a benzodiazepine and Z-drug deprescribing algorithm which has been endorsed by NICE which practices may find useful.

    https://deprescribing.org/wp-content/uploads/2019/02/BZRA-deprescribing-algorithms-2019-English.pdf
67. The Royal College of General Practitioners have produced a series of fact sheets about prescribed drug misuse which includes an approach to managing dependence on prescribed medication.

Practice Resources

Appendix 10: Patient Information Leaflet – Sleeping Tablets

Appendix 11: Patient Information Leaflet – Benzodiazepines for Anxiety

Appendix 16: Patient Information Leaflet – Stopping your medicines: Benzodiazepines and Z-drugs

Prescribing Drugs Likely to Cause Dependence or Misuse

68. The BNF advises that Prescribers have three main responsibilities when prescribing drugs likely to cause dependence or misuse:
    - To avoid creating dependence by introducing drugs to patients without sufficient reason.
    - To see that the patient does not gradually increase the dose of a drug, given for good medical reasons, to the point where dependence becomes more likely. The prescriber should keep a close eye on the amount prescribed to prevent patients from accumulating stocks. A minimal amount should be prescribed in the first instance, or when seeing a patient for the first time.
    - To avoid being used as an unwitting source of supply for addicts and being vigilant to methods for obtaining medicines. Methods include visiting more than one doctor, fabricating stories, and forging prescriptions.
69. The Royal College of General Practitioners has developed a Top Ten Tip: Dependence Forming Medications document which Practices may find useful:

    https://www.rcgp.org.uk/-/media/Files/CIRC/Desktop-guides/Top-Ten-Tips-Dependence-Forming-Medications-April-2019.ashx?la=en
70. Patients under temporary care should only be given small supplies of drugs unless they present an unequivocal letter from their own doctor.
71. Prescribers should also remember that their own patients may be attempting to collect prescriptions from other prescribers, especially in hospitals.

    Practice Resources

    Appendix 12: Benzodiazepines and Z-drug Policy

Identification of Prescription Benzodiazepine and Z-drug Dependent Patients

72. Dependence often presents in one or more of the following ways:
    - Patients gradually ‘need’ benzodiazepines to carry out normal day-to-day activities.
    - Patients continue to take benzodiazepines although the original indication for the prescription is no longer relevant.
    - Patients have difficulty in stopping treatment or reducing the dosage due to withdrawal symptoms.

- Short-acting benzodiazepines may cause patients to develop anxiety symptoms between doses.
- Patients contact their doctor regularly to obtain repeat prescriptions.
- Patients become anxious if the next prescription is not readily available.
- Patients may increase the dosage stated in the original prescription.
- Despite benzodiazepine therapy, patients may present with recurring anxiety symptoms, panic, agoraphobia, insomnia, depression and an increase in physical symptoms of anxiety.
- Taking higher doses than prescribed or running out of prescribed medication before expected
- Continually 'losing' medication so more prescriptions have to be written
- Seeking prescriptions from more than one healthcare professional, e.g., doctor, nurse, non-medical prescriber or from more than one practice
- Requesting a specific drug claiming that other medications 'don't work' or that (s)he is allergic to them
- Stealing, forging or diverting prescriptions
- Appearing to be intoxicated, sedated or experiencing withdrawal
- Excessive mood swings or hostility
- Increase or decrease in sleep
- Evidence of craving or other signs of dependence

73. Risk factors for benzodiazepine/z-drug dependence may include:

- Drug dose and length of exposure — frequent, long-term, high dose users are more likely to become dependent.
- Use of benzodiazepines with high potency and short elimination half-lives (such as lorazepam and alprazolam)— may lead to development of anxiety symptoms between doses, leading to more frequent dosing.
- Onset of effect — more fat-soluble drugs (such as diazepam) are absorbed faster and enter the central nervous system more rapidly, Rapid-onset drugs are associated with 'good' subjective effects, and therefore result in psychological reinforcement every time they are taken. Higher dose leads to better subjective effects.

- A history of current or past alcohol or other sedative-hypnotic dependence, or a family history of these.
- Use of recreational drugs.
- Co-morbid chronic psychiatric and personality problems, physical health problems (especially in older people), pain problems, or sleep difficulties.
- Age 16–45 years.
- Older people with complex physical and psychological needs complicated by pain.
- History of pre-adolescent sexual abuse.
- Certain psychological diseases (ADHD, obsessive–compulsive disorder, bipolar disorder, schizophrenia, depression).
- Exposure to peer pressure or a social environment where there is drug abuse.
- Easier access to prescription drugs, such as working in a healthcare setting.
- Lack of knowledge or understanding of the prescriber

74. It is sensible to reduce dosages steadily or to issue weekly or daily prescriptions for small amounts if it is apparent that dependence is occurring.

Practice Resources

Appendix 12: Benzodiazepines and Z-drug Policy

Appendix 17: Suggested withdrawal for long-term Benzodiazepines and Z-drugs

Appendix 1: Summary of NICE Guidance

Medicines Optimisation Key Therapeutic Topic – Hypnotics

Only use hypnotics if insomnia is severe, using the lowest dose that controls symptoms for the shortest period of time.

Z-drugs and the shorter-acting benzodiazepine hypnotics should only be considered for severe insomnia interfering with normal daily life.

They should be prescribed for short periods of time only, in strict accordance with their licensed indications.
There is no compelling evidence to distinguish between zolpidem, zopiclone or the shorter-acting benzodiazepine hypnotics.

Patients who have not responded to one of these hypnotic drugs should not be prescribed any of the others (switching from one of these hypnotics to another should only occur if a patient experiences adverse effects considered to be directly related to a specific agent).

NICE CKS Insomnia

If a hypnotic is required for insomnia the recommended choices are:

- Non-benzodiazepines (the 'z-drugs') – zopiclone and zolpidem (all are short acting).
- Short-acting benzodiazepines - temazepam, loprazolam, lormetazepam.
- Diazepam is not generally recommended, but it can be useful if insomnia is associated with daytime anxiety, prescribe 5 - 15 mg at bedtime.

Use the lowest effective dose for the shortest period possible. Treatment should not continue for longer than 2 weeks.

Sedative drugs other than hypnotics (such as antidepressants, antihistamines, chloral hydrate, clomethiazole, and barbiturates) are not recommended for the management of insomnia. Expert opinion from reviews suggests that there is insufficient evidence to support their use, and that the potential for adverse effects is significant.

Generalised anxiety disorder and panic disorder in adults: management (CG113)

Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short-term measure during crises. Benzodiazepines are associated with a less good outcome in the long term.

Benzodiazepines are associated with a less good outcome in the long term and should not be prescribed for the treatment of individuals with panic disorder.

CKS Generalised Anxiety Disorder

If a benzodiazepine is required for anxiety the recommended choice is diazepam:

- For anxiety, prescribe 2 mg three times a day.
- If needed, the dose can be increased to 15–30 mg daily in 3 divided doses
- Caution in the elderly, due to the increased risk of falls — the manufacturer advises halving the recommended doses.

Treatment should not Exceed 2–4 Weeks.

Depression in adults: recognition and management and Depression in adults with a chronic physical health problem: recognition and management

Benzodiazepines are only to be considered as an option if a person with depression prescribed an SSRI develops the side effects of anxiety, agitation and/or insomnia early in antidepressant treatment and symptoms are problematic. In this case short-term concomitant treatment with a benzodiazepine is one of several options that can be considered.

If a benzodiazepine is prescribed this should be for no longer than 2 weeks in order to prevent the development of dependence.

Benzodiazepines should not be used in people with chronic symptoms of anxiety.

Benzodiazepines should be used with caution in patients at risk of falls

Appendix 2: Patient Information Leaflet - The Good Sleep Guide

Develop a Regular Sleep Pattern

- Go to bed only when sleepy. Do not use the bedroom for anything but sleep (or intimacy).
- Set the alarm for the same time every morning for seven days a week, at least until your sleep pattern settles down.
- Get up at the same time every day, even if you did not fall asleep until late.
- Do not sleep during the day.

Look after Yourself

- Try to keep yourself fit by doing light exercise in the late afternoon or early evening (later than this can disturb your sleep).
- Avoid caffeine after noon.
- Avoid nicotine, alcohol, exercise and big meals within 2 hours of bedtime.
- Reduce the amount of caffeine you drink, such as coffee, tea and some soft drinks. Try decaffeinated milk-based or herbal drinks. Consider complete elimination of caffeine from your diet.
- Only have a light snack for supper.
- Keep your sleep for bedtime, avoid falling asleep or snoozing in the chair.

During the Evening

- Put the day 'to rest'. Think it through and use a notebook if needed. Tie up 'loose ends' in your mind and plan ahead.
- Have a regular routine before sleep, wind down during the course of the evening and avoid anything that is mentally demanding within 90 minutes of bedtime.

At Bedtime

- Go to bed when you are 'sleepy tired' and not before.
- Do not read or watch TV in bed.
- Turn the lights off when you get into bed.
- Relax and tell yourself that 'sleep will come when it's ready'. Enjoy relaxing even if you don't fall asleep at first.
- Do not try to fall asleep. Sleep cannot be switched on deliberately, but trying to do so may switch it off!

If You have Problems Getting to Sleep

- Make sure your bed is comfortable and the bedroom is not too cold or too warm and is quiet (use earplugs if necessary).
- Try not to get upset or frustrated as sleep problems are quite common and they are not as damaging as you might think.

- If you are awake in bed for more than 20-30 minutes, get up and go into another room.
- Do something relaxing for a while and don't worry about comorrow. Read, watch television or listen to quiet music and after a while you should feel tired enough to go to bed again.
- If not asleep within 20-30 minutes of returning to bed, repeat.
- Remember that people usually cope quite well even after a sleepless night. Only return to bed when you feel 'sleepy tired'.
- Developing a good sleep pattern may take a few weeks, however, you should remain confident that you will achieve it by working through this guide.
- Do not drink alcohol to help you sleep. It may help you fall asleep, but you will almost certainly wake up during the night.

Appendix 3: The Good Relaxation Guide

Dealing with Tension

- Finding and dedicating time to relax is essential. Give relaxation some of your best time, not just what's left over.
- Include relaxing things in your everyday life. Do not rush tasks or try too hard to resolve problems.
- Start a relaxation routine, but do not expect to learn without practice. Routines are available (audio recordings) which help to relieve muscle tension and teach you how to use breathing to help you relax.
- Try not to worry about tension symptoms, such as aches, stiffness, increased heart rate, sweating, stomach churning, etc.
- Keep fit and take part in regular exercise. Regular brisk walks or swimming can help relieve tension.
- Enjoy quiet moments, sit and listen to relaxing music, allow your mind to wander, picture yourself in pleasant situations.

Dealing with Worry

- Accept that worrying is normal and sometimes it may be useful - everyone worries sometimes.
- Write down your worries and decide which ones are more important.
- Work out a plan of action for each worry.
- Share your worries with friends, relatives or your GP, who may be able to give you helpful advice.
- Reading, crosswords, hobbies and interests can all help keep your mind active and positive.

Dealing with Difficult Situations

- Accept and confront situations that make you feel more anxious. BY
- Take a step-by-step approach to help face things and places which make you feel tense.
- Write a plan of how you are going to deal with difficult situations.
- Regular practice will help you overcome your anxiety.
- Reward yourself when you do well and tell other people.
- As you face up to difficult situations your anxiety symptoms should become less troublesome and your confidence will grow.
- Everyone has good and bad days. Expect more good days as time goes on.

Planning

Put together a plan based on the information in this guide and practice regularly. If something does not work, do not worry, change it and see what happens. Remember that expert guidance and advice is available if you need more help.

Relaxing is about slowing things down. Everyone is different — experiment until you find your best way to relax. Remember ten minutes ‘out’ of a busy day is a good investment for your health and well-being.

More information can be Found at:

https://www.nhs.uk/conditions/stress-anxiety-depression/

On the link below you will find a series of mental wellbeing podcasts or audio guides that you can listen to, to help you through times when your mood is low or you are feeling anxious. The series includes anxiety control training — guided relaxation; low mood and depression; overcoming sleep problems; low confidence and assertiveness; and unhelpful thinking.

https://www.nhs.uk/conditions/stress-anxiety-depression/moodzone-mental-wellbeing-audio-guides/

Appendix 4: Relaxation Exercises

There are various relaxation exercises that you can use to calm the mind and reduce the muscle tension that anxiety can cause.

You should try to set aside 30 minutes, 2 or 3 times each day to practise these techniques. The more you practise, the better you will get and the more effective they will be. It is important to keep using these techniques, even if you don't feel better straight away. It will take time and regular practise before you start to feel the benefits.

Relaxation Preparation

Before you start relaxing, make sure your mind, body and surroundings are just right. To prepare yourself:

- Find a cool and quiet room where you won't be disturbed
- Make sure your clothes are comfortable and take off your shoes
- Lie down or sit comfortably with your legs uncrossed
- Lightly close your eyes, or focus on a spot in front of you
- Clear your thoughts and focus on your breath

Don't worry if you can't relax immediately. Thoughts might pop into your mind. Don't focus on them, just let them pass through.

Breathing to Relax

Breathing too quickly and deeply can make you feel dizzy, faint or even more anxious. Taking slow, regular breaths can help you to control anxious thoughts and feelings and make you feel calmer.

To Control Your Breathing:

- Place one hand on your chest and the other over your stomach. You want your stomach to move more than your chest as you breathe
- Take a slow, regular breath in (through your nose if you can). Watch your hands as you breathe in. The hand on your stomach should move and your chest should not
- Breathe out slowly through pursed lips
- Repeat this 10 times, twice a day

It might take time to master this technique. Once you have, you won't need to watch your hands or put them on your chest and stomach.

Simple Visualisation Exercise

In your mind create an ideal spot to relax - your relaxation place:

- Somewhere you will find restful, calming, safe and happy
- A place you would want to return to whenever you feel the need to relax
- It can be a real place or imaginary

Imagine your relaxation place in as much detail as you can — use your senses to make it as real as possible — and see yourself comfortably enjoying this place.

Now close your eyes and take a slow, regular breath in through your nose. Become aware of your breathing. Focus on your relaxation place in all its detail and breathe out through your mouth. Do this exercise for 10 to 20 minutes.

Quick Muscle Relaxation

You can relieve tension in any part of your body just by tensing and relaxing each muscle in turn. If you have any physical injuries or conditions that may cause muscle pain, don't tense the muscle in that area.

- Sitting in a comfortable chair close your eyes and concentrate on your breathing. Slowly breath in through your nose and out through your mouth.
- Hands: Clench one hand tightly for a few seconds as you breathe in. You should you're your forearm muscles tense; then relax as you breathe out. Repeat with the other hand.
- Arms: Bend an elbow and tense all the muscles in the arm for a few seconds as you breathe in; then relax as you breathe out. Repeat the same with the other arm.
- Face: Try to frown and lower your eyebrows as hard as you can for a few seconds; then relax. Then raise your eyebrows (as if you were startled) as hard as you can; then relax. Then clench your jaw for a few seconds; then relax.
- Shoulders: Raise your shoulders as high as you can as you breathe in; then relax as you breathe out.
- Neck: Press your head back as hard as is comfortable and roll it slowly from side to side; then relax.
- Legs: Bend your feet and toes towards you as hard as you can; then relax. Then bend them away from you for a few seconds; then relax.

After Relaxation

Don't rush to get up after relaxation exercises. Sit with your eyes closed for a few minutes to avoid the possibility of feeling dizzy. Open your eyes and make sure you feel all right before you stand up.

Appendix 7: what to Discuss With the Patient When Considering Use of a Benzodiazepine or Z-drug

- Ensure the patient is aware that the medication is for short-term use alongside self-care.
- Ensure patients are aware of the risks of treatment including Central Nervous System (CNS) depressant effects, including 'hangover' effects, unsteadiness, reduced alertness and impaired memory, tolerance, dependence and withdrawal.
- The long-term use of benzodiazepines or Z-drugs is associated with a number of health conditions and an increased risk of death:
  - ✓ Over-sedation from long-term use can increase the risk of falls and accidents on the road and in the home.
  - ✓ Poisoning from overdose may contribute to increased mortality risk.
  - ✓ Studies have shown that users of hypnotics exhibit an increased risk of cancer that does not appear to be fully explained by preferential prescribing in people with poor health.
- Long-term use of benzodiazepines or Z-drugs (usually more than 4 weeks) may be associated with:
  - ✓ Tolerance — a higher dose is required to obtain the initial effect.
  - ✓ Dependence — the person feels they need the medication to carry out day-to-day activities, and/or withdrawal symptoms occur upon stopping or dose reduction.
- Other effects of long-term use of benzodiazepines include:
  - ✓ Cognitive effects, anxiety, agoraphobia, emotional blunting, reduced coping skills, and amnesia.
  - ✓ Reduced social functioning due to effects on memory, reduced ability to remember new people, appointments etc.
  - ✓ Depression, either for the first time, or aggravation of pre-existing depression with possible precipitation of suicidal tendencies.
- Older people are more vulnerable to the CNS depressant effects of benzodiazepines, possibly leading to confusion, night wandering, amnesia, ataxia, and hangover effects. Impaired cognitive function and memory may

be wrongly diagnosed as dementia. In the UK, it has been estimated that older adults receive 80% of all prescriptions written for benzodiazepine hypnotics.

Appendix 10: Patient Information Leaflet – Sleeping Tablets

Why are Doctors Reluctant to Prescribe Sleeping Tablets?

Sleeping tablets may cause significant problems, which include:

- Falls — people taking sleeping tablets have an increased risk of falling and bone fractures such as hip fracture.
- Accidents — people taking sleeping tablets are at a significantly increased risk of car accidents.
- Memory and mood problems — such as confusion forgetfulness, aggression and depression.
- Addiction and dependence -— feeling like you need the medicine to carry out day to day activities and/or withdrawal symptoms if you stop or reduce the tablets.
- Withdrawal — symptoms can include anxiety, irritability, difficulty sleeping, sweating, gastrointestinal symptoms. These are usually mild and usually only last for days to a few weeks.
- Dementia — there may be an increased risk of developing dementia and Alzheimer's disease in people taking sleeping tablets for more than 3 months.
- Death - people taking sleeping tablets have a significantly increased risk of death compared to people who do not take these medicines.

What is the Alternative to Sleeping Tablets?

Your doctor, nurse or pharmacist can give you advice on how to tackle poor sleep without taking medication. Advice includes reducing your intake of caffeine, more exercise and suggestions to improve your bedtime routine.

Advice If a Sleeping Tablet is Prescribed

Sleeping tablet prescriptions will usually only last a short period (a week or so). Please do not ask for more, or for it to be added to your repeat prescription.

- If you feel drowsy the next day, do not drive or operate machinery.
- Avoid alcohol.
- Never give your sleeping tablets to anyone and always keep them in a safe place such as a locked cupboard.

Sleeping Tablets and Driving

All sleeping tablets make you sleepy. When this happens do not drive or use tools or machinery.

Sleeping Tablets and Pain Killers

Use of sleeping tablets and opioid pain killers such as codeine, tramadol and morphine increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. If you are taking this combination it could be helpful to inform friends or relatives to be aware of these signs and symptoms. If you experience these symptoms you should seek medical attention immediately. If you are prescribed this combination you should make an appointment to discuss this with your doctor.

Some pain killers which you can buy from Pharmacies include codeine and you should avoid using these medicines if you are taking sleeping tablets.

What If You have been Taking Sleeping Tablets Regularly for Some Time?

- As a rule, you should consider reducing or stopping them with advice from your doctor
- Do it gradually; cut down the dose a little at a time.
- Pick a good time to do it; it is best to wait until any life crises have passed and your stress levels are as low as possible. Consider stopping the tablets whilst on holiday, or when you have less pressure from work, etc.

- You are likely to have worse sleep initially when reducing your tablets, however, most people who reduce or stop sleeping tablets say they feel much better mentally and physically.
- Look for possible causes of your sleep problems such as pain, indigestion, breathlessness or itching. These may interfere with your sleep and can often be treated without sleeping tablets. Check with your doctor or pharmacist whether any other medicines you are taking can cause sleeping problems.

Developing a good sleep pattern may take a few weeks. Remember you should be confident that you will achieve it by working through the guidance you have been given.

Speak to your Doctor, Pharmacist or Nurse if you need more help.

IMPORTANT: Do not stop your sleeping tablets suddenly if you have been taking them for longer than 4 weeks as this can cause problems. Make an appointment with your doctor to discuss how to stop your sleeping tablets safely.

Appendix 11: Patient Information Leaflet – Benzodiazepines for Anxiety

Treating Anxiety

Benzodiazepines are a group of drugs that may be used as a short term measure to treat severe anxiety eg during crises and include diazepam, lorazepam, oxazepam and chlordiazepoxide.

They should not be used to relieve mild nervousness or tension caused by daily stress, to treat panic attacks or for more than 4 weeks.

Treatment for anxiety and panic attacks should include psychological therapy and if drugs are needed antidepressants are often used.

Why are Doctors Reluctant to Prescribe Benzodiazepines for Anxiety?

Benzodiazepines may cause significant problems, which include:

- Falls — people taking benzodiazepines have an increased risk of falling and bone fractures such as hip fracture.
- Accidents — people taking benzodiazepines are at a significantly increased risk of car accidents.
- Memory and mood problems — such as confusion forgetfulness, aggression and depression.
- Addiction and dependence — feeling like you need the medicine to carry out day to day activities and/or withdrawal symptoms if you stop or reduce the tablets.
- Withdrawal — symptoms can include anxiety, irritability, difficulty sleeping, sweating, gastrointestinal symptoms. These are usually mild and only last for days to a few weeks.
- Dementia — there may be an increased risk of developing dementia and Alzheimer's disease in people taking benzodiazepines for more than 3 months.
- Death - people taking benzodiazepine have a significantly increased risk of death compared to people who do not take these medicines.

What is the Alternative to Benzodiazepines?

Your doctor or nurse will give you advice on how to tackle anxiety without using benzodiazepines. Advice includes finding time to relax, developing a relaxation routine, more exercise and using relaxation techniques.

If your symptoms are more severe your doctor will discuss psychological therapy and may consider drug treatment.

Advice If a Benzodiazepine is Prescribed

- Benzodiazepine prescriptions will usually only last a short period (a couple of weeks). Please do not ask for more, or for it to be added to your repeat prescription.

- If you feel drowsy the next day, do not drive or operate machinery.
- Avoid alcohol.
- Never give your tablets to anyone else and always keep them in a safe place.

Benzodiazepines and Driving

Benzodiazepines can make you sleepy. When this happens do not drive or use tools or machinery.

Benzodiazepines and Pain Killers

Use of benzodiazepines and opioid pain killers such as codeine, tramadol and morphine increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. If you are taking this combination it could be helpful to inform friends or relatives to be aware of these signs and symptoms. If you experience these symptoms you should seek medical attention immediately. If you are prescribed this combination you should make an appointment to discuss this with your doctor.

Some pain killers which you can buy from Pharmacies include codeine and you should avoid using these medicines if you are taking benzodiazepines.

What If You have been Taking Benzodiazepines Regularly for Some Time?

- As a rule, you should consider reducing or stopping them with advice from your doctor
- Do it gradually; cut down the dose a little at a time.
- Pick a good time to do it; it is best to wait until any life crises have passed and your stress levels are as low as possible. Consider stopping the tablets whilst on holiday, or when you have less pressure from work, etc.
- Anticipate and accept that you are likely to have a period of increased anxiety when reducing these tablets. However, most people who reduce or stop benzodiazepines say they feel much better mentally and physically.
- Check with your doctor or pharmacist whether any other medicines you are taking are likely to cause anxiety problems.

- Use the ‘Good relaxation guide’; copies are available from your GP practice.

IMPORTANT: Do not stop benzodiazepine medication suddenly, as this may cause problems. You should discuss this with your doctor first.

Appendix 12: Benzodiazepine/Z-drug Policy

A controlled substance is a drug or chemical whose manufacture, possession, or use is regulated by the government because of the potential for abuse or addiction. Such drugs include those classified as narcotics, stimulants, depressants, hallucinogens, and cannabis.

A list of the most commonly encountered controlled drugs can be found at:
https://www.gov.uk/government/publications/controlled-drugs-list--2

Many of our patients require strong, potentially addictive medication to help manage their condition(s). Of concern are ‘drugs of dependence’ (e.g. opioid medications, benzodiazepines and Z-drugs), particularly when these are prescribed on an on-going basis.

Appendix 14: Benzodiazepine and Z-drug Approximate Equivalent Doses to Diazepam 5mg and Duration of Action

- alprazolam 250micrograms
- chlordiazepoxide 12.5mg
- clobazam 10mg
- clonazepam 250micrograms
- flurazepam 7.5-15mg
- loprazolam 0.5-1mg
- lorazepam 500micrograms
- lormetazepam 0.5-1mg

- nitrazepam 5mg
- oxazepam 10mg
- temazepam 10mg
- zopiclone 7.5mg
- zolpidem 10mg

Short-Acting (Half-life of drug and metabolites shorter than 6 hrs)	**Intermediate-Acting** (Half-life of drug and metabolites 6-24 hours)	**Long-Acting** (Half-life of drug and metabolites longer than 24 hrs)
Midazolam Zopiclone Zolpidem	Alprazolam Loprazolam Lorazepam Lormetazepam Oxazepam Temazepam	Chlordiazepoxide Clobazam Clonazepam Diazepam Flurazepam Nitrazepam

Benzodiazepines with high potency and short elimination half-lives (e.g. lorazepam and loprazolam) are more likely to lead to dependence problems.

Those with an intermediate half-life (e.g. temazepam) cause fewer problems when used for a short period.

Those with long half-lives (e.g. nitrazepam, diazepam) can have residual effects the following day (e.g. daytime sedation and falls); some people are more susceptible to these effects than others.

Problems, Which Include:

- Falls
- Accidents
- Memory and mood problems
- Addiction and dependence
- Withdrawal

What are the Benefits If Stop Taking a Benzodiazepine or Z-drug?

If you have used it for a long time and the medicine has lost its effect, it will no longer help with the condition you are taking it for.

You may Become, or may have Already Become, Dependent on It.

If you stop, you will have fewer side effects, so you will be:

- More alert and able to concentrate
- Less drowsy
- Less irritable and depressed
- Less likely to have an accident such as a fall or car accident

Self help

There are many self help techniques you can use when stopping taking a benzodiazepine or Z-drug. Put together a plan based on the information given to you by your doctor and practise regularly. Relaxing is about slowing things down. Everyone is different — experiment until you find your best way to relax. Ten minutes 'out' of a busy day is a good investment for your health and well -being. Remember that expert guidance and advice is available if you need more help.

Appendix 17: Suggested Withdrawal for Long-term Benzodiazepines and Z-drugs

Withdrawal should be gradual (dose tapering, such as 5–10% reduction every 1–2 weeks, or an eighth of the dose fortnightly, with a slower reduction at lower doses), and titrated according to the severity of withdrawal symptoms.

The following reduction regimes are taken from https://cks.nice.org.uk/benzodiazepine-and-z-drug-withdrawal and are adapted from the Ashton Manual (available online at www.benzo.org.uk).

From Diazepam 40mg Per Day or Less:

- Reduce dose by 2-4mg every 1-2 weeks until reaching 20mg per day, then
- Reduce dose by 1-2mg every 1-2 weeks until reaching 10mg per day, then
- Reduce dose by 1mg every 1-2 weeks until reaching 5 mg per day, then
- Reduce dose by 500 microgram-1mg every 1-2 weeks until completely stopped.
  - ✓ Estimated total withdrawal time:
    - ◆ From diazepam 40mg per day: 30-60 weeks.
    - ◆ From diazepam 20mg per day: 20-40 weeks.

Suggested Withdrawal Schedules for Temazepam, Nitrazepam, and Zopiclone without Diazepam Conversion:

From temazepam 20mg daily or less:

- Reduce daily dose by a quarter of a 10mg tablet (2.5mg) every 2 weeks.
- The target dose for when to stop is when the person is taking only a quarter of a 10mg tablet as a daily dose.
- If stopping is not possible at the target dose, offer temazepam liquid (10mg/5mL) and an oral syringe to achieve further reductions.
  - ✓ Estimated total withdrawal time: 16-20 weeks or longer.

From Nitrazepam 10mg Daily or Less:

- Reduce the daily dose by a quarter of a 5mg tablet (1.25mg) every 2 weeks.
- The target dose for when to stop is when the person is taking only a quarter of a 5mg tablet as a daily dose.
- If stopping is not possible at the target dose, offer nitrazepam (2.5mg/5mL) liquid and an oral syringe to achieve further reductions.
  - ✓ estimated total withdrawal time: 16-20 weeks or longer

From Zopiclone 7.5mg Per Day or Less:

- Reduce the daily dose by half of a 3.75mg tablet (1.875mg) every 2 weeks.
- The target dose for when to stop is when the person is taking only half of a 3.75mg tablet.
- If stopping is not possible at the target dose, one option is to convert to diazepam to complete the withdrawal, although this is controversial.
  - ✓ estimated total withdrawal time: 16-20 weeks or longer.

Benzodiazepine Prescribing Support Pack

NHS dorset clinical commissioning group

https://nhsdorset.nhs.uk/wp-content/uploads/2025/12/Benzodiazepines-Support-Pack-Aug16.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Background

Prescribing of benzodiazepine drugs is widespread but dependence (both physical and psychological) and tolerance occur. This may lead to difficulty in withdrawing the drug after the patient has been taking it regularly for more than a few weeks Hypnotics and anxiolytics should therefore be reserved for short courses.

When a Benzodiazepine is considered essential, the BNF makes the following recommendations:

1. Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling, or causing the patient unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness.

2. The use of benzodiazepines to treat short-term ‘mild’ anxiety is inappropriate

3. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or causing the patient extreme distress.

Tips for prescribing benzodiazepines safely

- Use the lowest possible dose for the shortest possible duration.
- Prescribe small quantities and do not issue further prescriptions without consultation.

- Prescribe on a "when required" basis to encourage the patient to take the drug only when they feel it is absolutely necessary
- Advise the patient of the potential for dependence and other side effects; stress that the prescription is for short term use only.
- Offer and regularly re-enforce self-help advice in addition to drug treatment.
- Record diagnosis/reason for prescribing using appropriate read codes.
- Make use of patient decision aids. An excerpt from the insomnia patient decision aid published by the National Prescribing Centre in 2010 is shown below – if 13 people over the age of 60 were prescribed a benzodiazepine for primary insomnia for 5 days, only one person would benefit.

Strategies for reduction in long term prescribing:

Evidence suggests that educational letters to patients detailing the problems associated with long term benzodiazepine use and encouraging them to gradually reduce, and if possible stop, their usage is a successful intervention, even in patients who have previously been advised to or attempted reduction.

There is also evidence that patient consultations encouraging benzodiazepine reduction are successful but this strategy is more time-consuming than patient letters and does not appear to result in significantly greater reductions.

Therefore it is recommended that practices send an educational letter to all suitable patients on the benzodiazepine register. Repeating the intervention, possibly on an annual basis, may improve success rates.

Reduction and withdrawal process

Discontinuation of benzodiazepine drugs should be gradual to minimise the risk of withdrawal effects such as confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens. The following stepwise discontinuation schedule, adapted from the BNF, can be used as a guide. The reduction schedule may be tailored to the individual patient as required.

A benzodiazepine can be withdrawn in steps of about one-eighth of the daily dose every fortnight. A suggested withdrawal protocol for patients who have difficulty is as follows:

1. Transfer to equivalent daily dose of diazepam (see appendix 8) preferably taken at night
2. Reduce diazepam dose every 2–3 weeks; if withdrawal symptoms occur, maintain this dose until symptoms improve
3. Reduce dose further, if necessary in smaller steps; it is better to reduce too slowly rather than too quickly
4. Stop completely; period needed for withdrawal can vary from about 4 weeks to a year or more

Benzodiazepine withdrawal syndrome may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine, but may occur within a day in the case of a short-acting one. It is characterised by insomnia, anxiety, loss of appetite and of body-weight, tremor, perspiration, tinnitus, and perceptual disturbances. Some symptoms may be similar to the original complaint and encourage further prescribing; some symptoms may continue for weeks or months after stopping benzodiazepines.

Appendix 9

Areas to be included in a practice policy for managing patients prescribed benzodiazepines

1. Benzodiazepines to be initiated and prescribed only as short term treatment (2-4 weeks only) in line with the advice in the BNF and other national guidance.
2. Benzodiazepines are controlled drugs (schedule 4) and should not be issued as repeat prescriptions.
3. Lowest possible doses should be prescribed.
4. Prescriptions should be limited to a maximum 28 day supply.

5. Where benzodiazepines are essential, ensure that the choice of drug is in line with local prescribing advice/formulary.
6. Where possible, patients should be moving towards taking their benzodiazepine on a PRN basis.
7. Ensure that all patients with insomnia / anxiety are advised about non-drug treatments and self help prior to use of benzodiazepines or z-drugs.
8. Maintain an active and up to date register of patients who are currently prescribed benzodiazepines, or those who have had more than 28 days treatment in the last year.
9. Review patients prescribed benzodiazepines or z-drugs frequently (as a minimum once in 12 months) to ensure that every opportunity to reduce and stop is taken.
10. Consider inviting patients to discuss reduction / stopping benzodiazepines by way of personalised letters annually. Keep records of these interventions.
11. Where there is suspicion that a patient is abusing/misusing benzodiazepines, ensure that the patient is referred into local drug misuse shared care schemes (e.g. CADAS or SEDCDAT).
12. Document in patient records all notes of discussions with patient in relation to potential tolerance, addiction, loss of effectiveness, falls risk, driving.

Standard of Practice Prescribing Benzodiazepines & Z-drugs (including Zopiclone & other drugs)

The College of Physicians & Surgeons of Manitoba

https://cpsm.mb.ca/assets/Standards%20of%20Practice/Standard%20of%20Practice%20Prescribing%20Benzodiazepines%20and%20Z-Drugs.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

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 registrants 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 registrants 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 registrant exercises their clinical judgment, which is to be that of a registrant acting reasonably in the circumstances with current medical knowledge.

*If prescribing for any of these conditions please include the medical condition on the prescription for the awareness of the pharmacist for dispensing purposes.

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 registrant 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. Registrants 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 ZDrugs 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. Registrants 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. Registrants 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, registrants 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 registrant 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®)	
Bromazepam (Lectopam®)	Midazolam (Versed®)	
Chlordiazepoxide (Librium®)	Nitrazepam (Mogadon®)	Eszopiclone
Clobazam *to be started by Neurologists only	Oxazepam (Serax®)	Zolpidem
	Potassium-Clorazepate	Zopiclone
Clonazepam (Rivotril®)	Temazepam (Restoril®)	
Diazepam (Valium®)	Triazolam (Halcion®)	
Flurazepam (Dalmane®)		

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.

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.
Diazepam	10 mg	10 mg	10 mg	10 mg
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.

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.

FREQUENTLY ASKED QUESTIONS

The Frequently Asked Questions (FAQs) are provided to support registrants in implementing this Standard of Practice. The FAQs do not define this Standard of Practice, nor should it be interpreted as legal advice. It is not compulsory, unlike a Standard of Practice. The FAQs may be edited or updated for clarity, new developments, or new resources at any time.

The College of Physicians & Surgeons of Manitoba (CPSM) has received calls from healthcare providers and patients about the new Standard for prescribing benzodiazepines and z-drugs. In this document we hope to address some of the common questions received.

What is the Standard of Practice about?

This Standard of Practice sets out the requirements related to prescribing benzodiazepines and z-drugs. The Standard exists to ensure quality care and to ensure patient and public safety. While your doctor applies clinical judgment and discretion to your individual care, your doctor is also expected to follow this Standard to ensure all patient care is safe and ethical. The Standard of Practice for Prescribing Benzodiazepines & Z-Drugs came into effect on November 1, 2020.

Why does CPSM get to make decisions that affect my medications?

To protect the public

CPSM's job is to protect the public and ensure quality in the practice of medicine. The Standard of Practice for Prescribing Benzodiazepines & Z-Drugs is evidence-informed and promotes safe and ethical care of all patients. The Standard outlines the expectations that doctors must follow to balance individual care and public safety.

Standards are created by a group of experts in the relevant field of practice, often including doctors, nurses, pharmacists, lawyers, and members of the public. Feedback is also sought from the public prior to finalization.

To promote current and quality medical care

As medicine evolves, new information is discovered. After decades of prescribing

benzodiazepines and z-drugs, we know more about the risks of these medications today, especially when it comes to long-term use and higher doses. As the evidence of the risks compared to benefits of these drugs evolves, doctors must adapt their prescribing to align with current medical knowledge. These drugs are helpful for many patients, but they also pose risks for some patients and the public. The Standard tries to strike the best balance possible between the benefits and the risks.

What are benzodiazepines and z-drugs? What are their effects?

Benzodiazepines are sedative medications often prescribed to treat anxiety and sleep disorders. Commonly prescribed benzodiazepines include, but are not limited to, alprazolam (Xanax®), lorazepam (Ativan®), temazepam (Restoril®), clonazepam (Rivotril®), and diazepam (Valium®). Zdrugs, like zopiclone or zolpidem, are chemically similar to benzodiazepines and have similar effects and risks associated with their use. These sedatives essentially slow-down the activity of the brain and this slows bodily functions like heart rate and breathing, which can make you feelmore calm or sleepy.

While these medications may be effective to decrease anxiety or improve sleep at first, regularuse leads to tolerance and physiological dependence. With regular, longer-term use, the brain and body become accustomed to the effect. For some people, escalating doses are needed for relief of symptoms. Similarly, cutting back or missing doses can create rebound symptoms (including anxiety), often reinforcing the perceived need for the medication. Long-term use, and/or higherdose use, increases the likelihood of side-effects and risk of harm.

Why are benzodiazepines and z-drugs considered so harmful?

For the same reason benzodiazepines and z-drugs make you feel calm or sleepy (by slowing some brain and body functions), they have associated side-effects and risks of harm. See the list of side effects and risks below. These harmful effects are worsened by long-term and/or high-dose use. Some patients can develop addiction to these medications and experience serious repercussions. Misuse, overuse, or combining these medications with other sedatives increases the risk of overdose and death. In Manitoba, benzodiazepines and z-drugs have become significant

drugs of abuse and are known to be sought after by substance users. The likelihood of diversion (sharing, selling, stealing) of these medications is very high and this has had a profound impact on public safety. Benzodiazepines and z-drugs are responsible for an increasing number of deaths in Manitoba, regardless of whether these drugs are prescribed alone or with painkiller medications like opioids or other prescription drugs.

What are the side-effects and risks of benzodiazepines and z-drugs?

Common side-effects and risks of benzodiazepines and z-drugs include:

- Sedation, confusion, drowsiness, and instability when standing/moving that can add to risk of falls and subsequent fractures.
- Impairment of psychomotor skills, judgment, and coordination that can increase 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.
- Tolerance and physiological dependence, leading to withdrawal with abrupt cessation, or large dose changes.
- Sedative-Hypnotic Use Disorder (addiction).
- Risky interaction with medications or herbals.
- Risk of sleep automatism (in the case of z-drugs), similar to sleepwalking, when a person acts out scenarios when sleeping or dreaming.

Benzodiazepines and z-drugs are also particularly problematic in older adults. 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.

Does my doctor have to taper my medication?

The Standard provides evidence for doctors to consider and discuss with patients before starting benzodiazepines and z-drugs, as well as guidelines to manage patients already taking these medications. Good clinical judgment and an evidence-informed approach are key to safe and appropriate prescribing. Your doctor should

discuss the reason for taking these medications, their potential side-effects and risks, and reasonable expectations for their effect. This is part of the clinical judgment applied to continuing or changing medications. Given the overwhelming evidence of the harm these medications can cause (see above), the Standard recommends your doctor attempt slow dose reductions, also known as step-downs or tapering. This is particularly important if the harm outweighs the benefit of taking the medication, especially if benzodiazepines and z-drugs have been prescribed for a long time and/or at a high dose.

Do I have to get my dose down to zero?

The Standard asks your doctor to partner with you to attempt tapering. It asks that your doctor help you make informed decisions about your care by evaluating the risks of continuing the medication compared to the benefits. With slow and steady dose reductions (tapering), over weeks to months, over even years, you may eventually take your dose down to zero. However, all taper attempts are worthwhile, and even small dose reductions can improve cognitive function (things like memory, concentration, range of affect) and improve safety. It is not mandatory to taper off your medication completely; with incremental step-downs your doctor may find the lowest dose that allows you wellness, function, and minimizes side-effects/risks.

Why am I being tapered off benzodiazepines and z-drugs if they work for me?

The Standard does not recommend your doctor stop prescribing or "cut off" these medications. It recommends that your doctor take a closer look at why they are prescribing them. The Standard promotes a discussion about the benefit versus harm benzodiazepines and z-drugs carry for you and how to improve safety around use. In the past two decades, clinical guidelines have recommended against long-term use of benzodiazepines and z-drugs. Their effectiveness to treat conditions like anxiety and insomnia is debated by doctors. They may work well for some patients, but it is important to be aware of the risk they carry to both individuals and the public. While they can have important therapeutic uses, the supply of these medications needs to be clinically safe and appropriate.

Can my doctor cut off my medications?

CPSM and the Standard encourage communication and collaboration between you and your doctor. However, based on clinical judgment and safety, a doctor may need to proceed with a taper when a patient may not agree. A doctor may also limit the amount dispensed to a patient at a time if safety concerns arise (e.g. medications may need to be dispensed weekly or daily from the pharmacy in some situations). There are times when safety, either individual, public, or both, takes precedence over the therapeutic relationship between doctor and patient. If a doctor learns that the medications they prescribe are being misused, abused, or diverted, rapid tapers or sudden cessation of prescribing may be necessary to manage risk of overdose or death, and for public safety.

What can I expect if my dose is reduced?

Because benzodiazepines and z-drugs are drugs of physiological dependence, which means the brain and body become used to them, changes in the dose can create rebound or withdrawal symptoms. This is normal for anybody who takes these medications over time.

With dose reductions, you may temporarily experience more worry or anxiety, mild sleep disturbances, heightened emotions, shakiness, sweating, twinging or restless limbs, or digestive upset. This does not mean your anxiety or insomnia will become uncontrollable; with small changes, these symptoms will settle and pass with time. Ideally, dose step-downs should be small, with enough time in between each change for you (your brain and body) to adjust to the decrease. These symptoms will settle with time; many people start to feel “normal” or back to baseline within two to four weeks of a change. Your doctor may wait until you feel closer to baseline function, or more like yourself again, before making the next change. This is a highly individualized process and should be discussed regularly with your doctor. Rapid tapers or changing medications

yourself is not recommended.

What is a reasonable timeframe to taper?

There is no one-size-fits-all approach to tapers. The process is individualized and considers starting dose, length of use, and concurrent medical conditions, as well as your life circumstances. Slow and steady step-downs tend to be more successful, as this allows your brain and body time to adjust to changes. If tapers progress too quickly, they can feel overwhelming and unmanageable. However, remember that even small changes can create discomfort, and it is important to know that this is a normal experience for many and that it will pass. You may need to draw on extra support during these changes. With the guidance of your doctor, you may also need to take tapering breaks and remain on a stable dose for a while, before taking the next steps in a taper. Psychological work done during such tapering breaks can increase your success with future taper attempts. Conversely, for safety reasons, your doctor may initiate a taper or the next step-down before you feel ready.

Why change my medication if it took years to find this balance?

Given the risks described before, being stable on a dose of a medication for years is not a reason to forgo reexamination. As bodies and lives change over time, medications should also be reevaluated over time. Particularly since the risks associated with benzodiazepines and z-drugs increase with age. However, if taper attempts are unsuccessful over time and there is a documented benefit of continuing a stable dose of medication that outweighs the harm, doctors and patients may choose to continue the benzodiazepines and z-drugs.

I've never abused my pills - why can't I have more than a month at a time?

While it may not feel like the risks, harms, or concerns apply to you, CPSM and doctors must set parameters to promote public safety. That means drawing a line between safe and unsafe amounts of medication that can be available at one time. This line must balance the needs and lifestyles of both well and unwell community members. CPSM has made similar prescribing rules for benzodiazepines and z-drugs, as with opioid pain medications, because of the known risks of these medications. The Standard makes firm recommendations, or rules, for prescribing and dispensing intervals to limit the supply of these drugs in the community and promote safety.

These recommendations are also to ensure that doctors are taking a frequent and active role in managing the use of these medications.

What are the new rules? Are there any exceptions?

Specifically, the prescribing and dispensing rules in the Standard are that:

- Benzodiazepines and z-drugs prescriptions can only be written for **a maximum of three months at a time; and Only a one-month supply can be dispensed at a time.**

Exceptions to this rule apply only if use is 1) infrequent (as in, taking a single dose for travel or having a CT scan), 2) you live in a remote community, or 3) for travel if you have been on a stable long-term prescription. For these exceptions of remote living and travel, your doctor may allow a dispensing interval of up to three months only. This limit also applies if you leave the country for longer than three months at a time; still only a maximum of three months' supply of benzodiazepines and z-drugs may be prescribed and dispensed at one time.

This means that simply fewer pills are available in a home and within the community at a given time. For example, even if you have never misused or lost your medications and always got 90- days at a time, what would happen if someone stole all your medication? What if someone who has never tried them before, such as a minor, gets access, takes them, and overdoses? These are the types of risks doctors and CPSM must balance with the needs of patients who take their medications as prescribed. One-month of medication has been determined to be an amount of pills that balances community risk with patient need. When safety concerns arise, doctors can choose to further limit dispensing intervals to ensure patient and public safety (e.g. medications may need to be dispensed weekly or daily in some situations). It is a good idea to lock up medications in your home.

Are there resources to help me?

The symptoms or reasons you started these medications may still exist and can feel distressing. Evidence shows that other non-medication treatments, such as

Cognitive Behavioural Therapy (CBT) for anxiety or CBT for insomnia, sleep hygiene techniques, mindfulness, and healthy exercise, are all effective ways to manage mental health issues, often with longer-term benefits than benzodiazepines and z-drugs. You can discuss optimizing non-medication and other medication-based treatments with your doctor. Ask for a referral to counselling or specialized services. If your distress becomes overwhelming, call or present to local crisis services. There are also peer-lead support groups that have helped many people recover from mental health issues, such as the Anxiety Disorders Association of Manitoba, the Mood Disorders Association of Manitoba, 12-Step programs, and other self-help groups that can offer more support.

Canadian Guidelines on Benzodiazepine Receptor Agonist (BZRA) Use Disorder Among Older Adults

Canadian Coalition for Seniors' Mental Health (CCSMH) (2019).

https://ccsmh.ca/wp-content/uploads/2019/11/Benzodiazepine_Receptor_Agonist_Use_Disorder_ENG.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

BZRA Use Disorder: This refers to a problematic pattern of BZRA use leading to clinically significant impairment or distress. According to DSM-5 criteria BZRA use disorder is manifested by at least two of the criteria below occurring within a 12-month period (American Psychiatric Association, 2013).

- The BZRA is taken in larger amounts or over a longer period of time than intended.
- Persistent desire or unsuccessful efforts to cut down or control BZRA use.
- A great deal of time is spent in activities to obtain BZRAs, use them, or recover from their effects.
- Craving, or a strong desire or urge to use a BZRA.
- Recurrent BZRA use resulting in a failure to fulfill major role obligations at work, school, or home.
- Continued use of the BZRA despite persistent or recurrent social or interpersonal problems caused or exacerbated by their effects.
- Important social, occupational, or recreational activities are given up or reduced because of BZRA use.
- Recurrent BZRA use in situations in which it is physically hazardous.

- Continued use of the BZRA despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by drug use.
- Tolerance as defined by either a need for markedly increased amounts of the BZRA to achieve intoxication or desired effect OR a markedly diminished effect with continued use of the same amount of the BZRA (note: criterion not considered to be met for an individual taking the drug under medical supervision).
- Withdrawal as manifested by either characteristic withdrawal symptoms (i.e., autonomic hyperactivity, hand tremor, insomnia, nausea or vomiting, transient sensory hallucinations or illusions, psychomotor agitation, anxiety, and/or seizures) OR the BZRA (or a closely related substance such as alcohol) is taken to relieve or avoid withdrawal symptoms.

Diagnosis

- 1 symptom or less, no diagnosis
- 2–3 symptoms, mild BZRA Use Disorder
- 4–5 symptoms, moderate BZRA Use Disorder
- 6 or more symptoms, severe BZRA Use Disorder

Remission

- 3–12 months with no criteria other than craving is considered early remission.
- More than 12 months is considered sustained remission.

RECOMMENDATION #1:

Long-term use of BZRAs (> 4 weeks) in older adults should be avoided for most indications because of their minimal efficacy and risk of harm. Older adults have increased sensitivity to BZRAs and decreased ability to metabolize some longer-acting agents, such as diazepam. All BZRAs increase the risk of cognitive impairment, delirium, falls, fractures, hospitalizations, and motor vehicle crashes.

Alternative management strategies for insomnia, anxiety disorders, and the behavioural and psychological symptoms of dementia (BPSD) are recommended. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #2:

Appropriate first-line non-pharmacological options for the treatment of insomnia and anxiety disorders include cognitive behavior therapies (CBTs) provided in various formats. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #3:

A BZRA should only be considered in the management of insomnia or anxiety after failing adequate trials of non-pharmacological interventions or safer pharmacological alternatives OR for shortterm bridging until more appropriate treatment becomes effective. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #4:

An assessment of risk for BZRA use disorder and other potential adverse effects from these agents should be done prior to prescribing a BZRA. [Consensus]

RECOMMENDATION #5:

If a BZRA is being considered, the older adult should be informed of both the limited benefits and risks associated with use, as well as alternatives, prior to deciding on a management plan. [Consensus]

RECOMMENDATION #6:

Initiating treatment with a BZRA should be a shared decision between the prescriber and the older adult (or their substitute decision-maker). There should be agreement and understanding on how the BZRA is to be used (including planned duration of no more than 2 to 4 weeks) and monitored. [Consensus]

RECOMMENDATION #7:

Older adults who are receiving a BZRA should be:

a. Educated and provided the opportunity to discuss the ongoing risks of taking BZRAs. [GRADE: Evidence: Moderate; Strength: Strong]

b. Encouraged to only take the BZRA for a short period of time (2 to 4 weeks or less) at the minimally effective dose. [GRADE: Evidence: Moderate; Strength: Strong]

c. Monitored during the course of their prescription for evidence of treatment response and effectiveness, current and potential adverse effects, concordance with the treatment plan, and/or the development of a BZRA use disorder. [Consensus]

d. Supported in stopping the drug, which may require a gradual reduction until discontinued. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #8:

Health care providers and organizations should consider implementing interventions to decrease inappropriate use of BZRAs in their practice settings. These include medication reviews, prescribing feedback, audits and alerts, multidisciplinary case conferences, and brief educational sessions. Regulators, health authorities, and professional organizations should consult with clinical leaders and older adults to develop and implement policies that aim to minimize inappropriate use of BZRAs. [GRADE: Evidence: Low; Strength: Strong]

RECOMMENDATION #9:

Health care institutions, including acute care hospitals and long-term care facilities, should implement protocols that minimize new prescriptions for BZRAs because of the potential for harm and the risk of this leading to long-term use following discharge to the community or other transitions in care. [GRADE: Evidence: Low; Strength: Strong]

RECOMMENDATION #10:

Health care practitioners, older adults, and their families should advocate for

adequate access and funding of effective non-pharmacological alternatives for the management of insomnia, anxiety disorders, and BPSD. [GRADE: Evidence: Low; Strength: Strong]

RECOMMENDATION #11:

Clinicians should be aware that BZRAs are prescribed more frequently to women and the potential implicit bias that may lead to inappropriate use. [GRADE: Evidence: Low; Strength: Weak]

RECOMMENDATION #12:

All older adults should be asked about current and past consumption of substances that might lead to substance use disorders, including BZRAs, during periodic health examinations, admissions to facilities or services, perioperative assessments, when considering the prescription of a BZRA, and at transitions in care. [Consensus]

RECOMMENDATION #13:

Health care practitioners should be aware of and vigilant to the symptoms and signs of substance use disorders, including BZRA use disorder. Particular attention should be paid to this possibility when assessing common conditions encountered in older adults, such as falls and cognitive impairment. [Consensus]

RECOMMENDATION #14:

Assessment of older adults suspected of having a BZRA use disorder should include indication, dose, duration, features indicative of BZRA use disorder, readiness to change, and presence of both medical and psychiatric comorbidities, including any other past or current substance use or misuse. [Consensus]

RECOMMENDATION #15:

a. Multiple substance use is common and should be considered and inquired about in all older adults with a BZRA use disorder. [GRADE: Evidence: Moderate; Strength: Strong]

b. Health care practitioners should avoid prescribing BZRAs concurrently with opioids whenever possible. [GRADE: Evidence: Moderate; Strength: Strong]

c. The combination of a BZRA with alcohol should be avoided. [GRADE: Evidence: Low; Strength: Weak]

RECOMMENDATION #16:

A person-centred, stepped-care approach to enable the gradual withdrawal and discontinuation of BZRAs should be used. Clinicians and patients should share in: a) planning and applying a gradual dose reduction scheme supported by appropriate education of the patient; b) identifying and optimizing alternatives to manage the underlying health issue(s) that initiated or perpetuated the use of BZRAs; c) developing strategies to minimize acute withdrawal and managing rebound symptoms as needed; and d) establishing a schedule of visits for reviewing progress. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #17:

Abrupt discontinuation of a BZRA after intermediate to long-term use (> 4 weeks) in individuals with BZRA use disorder should be avoided due to the risk of withdrawal symptoms, substance dependence reinforcement, rebound phenomena, and/or higher likelihood of relapse with resumption of BZRA use. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #18:

Management of acute BZRA withdrawal symptoms should be monitored carefully and can be guided by a validated tool [e.g. Benzodiazepine Withdrawal Symptom Questionnaire, Clinical Institute Withdrawal Assessment-Benzodiazepine (CIWA-B)] and managed with symptom-driven judicious use of an appropriate BZRA. [GRADE: Evidence: Low; Strength: Weak]

RECOMMENDATION #19:

Regimens involving multiple BZRAs should be simplified and converted to a single BZRA. [Consensus]

RECOMMENDATION #20:

The routine switching of a short half-life BZRA with one having a long half-life to aid in withdrawing BZRAs is not generally recommended in older adults. Switching may have a role in certain situations, such as when withdrawal is being hindered by a limited number of available BZRA pill strengths or when alprazolam is the agent of dependence or misuse. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #21:

Psychological interventions such as CBT should be considered during efforts to withdraw BZRAs as they can improve the older adult's experiences and increase the likelihood of stopping the BZRA. [GRADE: Evidence: High; Strength: Strong]

RECOMMENDATION #22:

Substituting a pharmacologically different drug as a specific intervention to mitigate BZRA withdrawal symptoms during gradual dose reduction is not routinely recommended. [GRADE: Evidence: Moderate; Strength: Strong]

RECOMMENDATION #23:

Older adults with a BZRA use disorder whose drug use is escalating in spite of medical supervision, have failed prior efforts to withdraw their BZRA, are at high risk for relapse or harm, and/or suffer from significant psychopathology should be considered for referral to a specialty addiction or mental health service. [Consensus]

Guidance for the Use of Benzodiazepines in Psychiatric Practice

The Royal Australian and New Zealand College of Psychiatrists (RANZCP)

https://www.ranzcp.org/getmedia/cf85cf1c-b983-412d-b13d-0c7d384e0af0/ppg-5-use-of-benzodiazepines.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Introduction

As with all pharmacological treatments, benzodiazepines offer a range of beneficial, therapeutic effects, and also some potentially disadvantageous effects. Given the particular problems associated with dependence and risk of overdose, it is important to apply a clinically informed and evidence-based approach when prescribing benzodiazepines, to ensure treatment is safe and appropriate (RACGP, 2015). The Royal Australian and New Zealand College of Psychiatrists (RANZCP) has developed this resource to provide guidance to clinicians considering pharmacological treatment using benzodiazepines.

Recommendations

1. The prescription of benzodiazepines should be based on a comprehensive assessment of the patient that identifies a specific diagnostic reason or target symptoms for which good evidence exists for the efficacy of benzodiazepines. The situations where benzodiazepines may be considered include: acute mania, agitation (for example in acute psychosis or agitated depression), severe anxiety, catatonia, insomnia, alcohol withdrawal, akathisia.
2. In acute and long-term treatment the comparative benefits and disadvantages of benzodiazepines and of alternative treatments should be taken into account as

part of a comprehensive management plan. A plan for ceasing the medication should be documented. These drugs should not be discontinued abruptly.

3. In general, benzodiazepine use should be restricted to short term periods only. Longer term use should only be considered in patients who do not respond to adequate trials of other evidence-based pharmacological and psychological treatments.
4. Clinical experience indicates that there are a small number of patients, such as those with severe Generalised Anxiety Disorder (GAD), who are helped by long term benzodiazepine use, who do not escalate the dose, and for whom no other treatments prove as effective.
5. Patients should be advised that benzodiazepines may produce both tolerance and dependence, with the risk of withdrawal symptoms. Patients should also be informed of the full range of possible side effects, including cognitive impairment. Advice that the dosage and period of prescription are not to be exceeded should be clearly documented in the medical records. Patients should provide informed, formal consent when long term prescription of benzodiazepines is being considered and this should be documented in the notes.
6. The dosage used should be the lowest effective dose necessary to achieve symptomatic relief. Prescribers should be aware of the risk of dose escalation in long term use and ensure this does not happen.
7. Benzodiazepines are commonly associated with sedative side effects. Sedentary and elderly individuals and other vulnerable groups are at particular risk of developing problems due to sedation, as well as other motor effects such as ataxia, weakness and heightened risk of falls.
8. Benzodiazepine use in conjunction with anti-epilepsy medication may result in additive sedative effects and potentiation of central nervous system (CNS) depression with impaired psychomotor and cognitive function, particularly in elderly populations. Further risks may include falls, impaired swallowing, absence seizures, neutropenia, and agranulocytosis.
9. Caution should be exercised given benzodiazepines' effects on psychomotor coordination and the increasing understanding of medication contribution to motor vehicle accidents. Patients should be made aware of the dangers of driving motor or sea vehicles of any kind or operating machinery particularly at

times of initiation or dose changes, and that under certain circumstances use of benzodiazepines may affect employment. Patients should be made aware that use of other drugs, including alcohol, will increase the likelihood of these risks. Combined use of benzodiazepines with alcohol has been shown to increase the sedative and CNS depressive effects of the medication. This has been represented by increased risk of falls, disinhibition and alcohol and drug related presentations to emergency departments.

10. Benzodiazepine use has been associated with disinhibition and aggressive behaviour in some individuals. Caution should be exercised in prescribing benzodiazepines to patients who present with these risks.
11. Benzodiazepines are known to have contraindications for patients with sleep apnoea. Caution should be exercised in prescribing when any conditions with respiratory depression are present.
12. The concurrent prescription of more than one benzodiazepine should generally be avoided and if necessary requires justification.
13. Caution should be exercised where a history of misuse of alcohol and illicit or prescribed drugs is present. Individuals with a history of substance use disorder have a greater risk of developing benzodiazepine dependence1.
14. When benzodiazepines are prescribed, universal precautions should be applied to minimise the risk of dependence and diversion. These include having one prescriber, dose limits, controlled scripting and consideration of urine drug testing. Repeat prescriptions for benzodiazepines should not generally be provided without a clinical review.
15. Benzodiazepines are a common drug of abuse and have a significant black market value. The potential for diversion of prescribed medications should be considered with confirmation of use through urine drug screening.
16. Benzodiazepines are highly represented in patients presenting with intentional and accidental overdose. The risk can be reduced by use of controlled scripting and consideration of additional substance misuse.
17. The amnestic effects of benzodiazepines can confound clinical assessment. This is particularly relevant in the context of risk assessment following overdose.

Benzodiazepines: Good Practice Guidelines for Clinicians

Department of health and children an roinn slainte agus leanai

https://assets.gov.ie/15976/de072755b31c4c0993d4b6bfe960ac00.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Introduction

Benzodiazepines are one of the most widely used prescription medicinal products in the world. Benzodiazepines may be prescribed safely in the short-term and are a highly effective treatment for anxiety, insomnia and some forms of epilepsy and spasticity. Benzodiazepines are only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress. Dependence is now recognised as a significant risk in patients receiving treatment for longer than one month and the practitioner has to be conscious of this when evaluating the relative benefits and risks of continued prescription. It is recommended that every clinician examines the benefit:risk ratio in each individual case early in treatment, so that if dependence occurs, it is anticipated by therapist and patient alike. The decision to allow dependence to develop is sometimes defensible, but it must be appreciated that, once dependence has become established, it is often extremely difficult to treat and may become a long-term or even permanent state.

While this document deals with benzodiazepines, the information and recommendations made can also refer to other benzodiazepine receptor agonist such as Zopiclone, Zolpidem and Zaleplon which have similar effects to benzodiazepines.

Prescribing recommendations

Before looking at the use of benzodiazepines some general rules about the use of tranquillisers, and the benzodiazepines in particular are listed below:

General rules for treatment with tranquillisers/benzodiazepines

1. Benzodiazepine prescribing should never be purely symptom-oriented. A careful analysis of the causes of the symptom must be undertaken before benzodiazepines or other tranquillizers are prescribed.
2. Over and above the prescribing of the medication, some sort of psychotherapeutic guidance is required. It is important to spend time with the patient, and pay attention to what he/she is saying.
3. It is vital always to check carefully whether the patient might have a tendency to misuse drugs or alcohol.
4. It is important to individualize the dose for each patient, to ensure that there is neither under-dosage nor over-dosage.
5. Benzodiazepines should be prescribed only for as long as is necessary, aiming for the shortest possible time but no longer than 4 weeks.
6. If the medication is withdrawn abruptly, rebound anxiety or insomnia can occur. This should not be confused with recurrence of the original symptoms. The patient may require a tapering-off of medication, with ongoing support.
7. Reduction of the dose and discontinuation of benzodiazepine therapy should take place under careful medical observation and with appropriate psychological interventions.

So, before prescribing:

Take a full history including an alcohol and licit and illicit drug history.

Inform the patient of the side-effect profile of benzodiazepines and offer an information leaflet.

Consider and treat, if possible, any underlying causes. Consider referral to other services.

Consider alternative therapies.

Consider delaying prescribing until a subsequent visit.

When prescribing for the first time:

Initiate with the lowest recommended dose, but this may need to be adjusted depending on patient's response.

Do not prescribe for longer than 4 weeks. Use phased dispensing where possible.

Ensure that agreements between doctor and patient are documented.

Record all details of medication prescribed and duration of treatment.

Clear, effective and speedy communication concerning benzo diazepine usage should always take place between the prescribing professionals both within and between services.

For patients dependent upon benzodiazepines or patients in receipt of continuing prescribing

Issue small quantities at a time (usually not more than one week). Review regularly (usually monthly).

Use a long acting benzodiazepine in dosages no higher than diazepam 5 mg three times daily or equivalent.

Ensure that all patients are made aware of the risks of long term benzodiazepine use and document this communication.

Signed consent forms should be used where appropriate.

Encourage all patients with dependency to withdraw and offer them a detoxification programme at regular intervals (at least annually) and document all communication. A significant number of requests for repeat benzodiazepine prescribing are associated with addiction problems, primarily alcohol, or in urban areas, opiate misuse. A doctor who suspects this is the case should seek specialist advice.

INDICATIONS

Anxiety

Benzodiazepine anxiolytics should be prescribed primarily for the short-term relief of anxiety and related symptoms when it is disabling and severe resulting in

significant distress or problems in social functioning. Other forms of anxiety may be treated by psychological means or pharmacological treatments suitable for long-term use. The underlying cause should be determined and addressed.

Benzodiazepines should not usually be prescribed for longer than one month.

There are circumstances in which longer-term prescription of benzodiazepines may be considered desirable because the alternative is considered less beneficial. This may be in conditions such as chronic treatment-resistant anxiety or in patients who have established dependency and are unable to withdraw successfully. There are other situations where anxiety is complicated by other illnesses and where the risk of dependence may be considered acceptable because of the severity of the other disorders.

Sleep

Benzodiazepines are effective, safe and approved hypnotics for the short-term treatment of insomnia. The following guidelines should be noted:

Prescription should be:

- limited to between 2 and 4 weeks;
- at the lowest effective dose; and
- prescribed intermittently.

Care should be taken to exclude any other primary condition such as depression or substance misuse as a cause for insomnia. It may be useful to inform the patient when treatment is started that it will be of limited duration, and explain precisely how the dosage will be progressively decreased. Moreover, it is important that the patient be made aware of the possibility of rebound insomnia, thereby minimising anxiety over such symptoms should they occur while the medication is being discontinued.

Before starting any pharmacological treatment it is important to discuss sleep problems with patients and present them with information which may help them to overcome their sleep difficulties:

- the normal amount of sleep varies widely and usually decreases with age
- temporary sleep problems are common at times of stress or physical illness
- worry about not being able to sleep can worsen insomnia
- alcohol may help in falling asleep, but can lead to restless sleep
- stimulants (including tea and coffee) can cause or worsen insomnia

The choice of benzodiazepine (and dose) depends on the type of sleep disorder:

- Patients who have difficulty in falling asleep can be treated effectively with short or intermediate-acting benzodiazepines.
- Patients experiencing situational insomnia or periods of wake- fulness during the night, or early awakening, need a benzodiazepine with an intermediate half-life. Long-acting benzodiazepines, in general, should not be prescribed, to ensure there is no sedative hangover during the day.

UNWANTED EFFECTS

Withdrawal symptoms

Withdrawal symptoms may occur on cessation or reduction of benzodiazepine and are characterised by anxiety/nervousness, irritability, depressed mood, insomnia, fatigue or lethargy, lack of energy, restlessness and agitation, tremors, dizziness, headaches, muscle aches or stiffness, weakness and difficulty concentrating and remembering. These symptoms may be difficult to distinguish from the original presenting symptoms. Occasionally, withdrawal phenomenon is so severe that the patient may experience seizures.

The incidence and severity of withdrawal symptoms are dependent on speed of tapering-off, the elimination half-life of the drug, the duration of benzodiazepine therapy and the daily dose. Although the general principles of pharmacology

suggest that withdrawal symptoms are linked to a rapid fall in blood concentrations, the clinical emergence of withdrawal symptoms is complex, and is modulated by a number of important factors, including, personality, concurrent diagnoses, patient expectation, social situation, lifestyle and peer influences.

The withdrawal syndrome is more likely if: (a) the benzodiazepine has been taken in regular dosage for more than several months; (b) higher dosages have been used; (c) the drug is stopped suddenly; and (d) a benzodiazepine with a short elimination half-life has been taken (systemic kinetics determine the intensity and time-course of discontinuation phenomena, with these being more florid and more intense in those who were abruptly switched off short elimination half-life drugs such as lorazepam and alprazolam). The true pharmacological withdrawal syndrome is most likely to occur when there is a rapid fall in blood benzodiazepine concentrations.

The syndrome can best be avoided by the prescription of a benzodiazepine for less than 4 weeks with an intermediate or long elimination half-life and by gradual reduction of dosage when a decision is made to discontinue treatment.

Dependence

Dependence on benzodiazepines is mainly manifest by withdrawal symptoms on cessation, which may sometimes be prolonged and result in symptoms which may be hard to distinguish from other anxiety related disorders such as panic disorder. In general, withdrawal reactions are short-lived, lasting for up to a month, but there is controversy about whether symptoms persisting longer are really withdrawal reactions or the manifestations of a chronic underlying neurosis or an exacerbation of the underlying condition triggered by tranquilliser withdrawal.

During therapeutic use, the risk of developing benzodiazepine depend- ence increases with the dose and duration of treatment, the nature of the illness, the severity of symptoms, the expectation of beneficial effect and the intensity of stress factors.

Patients especially at risk are those with:

- a history of addiction
- chronic physical illness, especially if associated with pain
- dysthymic and personality disorders
- chronic sleep disorders.

Long-term dependence should be treated by gradual withdrawal. Psychological support with the addition of cognitive-behavioural therapy should be offered where appropriate and where services are available in order to attenuate any symptoms which may occur. Contact should be made with local health board psychiatric services for assistance in assessing treatment options for difficult cases.

Pharmacological and psychological aids may only have limited benefit and many patients are unable to stop their drugs, or show persistent symptoms after withdrawal. In patients with persistent symptoms, a decision needs to be taken about whether they are generally better off with or without the medication. This decision needs to be taken in conjunction with the patient.

The long-term risks of using benzodiazepines need to be balanced against the benefits. If a decision to prescribe maintenance benzodiazepines is made then the following recommendations are suggested;

- Use a long acting benzodiazepine
- Do not exceed the equivalent of diazepam 5 mg tds
- Issue small quantities at a time (usually not more than one-week)
- Review regularly (usually monthly)
- Ensure that all patients are made aware of the risks of long-term benzodiazepine use and document this communication
- Signed consent forms should be used where appropriate
- Encourage all patients with dependency to withdraw and offer themawithdrawal programme at regular intervals (at least annually) and document all communication

Seek specialist advice before prescribing to patients who have become dependent as a result of substance abuse.

Anterograde amnesia

All benzodiazepines may induce anterograde amnesia. This means that someone given a benzodiazepine may remember information before benzodiazepine administration, but there may be difficulties in later recall of information received after the benzodiazepine was given, until the effects of the drug have worn off.

Anterograde amnesia usually occurs several hours after the drug is taken: to reduce the risk, patients given benzodiazepines as hypnotics should ensure that they will be able to have 7-8 hours uninterrupted sleep.

Paradoxical reactions

Paradoxical reactions such as restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should any of these occur, the drug should be stopped. They are more likely to occur in children and the elderly. Another group to pay particular attention to in relation to paradoxical reactions are drug misusers who may take high and fluctuating amounts of benzodiazepines.

Drowsiness and other effects

Drowsiness during the day, 'flat'emotions, reduced alertness, confusion, fatigue, headache, dizziness, muscle weakness, ataxia or double vision are all possible unwanted effects of benzodiazepine treatment. Such phenomena occur predominantly at the start of therapy but usually disappear with repeated administration. Other side-effects, such as gastrointestinal disturbances, changes in libido or skin reactions have been reported occasionally.

OVERDOSAGE

Symptoms

Benzodiazepine overdose usually results in central nervous system depression, ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, coma (rarely) and death (very rarely). However, overdose does not usually present a threat to life unless combined with other CNS depressants (e.g. alcohol).

Treatment

In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken. Following overdose with oral benzodiazepines, vomiting should be induced (within 1 hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiac function in intensive care. Flumazenil may be useful as an antagonist. Caution should be observed in the use of flumazenil in epileptics treated with benzodiazepines.

Interactions

If benzodiazepines are taken in combination with other CNS depressants (including alcohol), the central depressant effect may be enhanced. This can occur with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, opioid compounds, antiepileptic drugs, anaesthetics and sedative antihistamines. In the case of opioid compounds, enhancement of euphoric effects may also occur.

Compounds which affect certain hepatic enzymes may alter the effect of benzodiazepines. Such reactions are known to occur with a wide variety of medications.

PRECAUTIONS AND CONTRAINDICATIONS

Precautions

Effects on ability to drive or use machines

Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or use machines. This effect may be greatly enhanced if other drugs such as opioid compounds are being taken by the patient. Patients should be advised not to drive or operate machinery if they experience drowsiness or are on opioid compounds.

Depression

Benzodiazepines should not be used alone to treat depression or anxiety associated with depression, as they may mask the symptoms of depression. This can have serious consequences, denying the patient the opportunity of effective antidepressant medication, or resulting in disinhibition which may lead to suicide attempts. Withdrawal from benzodiazepines may, in other cases, precipitate a depression. The need for an anti-depressant is best judged when benzodiazepine issues have been settled either by withdrawal or maintenance therapy.

A lower dose is recommended in patients with chronic respiratory insufficiency, due to the risk of respiratory depression. Patients with impaired liver function should also receive a reduced dose.

Street Diversion

Doctors should be aware that medication they prescribe may be diverted from the intended patient and fall into the wrong hands and be abused. It is not always possible to know which of our patients will divert some or indeed all of their medication to unintended sources. For instance it is known that patients, even in the older age group, may sell on their prescribed medication. For this reason supplies of benzodiazepines should be dispensed in limited quantities, ideally weekly aliquots. By writing “phased dispensing weekly/daily” as appropriate the pharmacist will dispense as requested for both GMS and non GMS prescriptions. It is recognised, however, that this recommendation may be more appropriate in younger rather than older people.

Contraindications

Benzodiazepines are generally contraindicated in patients with: myasthenia gravis hypersensitivity to benzodiazepines severe respiratory insufficiency sleep apnoea syndrome severe hepatic insufficiency

Benzodiazepines are not recommended for the primary treatment of psychotic illness. They are contraindicated for use as hypnotics in children.

SPECIAL PATIENT GROUPS

1) Elderly Patients

Benzodiazepines are the most commonly used psychotropic drug in older people and can be very effective anti-anxiety agents. However, adverse effects in this group include impaired cognition and gait and the development of tolerance dependence and withdrawal. Reduced drug clearance with consequent higher plasma levels may be responsible for increased adverse effects in older people. Benzodiazepines with a long duration of action are particularly likely to accumulate and therefore have an even greater potential for sedative effects and psychomotor impairment. Long acting benzodiazepines, therefore, with active metabolites should usually be avoided in the elderly e.g. diazepam, chlordiazepoxide, flurazepam, nitrazepam. When benzodiazepines are prescribed in older people, short acting benzodiazepines with few active metabolites are preferable e.g. lorazepam 0.5mg bd/tid, temazepam 10-20mg nocte, alprazolam 0.25mg bd/tid.

Older people should be checked regularly at the start of treatment in order to minimize the dosage and/or the frequency of administration to prevent undesirable effects due to accumulation.

Older people who are taking benzodiazepines with a long elimination half-life have been shown to have an increased risk of falls and involvement in road traffic accidents compared to users of short-acting benzodiazepines.

Late life depression can present with anxiety symptoms and should primarily be treated with antidepressant medication rather than benzodiazepines. Benzodiazepines may also be used on a time limited period for the short term treatment of severe insomnia.

Many elderly patients have been taking benzodiazepines on a long term basis and are physiologically and psychologically dependent. It is appropriate to try and taper and discontinue benzodiazepines in these cases; however it may be very difficult to discontinue benzodiazepine use completely. Best practice would be to discuss the issue with the patient and see if the patient will agree to a slow taper and possible discontinuation.

It is important for physicians to read the prescribing information for a particular benzodiazepine very carefully and to observe the relevant warnings.

2) Use During Pregnancy and Lactation

If a product is prescribed to a woman of child bearing potential, she should be warned to contact the prescriber regarding discontinuance of the product if she intends to become, or suspects she is pregnant.

If, for compelling medical reasons, the product is administered during the late stage of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due the pharmacological action of the compound.

Infants born to mothers who took benzodiazepines chronically during the later stages of pregnancy may have developed physical dependence and may be at risk of developing withdrawal symptoms in the postnatal period.

Since benzodiazepines are found in breast milk, they should not be pre- scribed to breastfeeding mothers.

3) Hospitals and Institutions

Many patients find admission to hospital a traumatic experience which causes understandable anxiety. The unfamiliar surrounding and noise of a busy hospital ward may also cause loss of sleep. In some hospitals, the prescription of benzodiazepines to overcome anxiety and loss of sleep has become a routine practice and can lead to patients who have not previously received these drugs being prescribed them during the admission and stay and then subsequently discharged on them. Therefore, where patients are prescribed benzodiazepines during a hospital admission this should be for a short period only (say, up to five days).

The short-term nature of the treatment should be explained to the patient and the continued need for benzodiazepines reviewed at discharge. Patients should be advised of the risk of dependency if drug treatment is continued following discharge from the hospital. Where drug treatment is continued following discharge the general practitioner should be fully informed of the indication for the new prescription and the proposed duration.

The creation of new chronic benzodiazepine users by a hospital admission must be considered unacceptable.

The opposite problem can also occur whereby chronic benzodiazepine users may not be prescribed their usual medicines on admission and their illness may be then complicated unnecessarily by withdrawal symptoms.

In order to avoid this problem, at each hospital admission, it should be determined whether the patient is a non-user, occasional user or routine user of benzodiazepines. Regular users should not have their treatment suddenly stopped but it should be recognised that the hospital admission presents an opportunity to encourage withdrawal or dose reduction in all users of benzodiazepines.

Special problems can arise during long-term care where routine prescribing and administration of benzodiazepines (especially as hypnotics on long stay hospital wards such as elderly care units) may cause problems of dependence. In such cases, patients receiving benzodiazepines should be regularly reviewed, as the only clinical justification for continuing use is dependence. Planned withdrawal of patients dependent on benzodiazepines should be considered. Attempts should be made to improve levels of mental stimulation and physical activity on long stay wards.

Alternative strategies for reducing anxiety and insomnia during an admission other than by the prescription of benzodiazepines should be considered. Suggestions include the reduction of unnecessary noise on wards during normal sleeping hours and the availability of counselling for patients suffering from anxiety. The prescription of alternative hypnotics and sedatives with similar dependence potential to benzodiazepines (e.g. chloral products) and the inappropriate use of antidepressants and anti-psychotics should be discouraged.

4) Alcohol Withdrawal and Benzodiazepines

In an individual with an established alcohol dependence syndrome, the sudden cessation of alcohol can precipitate the onset of an alcohol withdrawal syndrome. The withdrawal syndrome can vary in intensity from mild symptoms of anxiety and sweating to a severe delirium state with associated seizures and mortality. Effectively controlling the symptoms of withdrawal is an important intervention carried out to reduce morbidity. Traditionally benzodiazepines have been used to alleviate the symptoms of withdrawal. These compounds act on specific receptors in the brain called GABA receptors.

These are the principal inhibitory receptors in the brain and action on these results in decreasing noradrenaline release which is thought to be responsible for at least some of the symptoms of withdrawals experienced by alcohol dependent individuals. Benzodiazepines may affect, at least in part, the alcohol related mental confusion, depression and fatigue.

Thus benzodiazepines are safe and effective drugs to use in alcohol withdrawals, however the side effects of memory impairment, drowsiness and lethargy as well as the potential for dependence means that they may interfere with other therapeutic approaches dealing with stress management, coping behaviour or drinking behaviour modification. Therefore benzodiazepines used for this purpose should be in reducing dosages over a relatively short period of time, usually for no more than two weeks.Cross dependence between benzodiazepines and alcohol is also a recognised complication presenting to those dealing with both groups of patients.

5) Substance Misusers

Benzodiazepine prescribing would normally not be initiated in this group. It is recommended that before maintenance benzodiazepine is prescribed specialist advice be sought. (See list of health board contacts at Appendix 3). Benzodiazepine misuse is a great problem amongst the drug misusing community. It is often taken in large quantities in order to achieve an altered state of consciousness and euphoric effect. This is often associated with disinhibition which may lead to aggressive and irresponsible behaviour. It is also taken to help the addict tolerate heroin or cocaine withdrawal.

Very often benzodiazepine dependency develops and compounds the problem, leading to a continuous pattern of benzodiazepine misuse. It should be remembered however that there is a high incidence of mental illness, sexual abuse and social deprivation amongst this group that often contributed to their drug problem.

The use of maintenance benzodiazepines amongst this group, however, remains controversial as they are often used to supplement benzodiazepines acquired illegally.

It is recommended that before maintenance benzodiazepine is prescribed specialist advice be sought. See Appendix 4 for Guidelines for drug misuse treatment services.

Appendix 1

Alternative Strategies to the Prescribing of Benzodiazepines

Insomnia

a) Discussion - frequently talking about what is keeping a person from sleeping is sufficient to address the problem.

b) Relaxation therapy.

c) Avoidance of stimulant drugs and beverages during the evening e.g. coffee, tea, alcohol.

d) Increased physical activity.

e) Increased mental stimulation during the day.

f) Explanation that some people (particularly the elderly) require less than a 'full' night's sleep and that five hours is often sufficient.

g) Avoidance of 'catnapping' during the day.

h) A relaxing bath or a good book can facilitate sleep.

i) It is important to rule out the presence of a depressive illness, the treatment of which is commonly with anti-depressant medication.

j) Yoga -transcendental meditation- exercise.

k) Consider alternative medication ref: British National Formulary. Caution should be used particularly in the prescribing of Chlormethiazole (Heminevrin).

l) If an hypnotic must be prescribed it should be used intermittently, e.g. on only 2 - 3 nights per week.

Anxiety

a) Discussion.

b) Relaxation.

c) Exposure.

d) Increased physical activity.

e) Yoga - transcendental meditation- exercise.

f) Self help books - local library, book shops.

Appendix 2

Methods for Benzodiazepine Withdrawal

Any benzodiazepine withdrawal programme should be carefully planned and structured, the aim being to gradually reduce to zero the amount of drug being taken.

There is no single best technique for withdrawal, but simple dose reduction is successful for most patients. Equally there are no specific data relating to the rate of withdrawal or the total time involved. Nevertheless, whichever technique is used, the regimen must be discussed with the patient, and the goals must be simple and attainable.

Withdrawal can be achieved by many methods. Each involves regular supervision by the general practitioner. For example, the general practitioner can simply gradually reduce the daily dose of the patient's current benzodiazepine over a period of several weeks; or the general practitioner can switch the patient's short-acting benzodiazepine for a long-acting one before attempting withdrawal; alternatively, the withdrawal programme can be supplemented with concomitant therapy.

Listed below are four methods which follow the general structure discussed above. They should be regarded purely as guidelines; the exact withdrawal programme should be tailored to the individual's response due to the wide variation in subjective response.

Method 1

Gradual reduction in dosage

This is the simplest and most common method for withdrawing a benzodiazepine. For example, it is recommended that temazepam be gradually withdrawn, taking 10mg for 2 weeks, 5mg for 2 weeks and then 2.5mg for 2 weeks. Some authorities feel, however, the method is more appropriate for long-acting benzodiazepines, and for short-acting compounds they would recommend method 2.

Method 2

Substitution

1. Substitute the short-acting benzodiazepine with an approximately equivalent dose of a long-acting drug such as diazepam. Because of diazepam's long elimination half-life, the withdrawal symptoms appear to be less severe with little associated 'craving'. However, there may be a problem with daytime sedation if the short-acting benzodiazepine was for night sedation.
2. Substitution should be gradual and the benzodiazepines replaced in increments of one dose per day. This can usually be accomplished within one week but should be tailored to the individual patient. Some patients require a slightly higher dose than the approximate equivalent.
3. Once substitution is achieved, a gradual reduction of the diazepam dosage should follow. Diazepam is available in 2mg, 5mg, and 10mg tablets, all of which can be halved, and in an elixir 2mg in 5ml, which can be diluted.
4. Stepwise reductions in dosage should be made every week or fortnight, or even monthly, depending upon the patient's response. Suggested reductions are:

- Reduce by 2mg if daily dose 15mg to 20mg
- Reduce by 1mg if daily dose 10mg to 15mg
- Reduce by 0.5mg if daily dose 5mg

Tailor the dose reduction to patient response, i.e. weekly, fortnightly or monthly. Once patient is at a dosage of 0.5mg daily the dose interval can be increased to every two to three days.

Example

Replace the drug being used by equivalent doses of diazepam at the rate of one dose per day.

Patient's dosage: lorazepam 1mg three times daily

Day 1	Morning	Afternoon	Night
1 2 3 4 5 6	Lorazepam Lorazepam Lorazepam Lorazepam Diazepam 10mg Diazepam 10mg	Lorazepam Lorazepam Diazepam 10mg Diazepam 10mg Diazepam 10mg Diazepam 10mg	Lorazepam Diazepam 10mg Diazepam 10mg Diazepam 10mg Diazepam 10mg Diazepam 10mg

A few patients have difficulties in changeover and may need to achieve this over a longer period of time.

Method 3

Dose reduction then immediate substitution to long-acting benzodiazepine followed by reduction

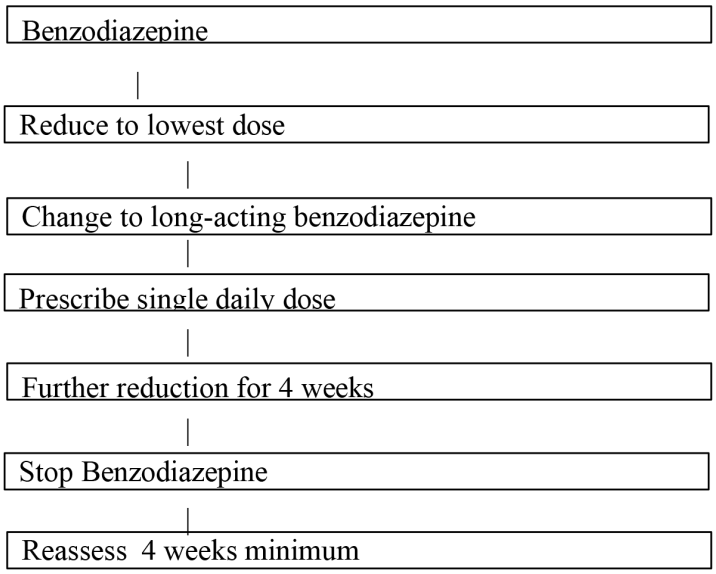
This approach combines Methods 1 and 2 and will make use of the greater flexibility in dosing of the longer acting preparations such as diazepam

Whichever method is chosen, if the patient experiences trouble- some abstinence effects after a reduction of dosage, the dose should be held at that level for a longer period before continuing the reduction at a slower rate. Try to avoid, if possible, increasing the dose at any stage.

Method 4

Adjuvant pharmacotherapy

Pharmacotherapy does not help with the psychological problems associated with benzodiazepine withdrawal, although it may help to reduce tension and anxiety with low doses of a sedative type antipsychotic drug.



However, it is possible to reduce some of the physical symptoms of withdrawal. The Table below shows the pharmacotherapy which is accepted by many general practitioners as valuable.

Manifestation	**Proposed drug or drug group**
Sympathetic overactivity, e.g. tremor, sweating	Propranolol for up to 3 weeks
Insomnia	A short course (about 2 weeks) of an effective hypnotic, e.g. antihistamines, sedative antidepressants, the dose of which is gradually reduced.
To avoid the risk of convulsions	Carbamazepine, or other anticonvulsants for up to 2 weeks may be necessary in rare cases

Adjuvant pharmacotherapy which helps to reduce the physical symptoms of benzodiazepine withdrawal.

Appendix 4

Guidelines for Drug Misuse Treatment Services

It is recommended that;

- Each health board should draw up guidelines for the management of benzodiazepine misuse within its own area. Ideally these guidelines should be drawn up via a consultative process of all relevant staff
- Ongoing evaluation of the implementation of these guidelines should take place
- Due to the complexity of the problems, a multidisciplinary approach should be used to create an individual care plan
- The objective of treatment shall normally be abstinence
- All patients who are considered to be dependent upon benzo diazepine be offered a detoxification programme by a multidisciplinary team
- Education and support including group support/therapy should form the mainstay of treatment
- Prescribed benzodiazepine should be dispensed daily when possible
- Urine metabolites should be monitored to evaluate compliance
- It is recognised that a small group of patients may require benzodiazepine maintenance prescribing. It is recommended that the general guidelines of the main document inform the decision as to which patients fall into this category. Cognisance should be taken of the duration and extent of benzodiazepine use, psychological status and otherpsycho- social stressors.

Guidance on Appropriate Prescribing of Benzodiazepines and Z-drugs (BZRA) for the Treatment of Anxiety and Insomnia

Medicines Management Programme, Ireland, 2021
https://www.drugsandalcohol.ie/34248/

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

6. Anxiety

Anxiety is an unpleasant emotional state characterised by feelings of fear and frequently involving distressing physical/somatic symptoms. Generalised anxiety disorder (GAD) is one of a range of anxiety disorders that include panic disorder (with and without agoraphobia), post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, specific phobias and acute stress disorder. The central feature of GAD is excessive worry about a number of different events associated with heightened tension.

6.1 Non-pharmacological treatments for anxiety

The management of anxiety conditions, however classified or caused, usually includes non-pharmacological measures that may range from low-intensity interventions to specific psychological techniques which can include anxiety management training, behaviour or cognitive therapy. National Institute for Health and Care Excellence (NICE) guidance Generalised Anxiety Disorder and Panic Disorder in Adults: management (2019), recommends that a stepped-care approach is used for patients with GAD, commencing with non-pharmacological measures as outlined in table 5.

Table 5: Stepped-care model for people with generalised anxiety disorder

Focus of intervention	Nature of intervention
STEP 1: All known and suspected presentations of GAD	Identification and assessment; education about GAD and treatment options; active monitoring
STEP 2: Diagnosed GAD that has not improved after education and active monitoring in primary care	Low-intensity psychological interventions: individual non-facilitated self-help*, individual guided self-help and psychoeducational groups
STEP 3: GAD with an inadequate response to step 2 interventions or marked functional impairment	Choice of a high-intensity psychological intervention (cognitive behavioural therapy/ applied relaxation) or a drug treatment
STEP 4: Complex treatment-refractory GAD and very marked functional impairment, such as self-neglect or a high risk of self-harm	Highly specialist treatment, such as complex drug and/or psychological treatment regimens; input from multi-agency teams, crisis services, day hospitals or inpatient care

*A self-administered intervention involving written or electronic self-help materials (usually a book or workbook), usually with minimal therapist contact e.g.an occasional short telephone call of no more than five minutes.

GAD: generalised anxiety disorder

6.2 Pharmacological treatments for anxiety

NICE guidance on the management of GAD and panic disorder (2019) recommends that selective serotonin reuptake inhibitors (SSRIs) should be offered as first-line pharmacological treatment for patients with GAD. Serotonin-noradrenaline reuptake inhibitors (SNRIs) may be used if there is no response to SSRIs. If the person cannot tolerate SSRIs or SNRIs, pregabalin can be considered.

Practice Tip

The MMP recommends selective serotonin reuptake Inhibitors (SSRIs) as first-line pharmacological treatment for generalised anxiety disorder (GAD).

6.2.1 Role of benzodiazepines in the treatment of anxiety

Although benzodiazepines have been used extensively as first-line pharmacological treatment of anxiety since the 1960s, public perception and concern for abuse liability and physical dependence with longer-term use gave rise to a great deal of controversy during the 1980s. The potential for cognitive impairment and associated dependency issues do not make them appropriate first-line pharmacological options.

6.2.2 Benzodiazepines licensed to treat anxiety

The benzodiazepines licensed to treat anxiety are:

- alprazolam
- bromazepam
- chlordiazepoxide
- clobazam
- diazepam
- lorazepam
- prazepam.

6.2.3 Recommended duration of use

Benzodiazepines should be restricted to short-term use during crises when the event is disabling and severe resulting in significant distress or problems in social functioning. ICGP Guidelines for the Management of Depression and Anxiety Disorders in Primary Care (2006), recommend benzodiazepines as adjunctive therapy for a maximum of two weeks. Similarly the consensus paper by the CPI (2012) recommend a short-term treatment duration (2 - 4 weeks) to reduce the risks of dependence and tolerance. Patients should be assessed regularly and the need for continued treatment should be evaluated. The Royal Australian College of General Practitioners (RACGP) Prescribing drugs of dependence in general practice (2015), recommends that patients being prescribed benzodiazepines should obtain all prescriptions from the same doctor so their risk of dependence can be monitored.

Practice Tip

The MMP recommends benzodiazepines should be prescribed for the shortest possible duration and for a maximum period of 2 – 4 weeks for the treatment of anxiety.

7. Insomnia

Insomnia is a disturbance of normal sleep patterns commonly characterised by difficulty in initiating sleep (sleep-onset insomnia) and/or difficulty maintaining sleep (sleep maintenance). Patterns of sleep vary greatly between people. Before a hypnotic medication is prescribed the underlying cause of the insomnia should be established and, where possible, underlying factors should be treated.

7.1 Types of Insomnia

Transient insomnia can occur in individuals who normally sleep well and sleep disturbance may be due to extraneous factors such as increased noise, shift work and jet lag.

Short-term insomnia is usually related to an emotional issue or medical illness. It may last for a few weeks and may recur whereas chronic insomnia can develop due to psychiatric disorders such as anxiety, depression, and abuse of drugs and alcohol.

Sleep-onset insomnia is characterised as difficulty initiating sleep while continuous sleep disturbance is characterised by ongoing sleep disturbance during the night.

The management of insomnia will differ depending on the duration of the problem (short-term versus chronic) and the type of insomnia (sleep-onset versus continuous).

7.2 Non-pharmacological treatments for insomnia

Before prescribing a hypnotic, the underlying cause of the insomnia should be identified and treated if possible. Patients should be provided with information which may help overcome their insomnia including:

- the normal amount of sleep varies widely and usually decreases with age;
- temporary sleep problems are common at times of stress or physical illness;
- alcohol may help in falling asleep, but can lead to restless sleep; and
- stimulants (including tea and coffee) can cause or worsen insomnia.

The American College of Physicians (ACP) guideline Management of Chronic Insomnia Disorder in Adults (2016), recommends that all adult patients receive CBT for insomnia as the initial treatment for chronic insomnia disorder. CBT for insomnia consists of a combination of treatments that include cognitive therapy around sleep, behavioural interventions (e.g. sleep restriction and stimulus control) and education (e.g. sleep hygiene). These non-pharmacological measures should be trialled before prescribing hypnotics (see table 6).

Table 6: Non-pharmacological interventions for the treatment of insomnia

Intervention	Intended effect
Sleep hygiene	Reduce behaviours that interfere with sleep drive or that increase arousal
Sleep restriction	Increase sleep drive and stabilise circadian rhythm
Stimulus control	Reduce arousal in sleep environment and promote the association between bed and sleep
Cognitive therapy	Restructure maladaptive beliefs regarding health and daytime consequences of insomnia
Relaxation therapy	Reduce physical and psychological arousal in sleep environment

Good sleep hygiene should be recommended to patients suffering from insomnia to make them more aware of behavioural, environmental, and temporal factors that may be affecting sleep. Patient guides for the encouragement of good sleep behaviour (The Good Sleep Guide) and relaxation (The Good Relaxation Guide) are available in Appendix B & C respectively and can be made available to patients as a first step in the treatment of both short-term and chronic insomnia.

Practice Tip

The MMP recommends ‘The Good Sleep Guide (Appendix B) as a first-line treatment for insomnia in new patients.

7.3 Pharmacological treatments for insomnia

7.3.1 Role of BZRA in the treatment of insomnia

BZRA should be prescribed for short periods of time only, in strict accordance with their licensed indications for the management of severe insomnia after consideration of the use of non- pharmacological measures. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or causing extreme distress. Similarly the z-drugs, zopiclone and zolpidem, are licensed for the short-term treatment of insomnia which is severe, debilitating or subjecting the individual to extreme distress.

NICE issued technology appraisal guidance (TA77) regarding the use of z-drugs in the short-term management of insomnia (2004). The guidance concluded that there was a lack of compelling evidence to distinguish between z-drugs (zaleplon, zolpidem, zolpiclone) or the shorter-acting benzodiazepine hypnotics.

NICE guidance recommends only switching from one z-drug to another if a patient experiences side-effects that are directly related to the specific z-drug. Patients who have not responded to one of these hypnotic drugs should not be prescribed any of the others.

In general, long-acting benzodiazepine hypnotics should not be prescribed. If prescribed, they tend to have next-day residual effects causing psychomotor impairment and affecting mental function. Short- or intermediate-acting benzodiazepines can be prescribed for patients with sleep-onset insomnia while patients experiencing continuous sleep disturbances or early awakening may require a benzodiazepine with an intermediate half-life.

Practice Tips for the Pharmacological Treatment of Insomnia

- Avoid long-acting benzodiazepine hypnotics.
- Zolpidem should only be prescribed for patients with sleep-onset insomnia.
- Zopiclone is suitable for continuous sleep disturbance.

Note: NICE: National Institute for Health and Care Excellence, UK.

7.3.2 BZRA licensed to treat insomnia

Table 7: BZRA licensed for the treatment of insomnia

Benzodiazepines	Diazepam
	Flurazepam
	Lorazepam
	Lormetazepam
	Nitrazepam
	Temazepam
	Triazolam
Z-drugs	Zolpidem
	Zopiclone

7.3.3 Recommended duration of use

Hypnotics should not be prescribed indiscriminately and routine prescribing is undesirable; they should be reserved for short courses in the acutely distressed. The Department of Health (DoH) Good Practice Guidelines for prescribing benzodiazepines (2002) recommend that hypnotic benzodiazepine prescriptions be limited to between 2 - 4 weeks.[43] The licensed duration of treatment for hypnotic benzodiazepines is a few days to a two-week period, with a maximum duration of four weeks including the tapering off process (see Appendix D).

The SmPC for zolpidem and zopiclone state that treatment duration should be as short as possible. The duration of treatment should usually vary from a few days to two weeks, with a maximum of four weeks including the tapering off process where clinically appropriate.

It may be useful to inform the patient when treatment is initiated that it will be of a limited duration.

In certain cases with BZRA, extension beyond the maximum treatment period may be necessary; this should not take place without clinical re-evaluation of the patient.

Practice Tip

The MMP recommends that BZRA should only be prescribed for a period of a few days to two weeks for the treatment of insomnia.

8. Safety concerns with the use of BZRA

When used appropriately BZRA can be effective for the short-term management of acute severe anxiety or insomnia. However, long-term use of BZRA is associated with problems such as tolerance, dependence and withdrawal symptoms. Patients should be made aware of the possibility of rebound phenomena to minimise anxiety should such symptoms develop when the BZRA is discontinued. Repeat BZRA prescriptions should not be issued without consultation.

8.1 Side-effects

BZRA side-effects include:

- psychomotor impairment and increased risk of motor vehicle accidents and falls
- impairment in judgement and dexterity
- forgetfulness, confusion, irritability, aggression and paradoxical disinhibition.

These side-effects may also occur with short-term use. Unwanted side-effects can largely be prevented by prescribing low dosages and courses of short duration in suitable patients.

8.2 Tolerance

With long-term use, BZRA lose the ability to increase the effect of GABA, resulting in the need to take higher doses to achieve a similar effect. Tolerance to BZRA progressively reduces their effectiveness for the treatment of insomnia or anxiety. Tolerance develops at different rates and degrees for the various actions.

Tolerance to the hypnotic effects of benzodiazepines develops rapidly, usually within days or weeks of regular use while tolerance to the anxiolytic effects develops more slowly, over months. Long–term efficacy of benzodiazepines is unreliable, particularly the hypnotics where tolerance to their effects can develop within 3 - 14 days of continuous use.

8.3 Dependence

The World Health Organisation (WHO) describes dependence syndrome as a cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or class of substances takes a much higher priority for the user than other behaviours that once had greater value.

Dependence is a significant risk in patients receiving treatment for longer than one month which the prescriber should be conscious of when evaluating the relative benefits and risks of continued prescribing. Psychological and physical dependence can develop within a few weeks or months of regular or repeated use.

Benzodiazepine dependence can present in a number of different ways including:

- patients “need” benzodiazepines to carry out normal day-to-day activities
- patients continue to take benzodiazepines even though the original indication for the prescription is no longer relevant
- patients have difficulty in stopping treatment or reducing the dosage due to withdrawal symptoms
- patients become anxious if their next prescription is not readily available
- patients may increase the dosage from that in the original prescription.

8.4 Safety concerns in special patient populations

8.4.1 Older people

The National Healthcare Quality Reporting System Annual Report (2019) highlighted that Ireland has the highest rate of chronic BZRA prescriptions (≥ 365 defined daily doses in one year) in patients aged 65 years and older compared to 15 other Organisation for Economic Co-operation and Development (OECD) countries. In Ireland, approximately 78 per 1,000 older people receive long-term

prescriptions for BZRA compared to an average of 25 per 1,000 across the OECD countries.

- BZRA should not be routinely prescribed in older people; if required they should be used at the lowest dose and with caution, as side-effects are likely to be enhanced e.g. sedation, disturbance of gait, falls, daytime drowsiness, cognitive impairment, hypotension, memory impairment and reduced psychomotor performance.
- Shorter half-life benzodiazepines are usually recommended for older adults (less accumulation and more rapid clearance); however they may be associated with a clinically significant discontinuation syndrome and have higher potential for abuse.
- A meta-analysis has shown that BZRA use in older people is associated with an increased risk of hip fractures. Patients who are newly prescribed BZRA are at the greatest risk.
- Benzodiazepine use has also been associated with an increased risk of Alzheimer's disease in older people. A case-control study showed an increased risk of Alzheimer's disease in older patients who were previously treated for more than three months with a benzodiazepine. The risk was higher with long-acting benzodiazepine use compared to short-acting benzodiazepine use.
- New benzodiazepine use in older people has been associated with an increased risk of dementia compared to non-users.

8.4.2 Pregnancy

- Specialist advice should be sought before prescribing benzodiazepines in pregnancy:
  - ✓ benzodiazepines and metabolites cross the placenta and accumulate in foetal circulation;
  - ✓ it is advisable to avoid in the first trimester due to the risks of teratogenicity (association with incidence of cleft palate); and
  - ✓ prolonged use of benzodiazepines in pregnancy is associated with low birth weight and in the third trimester may result in floppy baby syndrome. There is some evidence to suggest a link with congenital abnormalities such as cleft lip or palate, pyloric stenosis and alimentary tract atresia.

- Z-drugs should not be prescribed during pregnancy.

8.4.3 Hepatic and renal impairment

Prescribing in hepatic impairment

- BZRAs are not indicated in patients with severe hepatic insufficiency as they may precipitate encephalopathy.
- In general, manufacturers advise caution and dose reduction in mild-to-moderate hepatic impairment; benzodiazepines with a shorter half-life are considered safer.

Prescribing in renal impairment

- There is increased cerebral sensitivity to BZRA in patients with renal impairment.

8.5 Safety advice issued in relation to benzodiazepines and opioids

In March 2020, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a reminder that opioids co-prescribed with BZRA can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death. Healthcare professionals are advised to only co-prescribe BZRA and opioids if there is no alternative. If a decision is made to co-prescribe, the lowest possible doses should be given for the shortest duration and patients should be monitored for signs of respiratory depression.

8.6 Resources to raise public awareness of the potential harm associated with BZRA In July 2020, resources were developed for prescribers and pharmacists by the HSE in collaboration with the Medical Council, ICGP, DoH, PSI, HPRA, Office of the Nursing and Midwifery Services Director (ONMSD) and the Nursing and Midwifery Board of Ireland (NMBI) to raise public awareness of the potential harm associated with BZRA.

The resources include:

- Insomnia and Anxiety Medicines- Patient Guide

- Insomnia and Anxiety Medicines- poster for prescriber practice
- Insomnia and Anxiety Medicines- poster for pharmacy.

The patient guide includes information on BZRA, the potential harms associated with their use, and provides tips for improving sleep and managing anxiety. The resources are available on the MMP website:

www.hse.ie/eng/about/who/cspd/ncps/medicines-management/bzra-for-anxiety-insomnia/

Practice Tip

To reduce the risk of side-effects, tolerance and dependence with BZRA, only prescribe low doses and courses of short duration for acute severe symptoms in anxiety and insomnia.

9. Good Practice Guidelines

Good practice guidelines on benzodiazepine prescribing issued by the DoH (2002) in response to a report of the Royal College of Psychiatrists Benzodiazepines: risks, benefits or dependence (1997), stress the significant risk of dependence in patients receiving treatment for longer than one month.

The guidelines recommend that every clinician examine the benefit: risk ratio in each individual case early in treatment and recommend that benzodiazepines should not be prescribed for longer than one month in the treatment of anxiety and should be limited to between 2 - 4 weeks in the treatment of insomnia or sleep disturbance.

In the case of benzodiazepines used to treat insomnia, it may be useful to inform patients that treatment will be of a limited duration when initiated. Patients should be made aware of the possibility of rebound insomnia thereby minimising anxiety over such symptoms should they occur on discontinuation of the benzodiazepine.

Before prescribing a benzodiazepine, the prescriber should:

- Take a full history including alcohol, and licit and illicit drug history
- Inform the patient of the side-effect profile of benzodiazepines and offer an information leaflet
- Consider and treat, if possible any underlying causes
- Consider referral to other services
- Consider alternative therapies
- Consider delaying prescribing until a subsequent visit.

The guidelines outline good practice for prescribers when prescribing benzodiazepines for the first time and when prescribing for dependent patients (see table 8).

Table 8: Good practice guidelines for prescribing benzodiazepines

Prescribing for the first time	Prescribing for dependent patients
Initiate with the lowest dose and adjust according to response	Issue small quantities at a time
Do not prescribe for longer than four weeks	Review regularly, usually monthly
Use phased dispensing where appropriate	Ensure all patients are made aware of the risks of long-term benzodiazepine use and document this
Record all details of medication prescribed and duration of treatment	Encourage all patients with dependency to withdraw and offer them detoxification programmes at regular intervals and document all communications

12. Resources to support deprescribing of BZRA

12.1 Initial consultation

The first consultation with the patient should cover the following points:

- the risks associated with long-term use of BZRA e.g. tolerance, lack of effectiveness, dependency
- the risks of drowsiness, falls, cognitive impairment, confusion
- establish the reasons for sleep disturbance/anxiety
- the withdrawal plan including the tapering process
- advantages of reducing/stopping BZRA e.g. more refreshing sleep, alertness
- the possibility of withdrawal symptoms developing and how to deal with them
- GP practice policy with regard to lack of adherence and lost prescriptions.

12.2 Dose reduction schedules

Following initial consultation with the patient, two examples of dose reduction schedules are outlined below.

12.2.1 A suggested approach for managing patients who want to stop BZRA

*Summarised from NICE Clinical Knowledge Summary: Benzodiazepine and z-drug withdrawal

- Decide if the patient can reduce the dose and stop their current BZRA without switching to diazepam.
- Switching to diazepam should be considered for:
  - ✓ -patients on short-acting potent benzodiazepines (alprazolam and lorazepam);
  - ✓ -patients using preparations that do not easily allow for small reductions in dose (alprazolam, flurazepam, lormetazepam);
  - ✓ -patients experiencing difficulty or who are likely to experience difficulty withdrawing directly from temazepam, nitrazepam, or z-drugs, due to a high degree of dependency (associated with long duration of treatment, high doses, and a history of anxiety problems).
- Seek specialist advice before switching to diazepam in patients with hepatic dysfunction as diazepam may accumulate to toxic levels in these individuals.

- If switching patient to diazepam, carry out gradually in a stepwise manner. Consider making the first switch in the night-time dose to avoid day time sedation. Dose equivalences are set out in tables 9 and 10. Further information on switching to diazepam is available in NICE Clinical Knowledge Summary.
- Start dose withdrawal when conversion to diazepam is complete.
- Upon dose reduction of the patient's current BZRA or diazepam, negotiate a gradual withdrawal schedule which is flexible. Be guided by the patient in making adjustments so that they remain comfortable with the withdrawal process.
  - ✓ Dose tapering such as a 5 - 10% reduction every 1 - 2 weeks, or an eighth of the dose fortnightly, with a slower reduction at lower doses. The rate of reduction should take into account the drug, dose and duration of treatment, as well as personal circumstances.
  - ✓ Titrate dose according to severity of withdrawal symptoms. If the patient experiences difficulties with a dose reduction, encourage them to persevere and suggest delaying the next reduction. Do not revert to a higher dose. Make future dose reductions in smaller steps if necessary.
  - ✓ Review frequently to detect and manage problems, and to provide advice and encouragement.

See NICE Clinical Knowledge Summary: Benzodiazepine and z-drug withdrawal for further information. Examples of switching schedules to diazepam and withdrawal schedules for BZRA are available in the Aston Manual (www.benzo.org.uk/manual/bzsched.htm).

Table 9: Dose equivalence table if switching from current benzodiazepine to diazepam

Drug	Dose equivalent to diazepam 5 mg
Alprazolam	250 micrograms
Chlordiazepoxide	12.5 mg
Clobazam	10 mg
Clonazepam	250 micrograms

Flurazepam	7.5 - 15 mg
Lorazepam	500 micrograms
Lormetazepam	0.5 - 1 mg
Nitrazepam	5 mg
Temazepam	10 mg

Table 10: Dose equivalence table if switching from current z-drug to diazepam

Drug	Dose equivalent to diazepam 5 mg
Zopiclone	7.5 mg
Zolpidem	10 mg

12.2.2 A suggested protocol for withdrawal following long-term benzodiazepine use

- Transfer patient stepwise, one dose at a time over about a week, to an equivalent daily dose of diazepam (see table 9), preferably taken at night.
- Reduce diazepam dose, usually by 1 - 2 mg every 2 - 4 weeks (in patients taking high doses of benzodiazepines, initially it may be more appropriate to reduce the dose by up to one-tenth every 1 - 2 weeks). If uncomfortable withdrawal symptoms occur, maintain this dose until symptoms lessen.
- Reduce diazepam dose further, if necessary in smaller steps; steps of 500 micrograms may be appropriate towards the end of withdrawal. Then stop completely.
- For long-term patients, the period needed for complete withdrawal may vary from several months to a year or more.
- The addition of beta-blockers, antidepressants and antipsychotics should be avoided where possible.
- Counselling can be of considerable help both during and after the taper.

Provide patients with Stopping your benzodiazepine and z-drug: A guide for patients available in Appendix F.

Other examples of withdrawal schedules are available in the National Community Detoxification: Benzodiazepine Guidelines (2016) available at:

www.drugs.ie/downloadDocs/2017/Community-Detox-Guidelines-Benzodiazepines-2017.pdf

12.3 Withdrawal symptoms

Benzodiazepine withdrawal syndrome may develop at any time up to three weeks after stopping a long-acting benzodiazepine but may occur within a day in the case of short-acting agents. It is characterised by insomnia, anxiety, loss of appetite and of body-weight, tremor, perspiration, tinnitus and perceptual disturbances. Some symptoms may be similar to the original complaint and encourage further prescribing; some symptoms may continue for weeks or months after stopping benzodiazepines. The severity of withdrawal symptoms depends on several factors including treatment duration, drug dose, drug half-life, and baseline levels of anxiety and depression. The risk of withdrawal symptoms is greater with the short-acting benzodiazepines.

12.4 Managing patients who do not want to reduce or discontinue treatment

The following points should be considered in patients who do not want to reduce or discontinue treatment:

- do not pressurise patients to reduce or discontinue use unless they are motivated to do so;
- listen to concerns about the strategy, explain the benefits and advantages and reassure the patient;
- encourage even small reductions which may help the patient to realise that their fears are unfounded; and
- encourage patients to revert if they have any change in their circumstances which might facilitate them undergoing withdrawal. Likewise, prescribers should be alert to the opportunity for BZRA withdrawal that arises if a patient's circumstance changes.

Practice Point

There are two approaches to deprescribing of BRZA:

i. Withdraw slowly from current BZRA

ii. Switch patients on a BZRA to an equivalent dose of a long-acting slowly-metabolised benzodiazepine (e.g. diazepam) which is slowly tapered down.

13. Summary

Although BZRA can be effective for the short-term management of a range of medical and psychiatric conditions, it is important to exercise caution when prescribing these medicines and to only prescribe them for the shortest possible duration for treatment of insomnia and anxiety. Prescribers should consider non-pharmacological management options for patients with insomnia/anxiety prior to prescribing BZRA. When prescribing BZRA, the lowest dose which controls symptoms should always be prescribed. Repeat prescribing should be avoided as tolerance can develop within days or weeks of regular use to the hypnotic effects and more slowly, over months to the anxiolytic effects. Caution is especially relevant when prescribing for patients with a history of substance abuse or addiction. Prescribers must exercise appropriate judgement and consider whether the benefits associated with the use of these drugs outweigh the potential risks. Prescribing of BZRA should be avoided in older people as they are at a greater risk of developing ataxia and confusion leading to falls and injury.

BZRA in the treatment of anxiety and insomnia

- BZRA should only be initiated and prescribed at the lowest effective dose for as short a duration as possible.
- Non-pharmacological management options should always be considered as alternatives or additions to BZRA treatment.
- Prior to prescribing a BZRA, inform the patient of the side-effect profile of BZRA and offer an information leaflet.
- Patients being prescribed BZRA should obtain all prescriptions from the same doctor so their risk of dependence can be monitored.

- Repeat BZRA prescriptions should not be issued without consultation.
- Tolerance to hypnotic effects of benzodiazepines may develop after a few days or weeks of regular use while tolerance to the anxiolytic effects may develop more slowly over months.
- Dependence is a significant risk in some patients on treatment for longer than one month; consider this risk before initiating treatment.
- Patients should be encouraged to withdraw gradually (if appropriate) after long-term use to minimise the risk of withdrawal symptoms.

Overcoming Books: A self-help guide using Cognitive Behavioural Techniques

- OVERCOMING ANGER AND IRRITABILITY
- OVERCOMING ANOREXIA NERVOSA
- OVERCOMING ANXIETY BULIMIA NERVOSA AND BINGE-EATING
- OVERCOMING CHILDHOOD TRAUMA
- OVERCOMING CHRONIC FATIGUE
- OVERCOMING CHRONIC PAIN
- OVERCOMING COMPULSIVE GAMBLING
- OVERCOMING DEPERSONALIZATON AND FEELINGS OF UNREALITY
- OVERCOMING DEPRESSION
- OVERCOMING GRIEF
- OVERCOMING INSOMNIA AND SLEEP PROBLEMS
- OVERCOMING HEALTH ANXIETY
- OVERCOMING LOW SELF-ESTEEM
- OVERCOMING MOOD SWINGS
- OVERCOMING OBSESSIVE COMPULSIVE DISORDER
- OVERCOMING PANIC
- OVERCOMING ANXIETY
- OVERCOMING PARANOID AND SUSPICIOUS THOUGHTS
- OVERCOMING PROBLEM DRINKING
- OVERCOMING RELATIONSHIP PROBLEMS

- OVERCOMING SEXUAL PROBLEMS
- OVERCOMING SOCIAL ANXIETY AND SHYNESS
- OVERCOMING TRAUMATIC STRESS
- OVERCOMING WEIGHT PROBLEMS
- OVERCOMING WORRY AND GENERALISED ANXIETY DISORDER
- OVERCOMING YOUR CHILD'S FEARS AND WORRIES
- OVERCOMING YOUR CHILD'S SHYNESS AND SOCIAL ANXIETY

The above book titles can be bought online or in local book shops.

Appendix B: The Good Sleep Guide*

Establish a regular sleep pattern

- Set the alarm for the same time every morning for seven days a week, at least until your sleep pattern settles down.
- Get up at the same time every day, even if you did not fall asleep until late.
- Do not sleep during the day.

During the evening

- Ensure you 'put the day to rest'. Think it through and use a notebook if necessary. Tie up "loose ends" in your mind and plan ahead.
- Try to keep yourself fit by performing light exercise in the late afternoon or early evening (later than this can disturb your sleep).
- Have a regular routine before sleep, whereby you wind down during the course of the evening and avoid anything that is mentally demanding within 90 minutes of bedtime.
- Keep your sleep for bedtime (i.e. avoid falling asleep or snoozing in the armchair).
- Do not drink too much caffeinated substances (e.g. coffee, tea and certain soft drinks) and only have a light snack for supper. Try decaffeinated milk-based or herbal beverages.
- Do not drink alcohol to aid your sleep. It may help you fall asleep, but you will almost certainly wake up during the night.

- Make sure your bed is comfortable and the bedroom is not too cold (but not too warm) and is quiet (use earplugs if necessary).

At bedtime

- Go to bed when you are 'sleepy tired' and not before.
- Do not read or watch TV in bed.
- Turn the lights off when you get into bed.
- Relax and tell yourself that 'sleep will come when it's ready'. Enjoy relaxing even if you don't fall asleep at first.
- Do not try to fall asleep. Sleep cannot be switched on deliberately but attempting to do so may switch it off!

If you have problems getting to sleep

- Try not to get upset or frustrated as sleep problems are quite common and they are not as damaging as you might think.
- If you are awake in bed for more than 20 minutes, get up and go into another room.
- Do something relaxing for a while and don't worry about tomorrow. Read, watch television or listen to quiet music and after a while you should feel tired enough to go to bed again.
- Remember that people usually cope quite well even after a sleepless night. Only return to bed when you feel "sleepy tired".
- Establishing a good sleep pattern may take a number of weeks; however, you should remain confident that you will achieve it by working through this guide.

Appendix C: The Good Relaxation Guide*

Dealing with physical tension

- Finding and dedicating time to relax is essential. Give relaxation some of your time, not just what's left over.
- Incorporate relaxing activities into your lifestyle. Do not rush tasks or try too hard to resolve issues.

- Adopt a relaxation routine, but do not expect to learn without practice.
- Relaxation routines are available (audio recordings) which help to relieve muscle tension and teach appropriate breathing exercises.
- Try not to worry about tension symptoms, such as aches, stiffness, increased heart rate, perspiration, stomach churning, etc.
- Keep fit and try adhering to a physical exercise regime. Regular brisk walks or swimming can help relieve tension.

Dealing with worry

- Accept that worrying is normal and on occasion it may be useful.
- Write down your concerns and decide which ones are more important using a rating system (i.e. marks out of ten).
- Work out a plan of action for each problem.
- Share your worries with friends, relatives or your GP, as they may provide helpful advice.
- Mentally repeating a comforting phrase may help block out worrying thoughts. Similarly, reading, crosswords, hobbies and interests may all help keep your mind active and positive.
- Enjoy quiet moments (e.g. sit and listen to relaxing music). Allow your mind to wander and try to picture yourself in pleasant situations.

Dealing with difficult situations

- Build your confidence by accepting and confronting circumstances that make you feel more anxious. Adopt a step-by-step approach to help face things and places which make you feel tense. Regular practice will help you overcome these issues.
- Write a plan and decide how you are going to deal with difficult situations.
- For further encouragement, reward yourself and share with others when you overcome difficult situations.
- As you face difficult situations your confidence will grow and your anxiety symptoms should become less troublesome.
- Everyone has good and bad days. Expect more good days as time goes on.

- Try to put together a programme incorporating all the elements presented in 'The Good Relaxation Guide' that meets the needs of your particular situation. Remember that expert guidance and advice is available if you need further help.

Appendix D: BZRA licensed for the treatment of anxiety and insomnia-licensed dosage and duration as per SmPC

Anxiety

Benzodiazepine	Dose in adults	Dose in older people	Licensed duration
Alprazolam	Initially 0.5 mg - 1 mg daily in divided doses, with increments (no greater than 1 mg every 3 - 4 days), to the level of optimal control usually 3 to 4 mg daily.	Initially 0.25 mg twice daily	Maximum 8 - 12 weeks including a tapering off process
Bromazepam	3 - 18 mg daily in divided doses	Half the adult dose	Maximum 8 - 12 weeks including a tapering off process
Chlordiazepoxide	30 mg daily in divided doses	Half the adult dose	Maximum four weeks including a tapering off process
Clobazam	20 - 30 mg daily in divided doses or as a single dose given at night	10 - 20 mg daily	Maximum 8 - 12 weeks including a tapering off process
Diazepam	2 mg three times daily Maximum dose: 30 mg daily in divided doses	Half the adult dose	Maximum 8 - 12 weeks including a tapering off process. Treatment should not be continued at the full dose beyond four weeks
Lorazepam	1 - 4 mg daily in divided doses	Half the adult dose	A few days to four weeks including the tapering off process

Prazepam	30 mg daily in single or divided doses	Half the adult dose	Maximum 4 - 6 weeks including a tapering off process

Insomnia

BZRA	Drug Class	Dose in adults*	Dose in older people*	Licensed duration
Diazepam	Benzodiazepine	Insomnia associated with anxiety: 5 - 15 mg	Insomnia associated with anxiety: 2.5 - 7.5 mg	Maximum four weeks including tapering off process
Flurazepam	Benzodiazepine	15 - 30 mg	15 mg	Few days to two weeks, maximum four weeks including tapering off process
Lorazepam	Benzodiazepine	Insomnia associated with anxiety: 1 - 2 mg	Insomnia associated with anxiety: 0.5 - 1 mg	Few days to four weeks including the tapering off process
Lormetazepam†	Benzodiazepine	1 mg	0.5 mg	Few days to two weeks, maximum four weeks including tapering off process
Nitrazepam	Benzodiazepine	5 - 10 mg	2.5 - 5 mg	Few days to two weeks, maximum four weeks including tapering off process

Temazepam	Benzodiazepine	10 - 20 mg	10 mg	Few days to two weeks, maximum four weeks including tapering off process
Triazolam	Benzodiazepine	0.25 mg, 0.125 mg in patients previously untreated with hypnotics	0.125 mg	Few days to two weeks, maximum four weeks including tapering off process
Zolpidem	Z-drug	10 mg	5 mg	Few days to two weeks, maximum four weeks including tapering off process
Zopiclone	Z-drug	7.5 mg	3.75 mg	Few days to two weeks, maximum four weeks including tapering off process

*Hypnotic BZRA should be taken at night. See individual SmPCs for more information on times these medicines should be taken in relation to bedtime.

†The marketing authorisation holder, Bayer Ltd, has notified the Health Products Regulatory Authority (HPRA) of its decision to withdraw noctamid® (lormetazepam) from the Irish Market on 9 March 2020.

Appendix F: Stopping your medicine: benzodiazepines and z-drugs. A guide for patients

What are benzodiazepines and z-drugs, and why are they used?

Benzodiazepines are a group of medicines that can be prescribed for short periods to help with sleeping problems or to help with episodes of severe anxiety. Examples

include temazepam and nitrazepam for sleeping problems, and diazepam and lorazepam for anxiety.

Z-drugs act in a similar way to benzodiazepines and are used to help with sleeping problems. Examples of z-drugs are zolpidem and zopiclone.

Benzodiazepines and z-drugs are only available on prescription and must only be taken by the person they were prescribed for.

Benzodiazepines and z-drugs often work well for a short period of two to four weeks, but if you use them for longer, the medicine may lose its effect and you may become dependent on it.

What are the side effects of taking benzodiazepines and z-drugs?

Benzodiazepines and z-drugs act on the brain and may therefore:

- affect your memory and concentration
- make you feel confused or irritable
- make you feel drowsy
- make you more likely to have a fall
- make you more likely to have an accident, either at home, work or in the car.

Why should I stop taking a benzodiazepine or z-drug?

There are many good reasons why you should stop taking your benzodiazepine or z drug:

- If you have used it for a long time and the medicine has lost its effect, it will no longer help with the condition you are taking it for
- You may become, or may have already become, dependent on it. If you stop, you will have fewer side effects, so you will be:
  - ✓ More alert and able to concentrate
  - ✓ Less drowsy
  - ✓ Less irritable and depressed
  - ✓ Less likely to have an accident when driving.

How should I stop taking my benzodiazepine or z-drug?

1. DO NOT stop taking your medicine suddenly

You should discuss stopping your medicine with your doctor, pharmacist or practice nurse to make sure that you reduce your dose slowly. Different people will need to reduce their dose at different speeds. Once you have decided to stop, it is important that you make this a slow gradual process, as this will give you a better chance of long-term success. It is important that you take it at your own pace – one that feels right for you.

2. Plan how you will reduce and stop

Your doctor, pharmacist or practice nurse will give you advice on how you should reduce the dose of your medicine and help you think about other ways of dealing with your worries/sleep problems. Depending on which medicine you are taking, it may be easier to withdraw if you change to diazepam tablets. Diazepam tablets are available in a number of different strengths, which makes it easier to reduce your dose more slowly. Your doctor, pharmacist or practice nurse will let you know if you can change to diazepam and will tell you how you can reduce your dose. Most people find that about one to two weeks between each dose reduction works for them, but everyone should find their own level.

3. Keep a diary

Keeping a diary can help as it records your progress and achievements. This will give you more confidence and encouragement to carry on.

4. Don’t go back!

When people begin to reduce their dose, they often become more able to deal with normal day-to-day events and may feel much better. However, it is also common to have a bad patch at some time during the process. If you feel you are going through a bad patch, stick with the current dose until you feel ready to reduce again; this may take several weeks but it is important that you take it at your own pace. Any reduction in dose is a step in the right direction.

5. Be aware of possible side effects

If your medicine is reduced slowly it is unlikely that you will have any side effects, but it is a good idea to be aware of possible side effects as they will tell you that you may need to reduce more slowly:

- Aches and pains can be common when reducing the dose of benzodiazepines and z-drugs; taking painkillers can help you feel better.
- Sleeping problems may occur when reducing your dose, so it is important to get some exercise as this can help you sleep. Try not to worry about not sleeping; the more you worry about not getting sleep, the less sleep you are likely to get.
- Stomach and bowel problems, such as diarrhoea and irritable bowel syndrome may occur. These symptoms usually disappear after stopping the medicine completely, but you may wish to discuss them with your doctor or pharmacist.
- Sinus problems can cause sinus pain; taking painkillers can help.
- Vivid dreams and nightmares may occur. As you reduce your dose, your dreaming will return and although they may sometimes be disturbing, it is a sign that your sleep is returning to normal and that your body is re-adjusting successfully.
- Hot flushes and shivering. The feeling of burning and extreme heat and sweating is also common, while some people can suddenly feel cold.
- Panic attacks can be very distressing but they are never fatal and usually last no more than 30 minutes. Getting control of your breathing by taking slower and deeper breaths will help you feel less panic.
- Anxiety may be mistaken for the condition that your medicine was prescribed for in the first place.
- Agoraphobia is a type of anxiety disorder in which you fear and often avoid places or situations that might cause you to panic and make you feel trapped, helpless or embarrassed. Usually, as you continue to reduce your dose, these feelings go away.

With time these symptoms should pass – don’t give up. Good luck!

Prescriptions of Hypnotics, Benzodiazepines and Codeine Containing Cough Mixtures - Clinical Guidance and What You Need to Know About MOH Rules

Singapore Medical Council (SMC)

https://isomer-user-content.by.gov.sg/77/355fd8e0-23d2-442c-9d16-c0260fd5a84d/smc-newsletter-2022_20th-ed_nov.pdf

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

The improper prescribing of benzodiazepines (BZDs), hypnotics and codeine containing cough mixtures (CCCMs) all carry risk of misuse, abuse and dependence. All doctors are advised to familiarise themselves with the guidelines below and to comply with the requirements.

Benzodiazepines and Hypnotics

This section on BZDs and hypnotics takes reference from the following documents:

- The 2008 Ministry of Health (MOH) clinical practice guidelines (CPG) on the prescribing of benzodiazepines.
- The 2008 administrative guidelines on the prescribing of benzodiazepines and other hypnotics.

Definitions

Benzodiazepines (BZDs) are a class of drugs that have hypnotic, anxiolytic, muscle relaxant and anti-convulsant properties. Zopiclone (Imovane®) and Zolpidem (Stilnox®) are considered non-benzodiazepine hypnotics (non-BZDs).

In this article the non-BZDs are referred to as hypnotics.

The BZDs and non-BZD's have similar profiles with respect to side-effects, dependence and tolerance. Therefore, the prescription of Zolpidem and Zopiclone should be treated with the same cautions as BZDs.

Indications for Use

There is a need for every doctor to ensure that BZDs/hypnotics are used appropriately to treat insomnia, anxiety and other psychiatric and medical conditions. Their inappropriate use can lead to undesired results or tolerance and drug dependence.

- A short course of 2 to 4 weeks of a BZD/hypnotic may be considered in acute insomnia (less than 4 weeks) if it is severe, distressing and disabling. It should be prescribed for intermittent use and only when necessary.
- For chronic insomnia (> 4 weeks), non-pharmacological therapies are the mainstays of management and BZD/hypnotic drug use should be avoided as far as possible. Doctors should routinely warn patients about rebound insomnia with the use of BZDs/hypnotics and document such warnings accordingly.
- Similarly, BZDs are indicated for short-term relief (2 to 4 weeks only) of anxiety that is severe, disabling or subjecting an individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness.
- BZDs may also be added to anti-depressants in the short term to offset their initial excitatory effects in the treatment of depression and anxiety disorders and should be tapered and withdrawn by 4 weeks. BZDs should not be used as monotherapy in the treatment of depression.
- BZDs can be used in the management of medical conditions such as seizures, epilepsy and alcohol withdrawal. However, such complicated medical conditions should be referred to tertiary and specialist care.
- BZDs/hypnotics should be avoided in pregnant and breast-feeding women.
- It should also be avoided as first line treatment in children and adolescents, unless being used by specialists for specific indications.

- BZDs/hypnotics should be used with caution in older persons and only on a short-term basis and at a lower dose. Long-term use should be avoided due to the risk of cognitive impairment and falls.
- Care should be taken when prescribing BZDs/hypnotics in certain persons to avoid excessive sedation, which may pose a risk to the patient who drives or operates heavy machinery etc.

Abuse and Dependence

- Extended and long-term use of BZDs/hypnotics beyond 2 to 4 weeks is not recommended even when used at therapeutic doses, because efficacy is not clearly established.
- There must be appropriate clinical review, clear indications and adequate documentation for any continued or repeat BZD/hypnotic prescription.
- The concurrent use of two or more BZDs/hypnotics should be avoided.
- BZD/hypnotic use should be limited to short term symptomatic relief, at the lowest effective dose and taken intermittently, to minimise the side-effects and risks of dependence.
- BZDs should be gradually tapered, monitored and titrated to minimize withdrawal symptoms. For those on less than 4 weeks of BZDs, the dose can be discontinued or reduced over 1 to 2 weeks. For those on more than 4 weeks of BZDs requiring a withdrawal protocol, doctors can refer to the CPG for BZDs or refer to specialist care.
- All patients receiving BZDs/hypnotics should be routinely advised about the risk of developing dependence. Patients receiving BZDs/hypnotics should be advised to obtain all such prescriptions from the same doctor wherever possible, so that the risk of abuse and dependence may be monitored.
- Caution should be exercised when prescribing BZDs/hypnotics or avoided altogether for patients with known history or evidence of alcohol or substance abuse or those with signs of intravenous drug use. Doctors are strongly discouraged from prescribing highly addictive BZDs such as midazolam (Dormium®) and nimetazepam (Erimin®) as they are commonly abused.

- Under Regulation 19 of the Misuse of Drugs Regulation, a doctor who attends to a person who he considers, or has reasonable grounds to suspect, is a drug addict, shall within 7 days of the attendance, furnish to both the Director of Medical Services and the Director of the Central Narcotics Bureau, the particulars of that person.

Documentation

The standard required by the MOH BZD/hypnotic administrative guidelines on the documentation and maintenance of patient medical records states that:

- All information relating to a particular patient must be consolidated as one medical record relating only to that patient. Such information must be legibly documented.
- Each patient's medical record must be entirely reproducible upon request by the MOH or SMC.
- The following information must be documented in the medical record of every patient who is prescribed with BZDs/hypnotics:
  - Comprehensive history, including psychosocial history and previous use of BZDs/hypnotics.
  - Comprehensive physical examination findings, including evidence of misuse of BZDs/hypnotics or other drugs.
  - Withdrawal symptoms to BZDs/hypnotics previously experienced by the patient, if any.
- The following information must be documented in the medical records of every patient each time he/she is prescribed with BZDs/hypnotics, either initially or as repeat prescriptions:
  - The prescribed type/name of BZD/hypnotic, its dosage and duration of use.
  - Indication(s) and/or justification for prescribing BZDs/hypnotics.
  - Physical signs or evidence of tolerance, physical/psychological dependence or any illicit use or misuse of BZDs/hypnotics or other drugs.

Specialist Referrals

The following patients should not be further prescribed with BZDs/hypnotics, but referred to the appropriate specialist for further management:

- Patients who require or have been prescribed BZDs/hypnotics beyond a cumulative period of 8 weeks.
- Patients who are already on high-dose and/or long-term BZDs from their specialists or general hospitals; where possible, these patients should be referred back to their respective specialists for further management until they are weaned off BZDs/hypnotics.
- Patients who are non-compliant with professional advice or warnings to reduce intake of BZDs/hypnotics.

Patients who refuse to be referred to a specialist should be counselled appropriately. Such refusal should be documented in the patients' medical records. Patients who refuse and turn aggressive should be reported to the police.

Good Practices in the Prescription of Benzodiazepines and Other Sedative Hypnotics

Singapore Medical Journal, 64(3), 217–218, 2023.
https://doi.org/10.11622/smedj.2021232

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

Dear Sir,

Since the publication of the Ministry of Health's Clinical Practice Guidelines 'Prescribing of Benzodiazepines' and 'Administrative Guidelines in Insomnia' in 2008, there has not been any further update or local official guideline on this pertinent issue. Benzodiazepines and other sedative hypnotics are addictive and have adverse side effects.

To promote safe and responsible prescription, the Section of Addiction Psychiatry of the College of Psychiatrists, Singapore, and the National Addictions Management Service, Singapore, have worked together to produce the following set of good practice recommendations. It is a consensus among professionals working together in the field of addictions and presents a working set of recommendations for general practitioners (GPs) and non-psychiatrists working in Singapore.

1. Benzodiazepines and 'Z-hypnotics' (e.g. zolpidem, zopiclone) should not be used as first-line agents for the management of insomnia. GPs should discuss sleep hygiene with patients.

2. A course of sedating antihistamines, melatonin or sedating antidepressants may be considered. The side effects of such medications need to be discussed with patients. It is recommended that their use be limited to a short course (2–4 weeks).
3. A short (2–4-week) course of benzodiazepines may be considered for acute insomnia. Shorter-acting benzodiazepines (e.g. alprazolam) have a higher addictive potential than longer-acting ones. However, longer-acting benzodiazepines may cause daytime sedation. As such, their risks and benefits should be considered.
4. Patients with acute insomnia should not be prescribed more than one type of sedative hypnotic.
5. The mainstay of treatment for chronic insomnia is cognitive behavioural therapy for insomnia (CBT-I), and patients should be referred for professional help with a psychologist trained in CBT-I.
6. Patients with chronic (>3 months) insomnia should be referred to a specialist for thorough evaluation.
7. For patients with chronic insomnia who are already on benzodiazepine or 'Z-hypnotics' for many years, dosage reduction should be considered. These patients should be referred to psychiatrists, as they could be dependent on such drugs.
8. Benzodiazepines should not be the first line of treatment for anxiety disorders and should not be prescribed as monotherapy for anxiety disorders.
9. When prescribed for severe anxiety, benzodiazepines should be prescribed at their lowest effective dose for the shortest period of time, and should be avoided if the anxiety is mild.
10. Dosage of benzodiazepines and'Z-hypnotics'should be reduced in the elderly (>65 years old).
11. Benzodiazepines and'Z-hypnotics' should generally not be prescribed to patients with substance use disorders.
12. The risk of developing dependence and long-term side effects of benzodiazepines and'Z-hypnotics'should be discussed with patients and documented.

Summarizing The World Health Organization's 2023 Benzodiazepine Guidelines

By Benzodiazepine Information Coalition December 1, 2023 Comments

https://www.benzoinfo.com/2023/12/01/who-2023/

*** Note: 1. The content of this article is excerpted from the above reference.**
2. The order of arrangement (coding) in this article follows that of the original source.

On November 20, 2023, the World Health Organization's (WHO) 2023 (Third Edition) Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological, and substance use disorders introduced revised guidelines. The mhGAP guideline supports countries to strengthen their capacity to deal with the growing burden of mental, neurological, and substance use (MNS) conditions and narrow the treatment gap.

This new edition includes 30 updated and 18 new recommendations, alongside 90 pre-existing recommendations. This is the third iteration of the guideline and reflects 15 years of investment in the mhGAP program. The revised recommendations ensure that mhGAP continues to offer high-quality, timely, transparent, and evidence-based guidance to support non-specialist health workers in low-income and middle-income countries in providing treatment and care to individuals with MNS conditions.

Their findings regarding benzodiazepines are summarized below.

Anxiety Disorders

(see page 25 of the guideline)

The World Health Organization's new recommendation strongly discourages benzodiazepines for anxiety disorders, stating: Benzodiazepines are not recommended for the treatment of adults with generalized anxiety disorder (GAD)

and/or panic disorder. For emergency management of acute and severe anxiety symptoms, benzodiazepines may be considered but only as a short-term (3–7 days maximum) measure.

The WHO cautions that benzodiazepines carry a risk of dependence. They stress that benzodiazepines shouldn't be commonly prescribed for anxiety or distress; instead, they should be used in specific cases of acute and severe anxiety or distress where other treatments haven't worked or aren't available. They highlight the importance of obtaining informed consent before prescribing and encourage a gradual discontinuation process.

They also point out that there are research gaps—a limited number of studies on the long-term effectiveness and safety of benzodiazepines—and indicate that further research would help to quantify the risks of longer-term use.

Child and Adolescent Mental Disorders (CAMH)

(see page 43 of the guideline)

A new recommendation by the WHO states that since the harms of the intervention outweigh the benefits, a strong recommendation is made against use of pharmacological interventions for children and adolescents with anxiety disorders.

The justification for this recommendation comes from evidence in one meta-analysis, which showed no significant difference between all tricyclic antidepressants (pooled) and benzodiazepines when compared to pill placebo for improving anxiety symptoms. Group SSRIs and benzodiazepines had significantly more people stopping the treatment due to adverse effects compared to those receiving the placebo pill.

Epilepsy

(see pages 76-79 of the guideline)

The World Health Organization's guidelines mention that about 30–40% of adults with established status epilepticus don't respond to initial benzodiazepine treatment. These individuals require additional treatment with other intravenous anti-seizure medicines (ASMs). The guidelines caution that using phenobarbital and diazepam infusion carries the potential risk of sedation and respiratory depression, especially

if used after benzodiazepines. WHO also found that, like adults, 30-40% of all children do not respond to initial treatment with benzodiazepines. The WHO's recommendations on epilepsy are conditional and based on low to moderate certainty of evidence.

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食品藥物管理署
Taiwan Food and Drug Administration

Compilation of International Recommendations for Prescribing Benzodiazepine Receptor Agonists

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審　　核　祁若鳳　劉淑芬　張志旭　簡希文　鄭啓慧　莊佩鈴
出版年月　民國115年7月
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