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Dear Colleagues

This guidance is currently under review by the author.

Guidance For The Safe Prescribing Of Benzodiazepines And Z Drugs And Management Of Dependence In NHS Grampian, Version 3

This document has been risk assessed by the author and deemed appropriate to be used during this review period. A copy of the risk assessment can be provided on request.

If you have any queries regarding this, please do not hesitate to contact the Medicines Guidelines and Policy Group (MGPG) email at gram.mgpg@nhs.scot

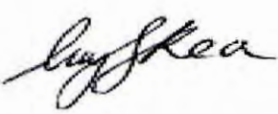
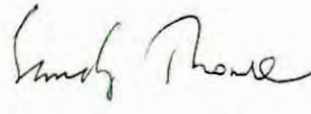
Yours sincerely



Lesley Coyle
Chair of MGPG, NHSG

**Guidance For The Safe Prescribing Of Benzodiazepines And Z Drugs
And Management Of Dependence In NHS Grampian**

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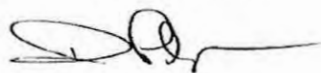
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Version 3

Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management



Signature: _____

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Identifier: NHSG/Guid/BenzoZ/MGPG904

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Author: Specialist Pharmacist in Substance Misuse, NHS Grampian

Subject Guidance

Key word(s): Benzodiazepine, dependence, withdrawal scale, diazepam, zopiclone, temazepam, zolpidem, reduction, misuse, z-drug, illicit drug use, psychological support, tolerance, gradual, zaleplon, BDEPQ, substance, valium, benzos, co-morbid.

Policy application: NHS Grampian – Substance misuse

Purpose: This guidance advises all staff in the community how to assess for dependence on benzodiazepines and z-drugs. It provides guidance on how to safely prescribe and withdraw benzodiazepines and z-drugs in dependent patients, along with advice and appropriate support.

Responsibilities for implementation:

Organisational: Management teams

Corporate: Senior Managers

Departmental: Substance misuse management team

Area: General practitioner practices and substance misuse clinics

Policy statement: It is the responsibility of supervisory staff at all levels to ensure that their staff are working to the most up to date and relevant guidance, policies, protocols and procedures. By doing so, the quality of the services offered will be maintained, and the chances of staff making erroneous decisions which may affect patient, staff or visitor safety and comfort will be reduced. Supervisory staff at all levels must ensure that staff using this guidance act within their own level of competence.

Review: This policy will be reviewed at least every three years or sooner if current treatment recommendations change.

This document is also available in large print and other formats and languages, upon request. Please call NHS Grampian Corporate Communications on (01224) 551116 or (01224) 552245.

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Revision History:

| Date of change | Approval date of Protocol that is being superseded | Summary of Changes (Descriptive summary of the changes made) | Changes Marked* (Identify page numbers and section heading) |
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| May 2017 | October 2014 | Added to key messages. If you choose to prescribe always check how the benzodiazepine may affect other co-prescribed drugs and the potential risks this may bring. This should include reducing tips and what to expect symptom wise while reducing. | Page 3 - Key Messages |
| May 2017 | October 2014 | Updated drug related death figures to most recent in Scotland 2016. Gabapentin, pregabalin. | Page 5 - Introduction |

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|-------------|--------------|--|---|
| August 2017 | October 2014 | Deleted section on insomnia from section 2 as this is covered in hypnotic policy. | Page 5 Section 2 “Prescribing for anxiety/insomnia acute requests” |
| May 2017 | October 2014 | Deleted “Where substance misuse CPNs (Community Psychiatric Nurses) are attached to a General Practice, they should be involved in the development of new, or update of existing, Practice policies on benzodiazepines”. | Page 6 Section 2.3. Service/practice prescribing policies |
| June 2017 | October 2014 | Added in sections on “properties and clinical actions of benzodiazepine drugs” and section on “problems associated with long term use. | Page 6/7 Sections 2.4 and 2.5 |
| August 2017 | October 2014 | Added advice about contact for specialist alcohol service. | Page 12 Section 5.4 |
| August 2017 | October 2014 | Moved section on pregnancy. | Page 12 Section 5.5 |
| August 2017 | October 2014 | Updated renal impairment to reflect BNF. | Page 15 Section 7.3 |
| August 2017 | October 2014 | Updated reducing regimen to “10 to 15% instead of 10 to 20% based on evidence for slower tapers. | Page 15 Section 7.2 |
| Nov 2017 | October 2014 | Re-organised to separate general advice around benzodiazepine prescribing from dependence and management of withdrawal. | Throughout document |

Guidance For The Safe Prescribing Of Benzodiazepines And Z Drugs And Management Of Dependence In NHS Grampian

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Key Messages Summary

- Benzodiazepines and Z-drugs carry a risk of dependence, tolerance and withdrawal effects. Patients taking benzodiazepines have an increased risk of overdose, falls and fracture risk¹ especially when combined with depressant drugs such as methadone, heroin, other opioids, gabapentin, pregabalin² and alcohol.
- Acute prescribing should be limited to a maximum of two weeks as signs of psychological and physical dependence can develop if prescribed for longer periods.
- If you choose to prescribe always check how the benzodiazepine may affect co-prescribed drugs and the potential risks this may bring.³
- Prescribing should be undertaken as per recommended guidance for licensed indications, e.g. [Generalised Anxiety Disorder](#) and [insomnia](#). Focus should be placed on resolving the underlying cause. Alternatives for anxiety management include non benzodiazepine pharmacotherapy and talking therapies (<https://www.nice.org.uk/guidance/qs53> generalised anxiety clinical management¹⁶ and <https://www.anxietyuk.org.uk/>).
- If you choose to prescribe outwith clinical recommendations for longer periods, patients should have their treatment reviewed frequently and be informed of the risk of addiction and dependence, as well as the potential for significant adverse effects which long term use can bring.
- Additional consideration should be given to patients in higher risk groups prior to initiating treatment, e.g. those with poly-pharmacy, older patients and patients with a previous history of dependence or drug seeking behaviours.
- Clinical services and Medical Practices should agree a prescribing policy for benzodiazepines and Z-drugs to ensure uniformity of practice between prescribers.

Key messages in Assessment and Management of Dependence

- There is very little evidence to suggest that long-term substitute prescribing for dependence reduces harm. There is clear evidence that prescribing more than 30mg diazepam equivalent per day may cause harm.
- Prescribing out with the recommended parameters, i.e. more than 30mg daily or shortened assessment period, must be undertaken by a prescriber with specialist experience in substance misuse.
- “Street” illicit benzodiazepines or Z-drugs may differ in constituents or strength. A patient may report to taking extraordinary amounts of drug however this should not be relied upon as an accurate account and should not be prescribed like for like.

- Provide patients with clear written information on the risks of continuing benzodiazepine use and the potential for symptoms of withdrawal whilst undergoing a reducing regimen. This should include reducing tips and what symptoms to expect while reducing.
- Illicit (street sources/non prescribed) should be assessed over a period of approximately 3 months before dependence is confirmed and/or a reducing regimen for diazepam initiated. Monitor the patient's pattern of use and reduce current non-prescribed usage to 30mg diazepam equivalent per day or less.
- Set realistic goals with the patient. Disagreement with the pace of reduction is likely to end in a poor outcome. Document the treatment plan in the patient notes.
- Whether prescribing for illicit or prescribed dependences, it is recommended that most benzodiazepines should be converted to the equivalent dose of diazepam. Its long half-life reduces the chances of sharp fluctuations in plasma levels.
- Aim for the lowest dose of diazepam which controls symptoms of withdrawal (daily dose of between 10mg and 30mg) with a maximum daily dose of no more than 30 mg per day according to patient response.
- For dependent patients, gradual dose reduction is safer and likely to be more manageable to the patient than abrupt discontinuation. As a rough guide the daily dose can be reduced by approximately 10-15% per fortnight depending on current intake.
- For reducing regimens the prescription should be dispensed in instalments, preferably as daily dispense and no more than one weeks supply at a time. Where co-prescribed an opioid substitute the frequency of instalment collection should match.
- If a patient is struggling with the reduction, hold the dose and reduction until the patient feels ready to continue. Do not increase the dose.
- Diazepam should be prescribed in 2mg and 5mg strengths only. Diazepam 10mg tablets have a higher street value and should not be prescribed.

Guidance For The Safe Prescribing Of Benzodiazepines And Z Drugs And Management Of Dependence And Withdrawal In NHS Grampian

1. Introduction

This guidance aims to reduce the risks associated with benzodiazepines and Z-drugs by promoting safe prescribing. It also outlines the recommended approach for managing benzodiazepine and Z-drug* dependence and withdrawal in NHS Grampian.

*Z- drugs (zaleplon, zolpidem and zopiclone) are non benzodiazepine hypnotics which may carry the same risks and dependence problems as benzodiazepines.

Historically both prescribed and illicit benzodiazepines/Z-drugs have been misused with opioids, stimulants, alcohol and other drugs. There is little evidence to support the long-term prescribing of benzodiazepine and/or Z-drugs.

Benzodiazepines factor heavily in Drug Related Deaths (DRDs) in Scotland. National records of Scotland reported that 867 drug-related deaths were registered in Scotland in 2016.⁴ This figure is more than double that of 2006 in which there were 421 and has increased since 2015.

Benzodiazepines (for example diazepam and etizolam) were implicated in, or potentially contributed to, 426 deaths (49%). Grampian accounted for 68 of the 867 deaths and benzodiazepines were implicated or contributed to 41 of these deaths. The majority were male and in the category of older drug user, i.e. 35 years and over and more likely to have co-morbid conditions.

Clinicians should be mindful of the risks associated with prescribing benzodiazepines and impact of co-prescribed medicines and co-morbidities. The risk of diversion and misuse of prescribed medicines along with illicit use should also be considered. These factors greatly increase the risk of overdose.

2. Advice For Safer Prescribing Of Benzodiazepines And Z-Drugs

2.1. Anxiety and Insomnia

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. The use of benzodiazepines to treat short-term 'mild' anxiety is inappropriate.⁵

In practice, prescribing of benzodiazepines should be limited to a maximum of two to four weeks as signs of psychological and physical dependence can develop if prescribed for longer periods.

- Prescribing should be undertaken as per recommended guidance for licensed indications, e.g. [Generalised Anxiety Disorder](#) and [insomnia](#). Focus should be placed on resolving the underlying cause. Alternatives for anxiety management include non benzodiazepine pharmacotherapy and talking therapies (<https://www.nice.org.uk/guidance/qs53> generalised anxiety clinical management¹⁶ and <https://www.anxietyuk.org.uk/>).
- If you choose to prescribe always check how the benzodiazepine may affect co-prescribed drugs and the potential risks this may bring.³

2.2. Acute requests for benzodiazepines

General practitioners should be alert to specific requests for supply of benzodiazepines for any acute condition, e.g. back/muscular pain. The patient should be thoroughly assessed and the appropriate prescribing guidance for any diagnosed conditions followed. Practice staff should be trained to recognise repeated requests for benzodiazepine or Z-drug prescriptions and refer patients back to GPs for review before a further supply is made.

2.3. Service/Practice Prescribing Policies

It is recommended that clinical services/General Practices formulate a practice prescribing policy for benzodiazepines and Z-drugs to ensure uniformity of practice between prescribers. This will help reduce the occurrence of patients selecting a prescriber on the basis of any personal prescribing policy.

Practice pharmacists may be able to assist in identifying those patients receiving long-term prescriptions and highlight or advise on a variety of methods to reduce prescribing levels, e.g. letters with information and self-help for patients.⁶

2.4. Properties and clinical actions of benzodiazepine drugs

- Benzodiazepines are rapidly and fully absorbed orally. The majority exhibit peak effects within a half-hour to 2 hours of ingestion.
- There are a large number of benzodiazepines available see [Appendix 4](#). All have similar properties, although their potency varies greatly.
- Those with long half-lives such as diazepam and nitrazepam are more likely to produce residual effects such as sedation and falls the next day.
- Rapid onset drugs are generally associated with increased abuse potential. They are associated with ‘good’ subjective effects and psychological effects are reinforced each time they are taken. This therefore leads to increasing doses in order to obtain a better ‘buzz’.
- Benzodiazepines enhance the activity of the inhibitory neurotransmitter gamma aminobutyric acid (GABA) which affects almost every part of brain function unselectively. This “inhibitory” effect is responsible for the characteristic effects of sedation, amnesia and motor discoordination.

2.5. Problems associated with long-term use⁷

Benzodiazepines and Z-drugs carry a risk of dependence, tolerance and symptoms of withdrawal. These typically occur after only a few weeks of regular use rendering them less effective for the management of the prescribed indication after this time. Nearly all of the associated disadvantages and problems are associated with long-term use and include:

- Cognitive impairment including memory impairment, emotional blunting, weakening of coping skills and amnesia. Patients may struggle with remembering recent events, the circumstances in which they occurred, and their sequence in time. This may impact on the efficacy of psychological interventions as patient recollection of consultations may be poor.
- Precipitating or aggravating depression including suicidal tendencies.
- Paradoxical excitement with increased anxiety, insomnia, nightmares and hallucinations at the onset of sleep, irritability, hyperactivity or aggressive behaviour. The extent of these effects will vary between individuals and depend on dose and duration of use. They will gradually reduce in most people 6-12 months after stopping the drug.
- Respiratory depression and overdose. Particularly when taken in combination with opioid drugs, alcohol and other depressant drugs such as gabapentinoids.
- Dependence on even small doses of benzodiazepines/Z-drugs can result in anxiety, insomnia and other distressing withdrawal symptoms if the drug is stopped abruptly. Gradual dose reduction is preferable to abrupt discontinuation. Symptoms may initially appear to worsen following dose reduction, however with slow withdrawal and psychological support, symptoms will often improve.
- Stopping after long-term use results in withdrawal symptoms in between 30% – 45% of people.
- Benzodiazepines can lead to an unpredictable and exponential increase in risk of respiratory depression particularly when taken in combination with opioid drugs, alcohol and/or other depressant drugs such as gabapentinoids.

3. Assessment Of Benzodiazepine/Z-Drug Misuse And Dependence

3.1. Definition of dependence

The **Diagnostic and Statistical Manual of Mental Disorders (DSM-5)** “Definition of Dependence” states that the presence of three or more of the following seven features, for a year or more would strongly indicate dependence.⁸

- **Tolerance:** a need for markedly increased amounts of the substance to achieve intoxication or desired effect **or** a markedly diminished effect with continued use of the same amount of the substance.
- **Withdrawal:** the characteristic withdrawal syndrome for the substance **or** taking the same (or a closely related) substance to relieve or avoid withdrawal symptoms.
- The substance is often taken in larger amounts or over a longer period than was intended.
- There is a persistent desire or unsuccessful efforts to cut down or control substance abuse.

- A great deal of time is spent in activities necessary to obtain the substance, use the substance or recover from its effects.
- Important social, occupational or recreational activities are given up or reduced because of substance use.
- The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

It is essential that a full assessment is undertaken in order to identify dependence on a benzodiazepine.

3.2. Establish type of dependency

- (i) Is drug prescribed or non-prescribed (illicit)?
- (ii) If prescribed, what was the original indication?
- (iii) Is the patient still experiencing symptoms of the original indication, e.g. stress or anxiety? Depending on timescales the prescribed drug may no longer be effective.
- (iv) Note details of and reason(s) for any illicit use whether sole or in addition to prescribed use.

3.3. Undertake full drug history

The following points should be covered to assist diagnosis of dependence.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/628634/clinical_guidelines_2017.pdf

- (i) Name of each drug taken, estimated daily dose, dosage interval, frequency of use and length of time taken, e.g. number of months, years.
- (ii) Co-morbid use of other drugs and/or alcohol. Practitioners should consider that there are a number of New Psychoactive Substances (NPS) governed by the New Psychoactive Substances Act (2016). Many of which mimic benzodiazepine like compounds which may or may not exhibit similar effects to licensed benzodiazepines.
- (iii) Time and duration of previous attempts at withdrawal and/or abstinence from benzodiazepines/Z-drugs.
- (iv) History of previous severe withdrawal (including history of seizures) or post-withdrawal reaction.
- (v) Concomitant severe medical or psychiatric illnesses.

3.4. Check for Evidence of Benzodiazepine/Z-drug Dependence

Note the patient's physical presentation – drowsiness, disinhibition, dilation of pupils, and the frequency or consistency of presentation over several weeks.

For illicit use, it is recommended that the patient's benzodiazepine use be assessed over a period of approximately 3 months before dependence is confirmed and/or a substitute prescription of diazepam supplied.

Prescribers should make use of the dependency questionnaires and drug diary sheets ([Appendix 1](#) and [3](#)) to monitor the patient's pattern of use and level of dependence. Patients should be supported to gradually reduce their illicit benzodiazepine intake.

Binge episodes of heavy benzodiazepine use should not be confused with dependence.

If there are exceptional circumstances, e.g. patient having withdrawal fits then prescribing can be considered at an earlier point but only under advice from a Specialist Substance Misuse Clinician.

3.5. Undertake urine/oral fluid drug testing

A minimum of two urine or oral fluid drug tests should be used to confirm constant presence of benzodiazepines. Bear in mind that higher dosing will result in a longer duration of detection. The request for a urine drug of abuse screen should clearly indicate "benzodiazepine testing" and highlight any prescribed and any known non-prescribed medications which may have been taken.

Consider whether the presence or absence of benzodiazepines fits with the patient's history, e.g. if a patient is regularly testing positive for cocaine and benzodiazepines, consider whether they are taking the benzodiazepines to deal with "come down effects" and therefore are not necessarily dependent.

Urine testing can also help identify other drugs of misuse and thus help decide if prescribing is appropriate or deemed too high risk.

In Grampian, neither oral fluid nor urine drug screening detects Z-drugs therefore usage, dependence and compliance cannot be confirmed this way.

Full guidance on the use of drug testing can be accessed in Drug Misuse and Dependence: UK guidance on clinical management.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/628634/clinical_guidelines_2017.pdf.

3.6. Dependence questionnaire/drug diary

The benzodiazepine dependence questionnaire (BDEPQ) is a self-report questionnaire developed to rate the severity of benzodiazepine dependence for people who use sleeping tablets or tranquillisers (benzodiazepines).¹⁰

A BDEPQ may be a useful aid in some patients. It may help elderly patients or those that may struggle with reading and writing to go through the questionnaire with them, perhaps covering a section at each appointment (see [Appendix 1](#)).

A drug diary is another simple tool to assist assessment through recording daily benzodiazepine and drug use. This process may help the patient to cut down quantities of the drug without the need for a prescription. It could also help those patients already in receipt of a prescription to identify triggers or reasons why they

use benzodiazepines at specific times. (See [Appendix 1](#), [2](#) and [3](#) respectively for self report BDEPQ questionnaire, scoring sheet and drug diary).

4. Supporting Patients With Withdrawal Symptoms

Stage One - Provide clients with education about dependence and withdrawal.

If the patient is fully aware of possible withdrawal effects and the length of time each effect may last, they may be more able to cope with them, particularly if they understand that steps can be taken to assist them to manage these symptoms. See [Heather Ashton manual](#) for advice and practical tips. Click on link for leaflet on benzodiazepine dependence and withdrawal.

<http://www.rcpsych.ac.uk/healthadvice/treatmentwellbeing/benzodiazepines.aspx>

Stage Two - Help clients deal with any negative symptoms that they experience as the drug is reduced.

These symptoms may affect the client both physically and psychologically. However anxiety and panic are the most common symptoms experienced. The use of cognitive behavioural approaches is recommended.

4.1. Psychological Interventions and support

The Matrix¹¹ summarises the current evidence base for the delivery of psychological interventions in Scotland. The Matrix specifies that treatment of benzodiazepine dependence, with and without co-morbid panic disorder, requires specialist psychological therapy at primary and secondary care levels. Individualised cognitive behavioural therapy is suggested for benzodiazepine dependence, whilst for benzodiazepine dependence with panic disorder, gradual tapering and group cognitive behavioural therapy is suggested. Ashton¹² summarized evidence for successful benzodiazepine reduction as including key strategies of gradual dose tapering and a range of psychological support from a single consultation or informational letter to cognitive-behavioural input focused on anxiety management and stress-coping strategies.

Tolerance to "episodic" memory loss (**Episodic memory** is the [memory](#) of [autobiographical](#) events) does not develop and should be taken into account during consultations as patients may struggle with remembering recent events, the circumstances in which they occurred, and their sequence in time. This may impact on the efficacy of psychological interventions as patient recollection of consultations may be poor.

Research suggests a high incidence of post-traumatic stress disorder among clients attending substance misuse services in the range of 19-35%, and with problematic alcohol use around 36-52%. Increasingly research suggests that the use of benzodiazepines is associated with worse outcomes in clients suffering from symptoms of traumatic stress, with benzodiazepine use being correlated with worse overall severity of Post Traumatic Stress Disorder (PTSD) symptoms.

Some support has been found for the use of self management approaches to discontinuing benzodiazepines for clients with anxiety problems¹³ (Otto et al, 2002).

The use of self-help style materials based on CBT has been trialled in clinical practice. This comprised of a collaborative approach of an initial period of psycho-education and support to stop benzodiazepine use.

Several agencies in Grampian are equipped to provide additional psychological support for benzodiazepine dependent patients. These include:

Alcohol and Drugs Action, Aberdeen 01224 557120.

North Aberdeenshire Recovery Service, Turning Point Scotland, Peterhead 01779 470490.

Arrows (a Quarriers service), Elgin 01343 543792.

In addition websites such as <http://www.benzo.org.uk/> have excellent links to patient forums and stories of recovery and withdrawal from benzodiazepines and excellent patient and professional advice and support on the subject.

5. Considerations Prior To Initiating A Reducing Regimen

5.1. Non-prescribed/illicit benzodiazepine use

Users of non-prescribed benzodiazepines should be motivated to reduce the dose of street benzodiazepine/Z-drug as much as possible without a prescription. NB: “Street” illicit benzodiazepines or Z-drugs may differ in constituents or strength which should be taken into consideration when prescribing, e.g. a patient may report daily use of 200mg “street” diazepam however there is no way of verifying this and the actual dose may be higher, lower or of an entirely different drug.

As a minimum patients should be supported to reduce current usage to therapeutic dose levels of 30mg diazepam equivalent per day or less. Prescribing should be considered as the last resort. By prescribing a benzodiazepine, prescribers may remove the principal motive for stopping use and may create dependency in the “intermittent” benzodiazepine/Z-drug user by giving them regular dosages. Psychological support is the mainstay to managing benzodiazepine dependence.

5.2. Co-existing mental health problems

It is important to take into account any mental health issues or conditions such as depression, schizophrenia or anxiety and any drugs already being prescribed for these. Drug interactions, respiratory depressant and sedative effects should be considered prior to commencing a benzodiazepine prescription. In these patient groups it would be appropriate to refer to the specialist service for assessment.

5.3. Opioid dependent patients

Patients who are also prescribed a substitute prescription for opioid dependence should be maintained on a stable dose prior to considering benzodiazepine detoxification and supported by urine drug screening, e.g. absence of other illicit drugs in the sample. Concurrent withdrawal from both medications is not recommended in a community setting. For patients whose other drug and alcohol misuse remains chaotic, the risk of overdose when introducing another respiratory depressant such as diazepam will greatly increase. Where opioid dependence is controlled it is easier to assess the need for and/or appropriateness of a benzodiazepine prescription.

Where required, advice should be sought from the Specialist Substance Misuse Service for support of more complex cases.

5.4. Alcohol dependent patients

Where patients exhibit a co-dependency on alcohol, the local specialist alcohol team should be consulted for advice prior to consideration of benzodiazepine withdrawal.

Aberdeen City - Integrated Alcohol Service (IAS), Tel: 01224 557845

Aberdeenshire North – Kessock Clinic – Tel: 01346 585160

Aberdeenshire South and Central Substance Misuse Team – Tel: 01224 557212

Moray Integrated Drug and Alcohol Service – Tel: 01343 552211

5.5. Pregnancy

The Essential Guide to Problem Substance use During Pregnancy¹⁴ states:

“There is no conclusive evidence that benzodiazepines cause congenital birth defects or other serious adverse effects on the developing fetus. However, an increased risk of low birth weight and preterm delivery has been reported and most studies have investigated low dose use, whereas many drug users report high dose intake. Whilst there have been some reports of facial abnormalities (i.e. cleft lip and palate) following high dose benzodiazepine use in early pregnancy, these findings have not been reliably reproduced.

Maternal use of benzodiazepines near term can also result in “floppy baby syndrome” where the newborn baby is lethargic, has reduced muscle tone and respiratory depression. Dependent benzodiazepine use by the mother is clearly associated with withdrawal symptoms in the newborn baby. Neonatal Abstinence Syndrome can be more severe and prolonged with benzodiazepines and the onset of withdrawal symptoms can be delayed, secondary to maternal opioid use”.

It is generally recommended that use of benzodiazepines is avoided in pregnancy unless there is a clear indication. However to reduce the risk of illicit use, those women who are dependent on benzodiazepines or Z-drugs should be stabilised on diazepam and where this can be tolerated without restarting illicit use, the dose reduced.

Recommended management for benzodiazepine use in pregnancy:

- **Outpatient:** General Practitioners should liaise closely with the obstetrician involved with the care of the patient who is benzodiazepine dependent in order to determine individual management. Follow this policy, speeding up reduction if possible by reducing the interval of reductions to weekly.
- **In-Patient:** In Aberdeen Maternity Hospital care will be jointly delivered by the consultant obstetrician and the specialist antenatal clinic.

6. Advice On Prescribing For Dependent Patients

Make sure the patient understands and is aware of the treatment plan. It may be helpful for patient and prescriber to sign the agreed plan and record this. Starting a reducing regimen with an unwilling patient is unlikely to result in a successful outcome. Encouraging and educating the patient on the benefits of reducing/stopping should help to engage the patient in a reduction plan.

Evidence would suggest that a change in drug taking behaviour is more likely when an individual themselves is motivated to make such changes. Whilst it is often tempting to point out to an individual the problems their drug use is causing them, it may be helpful to build on what positive changes the individual hopes to achieve by reducing their drug use. These frequently include improvements in physical and mental health, improved relationships, occupational performance and feeling of increased control over their lives. Reinforcing these positive long term goals may encourage the individual to move forward to make this change.

6.1. Initiating a reducing regimen

NB: It should be made clear at the outset that prescribing will be undertaken as a reducing regimen for a limited duration. Document the treatment plan in the patient's appropriate notes.

(i) Where a reducing regimen is deemed clinically appropriate, diazepam should be prescribed. **Aim for the lowest dose which controls symptoms of withdrawal (daily dose of between 10mg and 30mg) increasing to a maximum of 30mg per day according to patient response.** Daily doses greater than 30mg are not recommended and may cause harm.

(ii) Benzodiazepines and Z-drugs should be converted to diazepam using the benzodiazepine dose equivalent chart (see [Appendix 4](#)). **There is no justification for prescribing more than one benzodiazepine or Z-drug concurrently, except during the period of conversion.** Substitute one dose of current benzodiazepine to diazepam at a time, usually starting with the evening or night-time dose. Replace the other doses, one by one, at intervals of a few days or a week until the total approximate equivalent dose is reached before starting the reduction. **See [Appendix 6](#).**

The long half-life of diazepam should enable the patient to take a single daily dose at night or a twice daily dose at most.

(iii) **10mg strength tablets of diazepam should not be prescribed** as they have higher street value and are more likely to be diverted. Only 2mg and 5mg tablets should be prescribed. This has the additional benefit of allowing the patient to establish the lowest total dose required in a day.

(iv) **Excessive supplies of medication on one prescription should be avoided.** If a prescription is to be initiated this should initially be as a daily dispense arrangement. **It is recommended that no more than one week's supply should be prescribed to take away at a time and instalment dispensing (daily, three times per week, etc) should be used.** This is especially important where patients have a history of drug or alcohol misuse or are co-prescribed an opioid substitute medication such as methadone or a buprenorphine product (e.g. Suboxone®).

6.2. Reducing regimen

(i) Aim to reduce in steps of approximately 10% to 15% of the daily dose every fortnight with patient consent. The rate of withdrawal is often determined by an individual's capacity to tolerate symptoms.

(ii) If the patient is struggling with symptoms of withdrawal, halt the reduction and maintain the current dose until symptoms improve. Increases in dose are to be discouraged. Examples of reducing scale can be found in [Appendix 6](#).

(iii) Set realistic goals with the patient. Disagreement with the pace of reduction is likely to end in a poor outcome. Document the treatment plan in the patient notes.

(iv) Check that other substances such as cannabis, new psychoactive substances (NPS) or alcohol are not being added in or increased in response to the benzodiazepine reduction.

(v) The time needed for complete withdrawal may vary from 4 weeks to a year or more.

(vi) Automatic repeat prescriptions are not recommended. Patients should be seen for ongoing assessment and support, before further supplies of benzodiazepines are issued.

7. Contraindications, Cautions and Adverse Effects

A full list of contraindications, cautions and side effects for each drug can be found by accessing Medicines Complete platform:

<https://www.medicinescomplete.com/mc/bnf/current/>

7.1. Breastfeeding

Diazepam and other benzodiazepines are excreted into breast milk, albeit at relatively low levels. Manufacturers' advice on the use of diazepam whilst breastfeeding is to avoid if possible. There is a lack of research on benzodiazepine-dependent mothers who breastfeed, but if they wish to breastfeed and the benefits are deemed to outweigh the risks they should be supported to do so. Potential risks reported include lethargy, sedation and poor suckling. Mothers should be advised to keep the dose of benzodiazepine as low as possible whilst breastfeeding and the infant should be monitored for signs of over-sedation and low milk intake/poor weight-gain.

7.2. Hepatic impairment

In people with compromised hepatic function, long-acting agents are known to accumulate and metabolism will be slower necessitating prescribing of lower doses and closer monitoring. Benzodiazepines can precipitate coma in patients with hepatic impairment. The dose of Z-drugs should also be reduced if prescribing in these patients. Benzodiazepines and Z-drugs should be avoided in patients with severe hepatic disease - seek specialist advice. Seek specialist advice (preferably from a hepatic specialist) before switching to diazepam in people with hepatic dysfunction as diazepam may accumulate to a toxic level in these individuals. An alternative benzodiazepine without active metabolites (such as lorazepam) may be preferred.

7.3. Renal impairment

Patients with renal impairment have increased cerebral sensitivity to benzodiazepines; start with small doses in severe impairment.

7.4. Respiratory depression

Benzodiazepines and Z-drugs may cause respiratory depression which is exacerbated by the concomitant use of other CNS depressants such as alcohol, NPS and opioid drugs. Caution should be employed when prescribing benzodiazepines and Z-drugs in these instances. Patients should also be warned of the increased risks when mixing different respiratory depressants.

8. Driving status

It is the responsibility of the patient to inform the DVLA of any condition which may impair their ability to drive and the prescriber should inform patients of DVLA guidance. The DVLA has produced guidance regarding the professional responsibility of the prescriber available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/618072/assessing-fitness-to-drive-a-guide-for-medical-professionals.pdf¹⁵

9. Consultation

| | |
|---|---|
| Dr Steve Beason | Psychiatrist, NHSG Substance Misuse Service |
| Dr Carol Buchanan | GP with Special Interest in Substance Misuse |
| Dr Bruce Davidson | Consultant Psychiatrist and Clinical Lead, NHS Grampian Substance Misuse Service |
| Dr Alan Fraser | Sessional and out-of hours GP |
| Dr Dave Fowler | GP, Kincorth Medical Practice |
| Dr Sharin Garden | Principal Clinical Psychologist NHSG Substance Misuse Service |
| Linda Law | Senior Practitioner Social work |
| Dr Richard Legg | GP with Special Interest in Substance Misuse |
| Angela Macmanus | Principle Pharmacist, Mental Health and Learning Disability Services, Royal Cornhill Hospital |
| Dr Alison Mearns | GP with Special Interest in Substance Misuse |
| Fiona Raeburn | Specialist Pharmacist in Substance Misuse |
| Ruth Innes | Specialist pharmacist neonatal/maternity |
| Craig Rore | Lead Pharmacist Grampian Medicines Information Centre |
| Controlled Drug Pharmacists, NHS Grampian | |
| CPN Clinical Leads, NHSG Substance Misuse Service (combined feedback) | |
| NHS Grampian Mental Health Operational Medicines Management Group | |

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Appendix 1 - NHSG Benzodiazepine Dependence Questionnaire (BDEPQ)

In the questions that follows you will be asked about your experience using medications known as sleeping pills, sedatives, hypnotics, 'benzos' or tranquillisers. These medications are also known by their trade names: valium, temazepam, nitrazepam (or mogadon), chlordiazepoxide (Librium); or by their nicknames such as 'blues', 'moggies', 'tems', 'downers'.

When answering the questions please think only about your experiences **over the last month**. Place a tick or x in the box below the answer that best suits your experience in the last month.

1. **In the last month, have you taken another sedative or tranquilliser as soon as the effects of the previous one began to wear off?**

NEVER SOMETIMES OFTEN ALWAYS

2. **Have you taken sedatives, tranquillisers or sleeping pills in the last month because you like the way they make you feel?**

NEVER SOMETIMES OFTEN ALWAYS

3. **In the last month, have you felt that you cannot face anything out of the ordinary without a sedative or tranquilliser?**

NEVER SOMETIMES OFTEN ALWAYS

4. **Do you feel that you cannot get through the day without the help of your sedatives or tranquillisers?**

NEVER SOMETIMES OFTEN ALWAYS

5. **Do you need to carry your sedatives or tranquillisers with you?**

NEVER SOMETIMES OFTEN ALWAYS

6. **Have you tried to reduce the number of sedatives, tranquillisers or sleeping pills you take because they interfered with your life?**

A GREAT DEAL SOMEWHAT A LITTLE NO

7. **Have you found that you needed to take more tranquillisers, sedatives or sleeping pills to get the same effect in the last month compared to when you first took them?**

NEVER SOMETIMES OFTEN ALWAYS

8. **Do you need to take sedatives, tranquillisers or sleeping pills to deal with the problems in your life?**

NEVER SOMETIMES OFTEN EVERY DAY

9. Do you feel terrible if you do not take a sedative, tranquilliser or sleeping pill?

EVERY DAY OFTEN SOMETIMES NEVER

10a. In the last month, have you been worried that your doctor might not continue to prescribe the sedatives, tranquillisers or sleeping pills you are taking?

NEVER SOMETIMES OFTEN A LOT

10b. How strong has this worry been?

MILD MODERATE SEVERE

11. Could you stop taking sedatives, tranquillisers or sleeping pills tomorrow without any difficulties?

No, it would be impossible
Perhaps, with a lot of difficulty
Yes, with some difficulty
Yes, without difficulty

12. Do you count down the time until you can take your next sedative, tranquilliser or sleeping pill?

ALWAYS OFTEN SOMETIMES NEVER

13a. Have you experienced relief when you have taken sedatives, tranquillisers or sleeping pills in the last month?

NEVER SOMETIMES OFTEN ALWAYS

13b. How strong is that relief?

MILD MODERATE INTENSE

14a. In the last month, have you felt bad or sick as the effects of sedatives, tranquillisers or sleeping pills wore off?

Yes – Answer the next question
No – Skip to question 15

14b. Have you taken another sedative, tranquilliser or sleeping pill to reduce these unpleasant after-effects?

NEVER SOMETIMES OFTEN ALWAYS

15. In the last month, have you taken sedatives, tranquillisers or sleeping pills against the doctor's advice or more frequently than recommended?

NEVER OCCASIONALLY SOMETIMES OFTEN

16. Are you concerned about the number of sedatives, tranquillisers or sleeping pills you have taken in the last month?

A GREAT DEAL A LOT A LITTLE NOT AT ALL

17. Have you taken more sedatives, tranquillisers or sleeping pills in one day than you planned to?

EVERY DAY OFTEN SOMETIMES NEVER

18a Have you found the effects of sedatives, tranquillisers or sleeping pills pleasant?

NEVER SOMETIMES OFTEN ALWAYS

18b. How strong is the pleasant feeling?

MILD MODERATE INTENSE

19. Have you taken sedatives, tranquillisers or sleeping pills for a longer period than you intended when you started?

NEVER SOMETIMES OFTEN A LOT

20a. Have you felt tense or anxious as your prescription for sedatives, tranquillisers or sleeping pills began to run out?

NEVER SOMETIMES OFTEN EVERY TIME

20b. How strong have these feelings been?

MILD MODERATE SEVERE

21a. Have you felt an urge or desire to take sedatives, tranquillisers or sleeping pills in the last month?

NEVER SOMETIMES OFTEN EVERY DAY

21b. How strong is that urge or desire?

MILD MODERATE INTENSE

22. Have you taken sedatives, tranquillisers or sleeping pills in the last month when you did not really need them?

NEVER SOMETIMES OFTEN EVERY DAY

Instructions: In the next set of questions please tick the box below next to the answer that matches what you think.

23. I feel powerless to prevent myself taking a sedative or tranquilliser when I am anxious, uptight or unhappy.

STRONGLY DISAGREE SOMEWHAT DISAGREE SOMEWHAT AGREE STRONGLY AGREE

24. I would not be able to handle my problems unless I take a sedative or tranquilliser.

STRONGLY DISAGREE SOMEWHAT DISAGREE SOMEWHAT AGREE STRONGLY AGREE

25. I get so upset over small arguments, that I need to take a sedative or tranquilliser.

STRONGLY DISAGREE SOMEWHAT DISAGREE SOMEWHAT AGREE STRONGLY AGREE

THANK YOU

Appendix 2 - Scoring The BDEPQ

SCORING INSTRUCTIONS:

Scoring the BDEPQ requires no more than basic clerical skills. The following steps describe how to calculate a total score and scores on the three subscales.

1. Score the items as follows:

- a. Score most items as 0 1 2 3
- b. Except items 2, 5, 6,9,12,16,17,24, and 25 which are reversed. Score these as 3 2 1 0.
- c. Score the second part (b) of 2-part items as 0 if the first part (a) is scored 0.
- d. Ignore item 14a
- e. Score item 11 as
 - 3 No, it would be impossible
 - 2 Perhaps, but with a lot of difficulty
 - 1 Yes, with some difficulty
 - 0 Yes, without difficulty

2. Sum the items to give a total score.

3. Optionally calculate subscale scores as follows

- a. GENERAL DEPENDENCE SUBSCALE: Sum items 1, 6, 7, 10a, 14b, 15, 16, 17, 19, 20a, 20b, 21a, and 22
- b. PLEASANT EFFECTS SUBSCALE: Sum items 2, 13a, 13b, 18a, 18b, and 21b
- c. PERCEIVED NEED SUBSCALE: Sum items 3, 4, 5, 8, 9, 11, 12, 23, 24, and 25

INTERPRETATION

In general higher scores are associated with greater risk of future withdrawal symptoms, of continued benzodiazepine use, and are more likely to be associated with ICD-10 diagnosis of benzodiazepine dependence.

SCORING SHEET

| QUESTION No. | CIRCLE THE SCORE CORRESPONDING TO THE SUBJECT'S RESPONSE | | | |
|--------------|--|---|---|---|
| 1 | 0 | 1 | 2 | 3 |
| 2 | 3 | 2 | 1 | 0 |
| 3 | 0 | 1 | 2 | 3 |
| 4 | 0 | 1 | 2 | 3 |
| 5 | 3 | 2 | 1 | 0 |
| 6 | 3 | 2 | 1 | 0 |
| 7 | 0 | 1 | 2 | 3 |
| 8 | 0 | 1 | 2 | 3 |
| 9 | 3 | 2 | 1 | 0 |
| 10a | 0 | 1 | 2 | 3 |
| 10b | 0 | 1 | 2 | 3 |
| 11 | 3 | 2 | 1 | 0 |
| 12 | 3 | 2 | 1 | 0 |
| 13a | 0 | 1 | 2 | 3 |
| 13b | 0 | 1 | 2 | 3 |
| 14a | Ignore | | | |
| 14b | 0 | 1 | 2 | 3 |
| 15 | 0 | 1 | 2 | 3 |
| 16 | 3 | 2 | 1 | 0 |
| 17 | 3 | 2 | 1 | 0 |
| 18a | 0 | 1 | 2 | 3 |
| 18b | 0 | 1 | 2 | 3 |
| 19 | 0 | 1 | 2 | 3 |
| 20a | 0 | 1 | 2 | 3 |
| 20b | 0 | 1 | 2 | 3 |
| 21a | 0 | 1 | 2 | 3 |
| 21b | 0 | 1 | 2 | 3 |
| 22 | 0 | 1 | 2 | 3 |
| 23 | 0 | 1 | 2 | 3 |
| 24 | 3 | 2 | 1 | 0 |
| 25 | 3 | 2 | 1 | 0 |
| TOTAL | | | | |
| | TOTAL SCORE | | | |

SUBSCALES:

GENERAL DEPENDENCE

| Q | 1 | 6 | 7 | 10a | 10b | 14b | 15 | 16 | 17 | 19 | 20a | 20b | 21a | 22 |
|-------|---|---|---|-----|-----|-----|----|----|----|--------------|-----|-----|-----|----|
| Score | | | | | | | | | | | | | | |
| | | | | | | | | | | TOTAL | | | | |

PLEASANT EFFECTS

| QUESTION | 2 | 13a | 13b | 18a | 18b | 21b |
|----------|---|-----|-----|-----|--------------|-----|
| SCORE | | | | | | |
| | | | | | TOTAL | |

PERCEIVED NEED

| Q | 3 | 4 | 5 | 8 | 9 | 11 | 12 | 23 | 24 | 25 |
|---|---|---|---|---|---|----|--------------|----|----|----|
| | | | | | | | | | | |
| | | | | | | | TOTAL | | | |

Appendix 3 - NHSG Drug Diary

| Date and time | What did I use and how much? | What triggered me to use? | How was I feeling before I used? | Any consequences of taking drug? (good or bad) |
|---------------|------------------------------|---------------------------|----------------------------------|--|
| | | | | |
| | | | | |
| | | | | |
| | | | | |

Appendix 4 - Diazepam Equivalent Table

All Doses approximately equivalent To Diazepam 10mg -Table adapted from Heather Ashton¹⁷

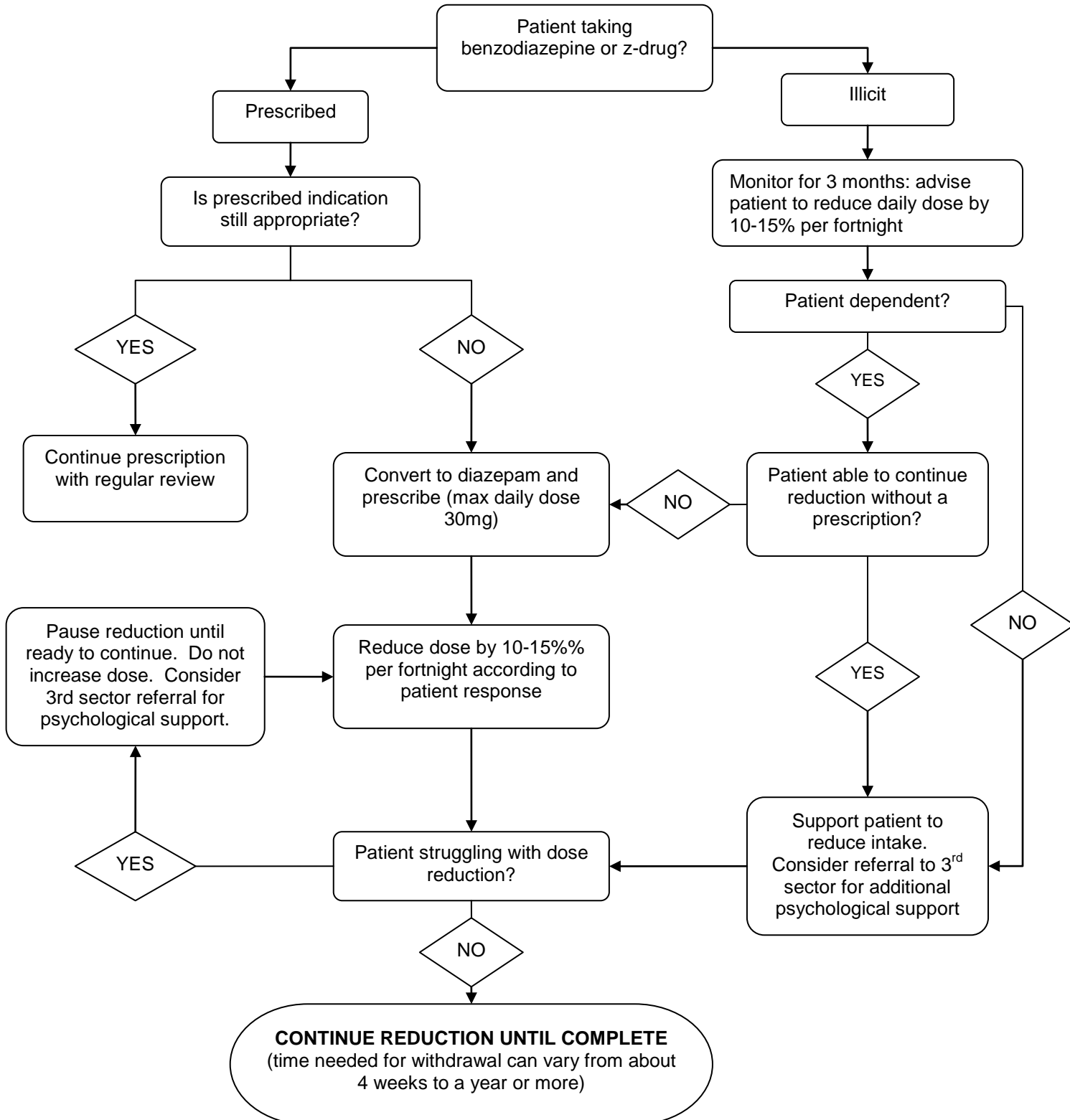
* **Half-life:** time taken for blood concentration to fall to half its peak value after a single dose. Half-life of active metabolite shown in square brackets. This time may vary considerably between individuals.

| Benzodiazepines ⁵ | Half-life (hrs)* [active metabolite] | Approximately Equivalent Oral Dosages (milligrams) |
|--|---|--|
| Alprazolam | 6-12 | 0.5 |
| Chlordiazepoxide | 5-30 [36-200] | 25 |
| Clobazam | 12-60 | 20 |
| Clonazepam | 18-50 | 0.5 |
| Clorazepate | [36-200] | 15 |
| Diazepam | 20-100 [36-200] | 10 |
| Flunitrazepam | 18-26 [36-200] | 1 |
| Flurazepam | [40-250] | 15-30 |
| Loprazolam | 6-12 | 1-2 |
| Lorazepam | 10-20 | 1 |
| Lormetazepam | 10-12 | 1-2 |
| Nitrazepam | 15-38 | 10 |
| Oxazepam | 4-15 | 20 |
| Temazepam | 8-22 | 20 |
| Non-benzodiazepines with similar effects | | |
| Zaleplon | 2 | 20 |
| Zolpidem | 2 | 20 |
| Zopiclone | 5-6 | 15 |

Appendix 5 - Treatment Algorithm

General principles that should be ongoing throughout any reduction regimen

- Teach HEALTHY coping techniques appropriate to patient
- Address underlying SLEEP HYGIENE issues
- Address any underlying PSYCHOLOGICAL PROBLEMS
- If withdrawal symptoms occur, maintain at same dose until symptoms improve and reduce in small steps; It is better to reduce slowly than too quickly



Appendix 6 - Sample Reducing Regimen¹⁷

NOTES: Stages 1-5 might be manageable with one week between reductions, but the later stages are better taken over 2 weeks.

A mixture of 5mg and 2mg tablets will be required. If intermediate reductions of 1mg are required, halve the 2mg (scored) tablets. Do not prescribe in 10mg tablets.

| DIAZEPAM REDUCING REGIMEN : STARTING AT 30MG DAILY | | | | | | |
|---|---------|---------|------------|-------|---------------|-----------------------|
| | | MORNING | AFTER-NOON | NIGHT | TOTAL FOR DAY | GP USE: TABS PER WEEK |
| STARTING DOSE | | 10mg | 10mg | 10mg | 30mg | 42 x 5mg |
| STAGE 1 | 2 WEEKS | 8mg | 8mg | 8mg | 24mg | 84 X 2mg |
| 2 | 2 WEEKS | 6mg | 6mg | 8mg | 20mg | 70 X 2mg |
| 3 | 2 WEEKS | 6mg | 6mg | 6mg | 18mg | 63 x 2mg |
| 4 | 2 WEEKS | 4mg | 6mg | 6mg | 16mg | 56 x 2mg |
| 5 | 2 WEEKS | 4mg | 4mg | 6mg | 14mg | 49 x 2mg |
| 6 | 2 WEEKS | 4mg | 4mg | 4mg | 12mg | 42 x 2mg |
| 7 | 2 WEEKS | 2mg | 4mg | 4mg | 10mg | 35 x 2mg |
| 8 | 2 WEEKS | 2mg | 2mg | 4mg | 8mg | 28 x 2mg |
| 9 | 2 WEEKS | 2mg | 2mg | 2mg | 6mg | 21 x 2mg |
| 10 | 2 WEEKS | 2mg | 0 | 2mg | 4mg | 14 x 2mg |
| 11 | 2 WEEKS | 0 | 0 | 2mg | 2mg | 7 x 2mg |
| <u>SOME GROUND RULES</u> | | | | | | |
| This is intended to be a slow process. Do not try to rush it. | | | | | | |
| If struggling take an extra week or two to complete a stage rather than going backwards by increasing the dose. | | | | | | |
| Tell a friend or partner what you are aiming for so that they can support/encourage you. | | | | | | |
| Consult your GP regularly, especially if you experience any fainting, fits, and depression or panic attacks. | | | | | | |

WITHDRAWAL FROM Zopiclone 15mg with diazepam substitution
(15mg Zopiclone is approx. equivalent to 10mg diazepam)

| | Night Time | Equivalent diazepam dose |
|--|---------------------------------|--------------------------|
| Starting dose | Zopiclone 15mg | 10mg |
| Stage 1 (1 week) | Zopiclone 7.5mg Diazepam 5mg | 10mg |
| Stage 2 (1 week) | Stop Zopiclone Diazepam 10mg | 10mg |
| Stage 3 (1-2 weeks) | Diazepam 9mg | 9mg |
| Stage 4 (1-2 weeks) | Diazepam 8mg | 8mg |
| Then continue reducing diazepam by 1mg every 1-2 weeks | | |

Appendix 7 – Blank Sample Reducing Regimen¹⁷

NOTES: Stages 1-5 might be manageable with one week between reductions, but the later stages are better taken over 2 weeks.

A mixture of 5mg and 2mg tablets will be required. If intermediate reductions of 1mg are required, halve the 2mg (scored) tablets. Do not prescribe in 10mg tablets.

| DIAZEPAM REDUCING REGIMEN : STARTING AT 30MG DAILY | | | | | | |
|---|---------|---------|------------|-------|---------------|-----------------------|
| | | MORNING | AFTER-NOON | NIGHT | TOTAL FOR DAY | GP USE: TABS PER WEEK |
| STARTING DOSE | | | | | | |
| STAGE 1 | 2 WEEKS | | | | | |
| 2 | 2 WEEKS | | | | | |
| 3 | 2 WEEKS | | | | | |
| 4 | 2 WEEKS | | | | | |
| 5 | 2 WEEKS | | | | | |
| 6 | 2 WEEKS | | | | | |
| 7 | 2 WEEKS | | | | | |
| 8 | 2 WEEKS | | | | | |
| 9 | 2 WEEKS | | | | | |
| 10 | 2 WEEKS | | | | | |
| 11 | 2 WEEKS | | | | | |
| <u>SOME GROUND RULES</u> | | | | | | |
| This is intended to be a slow process. Do not try to rush it. | | | | | | |
| If struggling take an extra week or two to complete a stage rather than going backwards by increasing the dose. | | | | | | |
| Tell a friend or partner what you are aiming for so that they can support/encourage you. | | | | | | |
| Consult your GP regularly, especially if you experience any fainting, fits, and depression or panic attacks. | | | | | | |