Guidance on appropriate prescribing of benzodiazepines and z-drugs (BZRA) in the treatment of anxiety and insomnia

Medicines Management Programme
February 2018

<table>
<thead>
<tr>
<th>Approved by:</th>
<th>Prof. Michael Barry, Clinical Lead, Medicines Management Programme (MMP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date approved:</td>
<td>01/02/2018</td>
</tr>
<tr>
<td>Version:</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Table of contents
1. Purpose .............................................................................................................................. 1
2. Scope ................................................................................................................................. 1
3. Definitions ........................................................................................................................ 2
4. Benzodiazepines and z-drugs .......................................................................................... 2
   4.1 Benzodiazepines ........................................................................................................... 2
      4.1.1 Difficulties arising from the use of benzodiazepines .............................................. 2
   4.1.2 Pharmacology of benzodiazepines ........................................................................... 3
   4.2 Z-drugs ........................................................................................................................ 5
      4.2.1 Difficulties arising from the use of z-drugs ............................................................ 5
      4.2.2 Pharmacology of z-drugs ..................................................................................... 5
5. Legislative requirements relating to BZRA ...................................................................... 5
   5.1 Misuse of Drugs Regulations ..................................................................................... 5
   5.2 Road Traffic Act ........................................................................................................... 9
6. Anxiety .............................................................................................................................. 10
   6.1 Non-pharmacological treatments for anxiety ............................................................ 10
      6.1.1 Counselling in Primary Care Service .................................................................... 11
   6.2 Pharmacological treatments for anxiety .................................................................. 11
      6.2.1 Role of benzodiazepines in the treatment of anxiety ............................................ 12
      6.2.2 Benzodiazepines licensed to treat anxiety ............................................................ 12
      6.2.3 Recommended duration of use ............................................................................ 13
7. Insomnia .......................................................................................................................... 13
   7.1 Types of Insomnia ....................................................................................................... 13
   7.2 Non-pharmacological treatments for insomnia ........................................................ 14
   7.3 Pharmacological treatments for insomnia ................................................................. 15
      7.3.1 Role of BZRA in the treatment of insomnia ......................................................... 15
      7.3.2 BZRA licensed to treat insomnia ....................................................................... 16
      7.3.3 Recommended duration of use ............................................................................ 16
8. Safety concerns with the use of BZRA ........................................................................ 17
   8.1 Side-effects .................................................................................................................. 17
   8.2 Tolerance ..................................................................................................................... 17
   8.3 Dependence ............................................................................................................... 18
   8.4 Safety concerns in special patient populations ........................................................ 18
      8.4.1 Older people ........................................................................................................ 18
Tables

Table 1: Duration of action of certain benzodiazepines................................................................. 4

Table 2: Examples of controlled drugs in Schedules 1, 2, 3, 4, or 5 of the Misuse of Drugs Regulations 2017 ................................................................................................................................. 6

Table 3: Controlled drug classification of BZRA licensed for the treatment of anxiety and/or insomnia ........................................................................................................................................ 7

Table 4: Prescription writing, dispensing and storage requirements for Schedule 3 and Schedule 4 Part 1 BZRA ........................................................................................................................................ 8

Table 5: Stepped-care model for people with generalised anxiety disorder .................................... 10

Table 6: Non-pharmacological interventions for the treatment of insomnia .................................... 14

Table 7: BZRA licensed for the treatment of insomnia..................................................................... 16

Table 8: Good practice guidelines for prescribing benzodiazepines .............................................. 20

Table 9: Equivalence table if switching from current benzodiazepine to diazepam ....................... 26

Table 10: Equivalence table if switching from current z-drug to diazepam ..................................... 26

Figures

Figure 1: Sample BZRA prescribing analysis report – PCRS ......................................................... 21

Figure 2: Total number of BZRA prescriptions on the GMS scheme in 2016 ................................. 23

Figure 3: Total expenditure on BZRA on the GMS scheme in 2016............................................... 24

Figure 4: Duration of use of BZRA on the GMS scheme in 2015 (based on total day’s supply over the year) ......................................................................................................................... 25
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP</td>
<td>American College of Physicians</td>
</tr>
<tr>
<td>BNF</td>
<td>British National Formulary</td>
</tr>
<tr>
<td>BZRA</td>
<td>Benzodiazepine Receptor Agonist</td>
</tr>
<tr>
<td>CBT</td>
<td>Cognitive Behavioural Therapy</td>
</tr>
<tr>
<td>CD</td>
<td>Controlled Drug</td>
</tr>
<tr>
<td>CIPC</td>
<td>Counselling in Primary Care</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>CPI</td>
<td>College of Psychiatry of Ireland</td>
</tr>
<tr>
<td>DoH</td>
<td>Department of Health</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma-aminobutyric acid</td>
</tr>
<tr>
<td>GAD</td>
<td>Generalised Anxiety Disorder</td>
</tr>
<tr>
<td>GMS</td>
<td>General Medical Services</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>HRB</td>
<td>Health Research Board</td>
</tr>
<tr>
<td>HSE</td>
<td>Health Service Executive</td>
</tr>
<tr>
<td>ICGP</td>
<td>Irish College of General Practitioners</td>
</tr>
<tr>
<td>IIOP</td>
<td>Irish Institute of Pharmacy</td>
</tr>
<tr>
<td>MBRS</td>
<td>Medical Bureau for Road Safety</td>
</tr>
<tr>
<td>MHI</td>
<td>Mental Health Ireland</td>
</tr>
<tr>
<td>MMP</td>
<td>Medicines Management Programme</td>
</tr>
<tr>
<td>NCHD</td>
<td>Non-Consultant Hospital Doctor</td>
</tr>
<tr>
<td>NCS</td>
<td>National Counselling Service</td>
</tr>
<tr>
<td>NMIC</td>
<td>National Medicines Information Centre</td>
</tr>
<tr>
<td>NDRDI</td>
<td>National Drug-Related Deaths Index</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PCRS</td>
<td>Primary Care Reimbursement Service</td>
</tr>
<tr>
<td>PSI</td>
<td>Pharmaceutical Society of Ireland</td>
</tr>
<tr>
<td>RACGP</td>
<td>Royal Australian College of General Practitioners</td>
</tr>
<tr>
<td>RNP</td>
<td>Registered Nurse Prescriber</td>
</tr>
<tr>
<td>RSA</td>
<td>Road Safety Authority</td>
</tr>
<tr>
<td>SmPC</td>
<td>Summary of Product Characteristics</td>
</tr>
<tr>
<td>SNRI</td>
<td>Serotonin Noradrenaline Reuptake Inhibitor</td>
</tr>
</tbody>
</table>
Acknowledgements
The Medicines Management Programme (MMP) wishes to acknowledge the following individuals and groups for their contribution to this document:

- National Medicines Information Centre (NMIC) review group
- Pharmaceutical Society of Ireland (PSI)
- Prof. Colin Bradley, University College Cork (UCC)
- Marie Carey (Clinical Nurse Specialist in Cognitive Behavioural Therapy; Registered Nurse Prescriber)
- Dr. Ide Delargy, Irish College of General Practitioners (ICGP)
- Bernard Duggan, Irish Institute of Pharmacy (IIOP)
- Denis O’Driscoll, HSE Addiction Services
- Eamonn Quinn, Department of Health (DoH)
- Dr. Anne Marie Liddy, Specialist Registrar, Pharmacology and Therapeutics, Trinity College Dublin

We also wish to thank the All Wales Medicines Strategy Group for permission to adapt material from their Educational Pack *Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales* (2016) for this document.
1. Purpose
This document aims to support the appropriate prescribing of benzodiazepines and z-drugs (BZRA) in Ireland. It contains information on initiation and review of BZRA, highlighting the potential dangers associated with long-term use and provides examples of resource materials which may support prescribers and pharmacists to manage the withdrawal of patients from these medicines. This guidance includes the recent changes made by the Misuse of Drugs Regulations 2017 which have replaced the now revoked Misuse of Drugs Regulations 1988, as amended. It is anticipated that the adoption of this guidance by prescribers will lead to a reduction in the long-term inappropriate prescribing of these drugs.

2. Scope
This document will focus on the use of BZRA as sedatives, hypnotics and anxiolytics in adults and will consider only oral medicines licensed for these indications which are reimbursed in Ireland. There are currently twelve benzodiazepines and two z-drugs which are licensed for the treatment of anxiety and/or insomnia available on the Health Service Executive-Primary Care Reimbursement Service (HSE-PCRS) reimbursable list. These benzodiazepines are alprazolam, bromazepam, flurazepam, lorazepam, nitrazepam, prazepam, temazepam and triazolam, and the z-drugs are zolpidem and zopiclone.

The use of benzodiazepines in the treatment of epilepsy, spasticity and other neurological and musculoskeletal disorders are outside the scope of this guidance. The safety and efficacy of BZRA for the treatment of anxiety and insomnia have not been established in children and adolescents below the age of 18 years and therefore their use is not recommended. Specialist advice should be sought before prescribing in this group of patients.

The information in this document is relevant to prescribers [i.e. General Practitioners (GPs), Registered Nurse Prescribers (RNPs), Non-Consultant Hospital Doctors (NCHDs) and Consultants]. The information will also be useful for Pharmacists and other Healthcare Professionals working in both Primary Care and the Acute hospital settings.
3. Definitions
The term benzodiazepine receptor agonist (BZRA) is used in this document when discussing both benzodiazepine and z-drugs in combination. When the agents are being discussed individually the terms “benzodiazepines” and “z-drugs” will be used.
The term hypnotic is often used to describe medications that induce sleep. The z-drugs and some benzodiazepines may also be referred to as hypnotics in this document.

4. Benzodiazepines and z-drugs
4.1 Benzodiazepines
Benzodiazepines are a class of psychoactive drugs which act on the central nervous system (CNS) to enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABA-A receptors in the brain. The various subtypes of benzodiazepine receptors have slightly different actions, Alpha 1 is responsible for sedative effects, Alpha 2 for anxiolytic effects and Alpha 1, Alpha 2 and Alpha 5 for the anticonvulsant effects. Benzodiazepines can be used in the treatment of a number of conditions depending on their potency, duration of action and receptor site affinities. Some of these therapeutic areas include treatment of insomnia, anxiety, addiction, agitation and neurological disorders. Benzodiazepines are also widely prescribed in the treatment of muscle spasticity, involuntary movement disorders, detoxification from alcohol, and anxiety associated with cardiovascular or gastrointestinal conditions. In the late 1970’s, benzodiazepines were the most commonly prescribed drugs worldwide.

4.1.1 Difficulties arising from the use of benzodiazepines
There are various problems associated with benzodiazepine use including:

- misuse,
- dependency,
- diversion,
- driving impairment,
- morbidity and mortality related to overdose and withdrawal,
- tolerance.

Older people are more vulnerable to the adverse effects of benzodiazepines and their use has been associated with cognitive deterioration, dementia and falls.
Dependence to benzodiazepines is recognised as a significant risk in patients receiving treatment for longer than one month. Continuing treatment may only assist in preventing withdrawal symptoms which include insomnia, anxiety and agitation.

Before prescribing a benzodiazepine, prescribers should check whether the person might have a tendency to misuse drugs or alcohol, or a history of same and referral to a specialist addiction service should be considered in this instance. Drug-related behaviours may be a feature in some patients who are prescribed benzodiazepines. These may include diversion of valid prescriptions, illicit sale or use in manners alternate to the prescribed dosage, route and frequency. The United Nations Office on Drugs and Crime (UNODC) monitors the international use of illicit drugs and misuse of prescription medications. In their World Drug Report (2012), it noted that benzodiazepines were the main substances of concern in the class of CNS depressants, having largely replaced barbiturates.

In Ireland, the National Drug-Related Deaths Index (NDRDI), a census of drug-related deaths and deaths among drug users was established by the Health Research Board (HRB). The NDRDI reports on poisoning deaths (also known as overdose) and on non-poisoning deaths, which are deaths among drug users as a result of medical reasons or trauma. Drugnet Ireland is the HRB drug and alcohol research and policy newsletter. The Spring 2017 edition published data relating to the NDRDI from 2004 to 2014. In 2014, it reported 354 poisoning deaths and it noted the following:

- Prescription drugs were implicated in 259, or three in every four poisoning deaths
- Benzodiazepines were the most common prescription group implicated in poisoning deaths
- Diazepam was the most common single prescription drug, implicated in 115 (32%), of all poisoning deaths.

Polydrug use is a significant risk factor for poisoning deaths; 235 (66%) of poisoning deaths were due to a combination of drugs in 2014, with an average of four different drugs taken.

- 92% of deaths where methadone was implicated and 81% of deaths where heroin was implicated involved other drugs mainly benzodiazepines.

4.1.2 Pharmacology of benzodiazepines
Benzodiazepines can be categorised as short-, intermediate- or long-acting depending on how quickly they are eliminated from the body. There are conflicting estimates of elimination half-lives between different resources. A consensus statement on the use of benzodiazepines in specialist...
mental health services by the College of Psychiatry of Ireland (CPI) (2012) places benzodiazepines into the three categories (short-, intermediate-, and long-acting) as outlined in table 1.11

**Table 1:** Duration of action of certain benzodiazepines11

<table>
<thead>
<tr>
<th>Short-acting</th>
<th>Intermediate-acting</th>
<th>Long-acting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triazolam (1.5-5.5 hours)</td>
<td>Alprazolam (10-12 hours)</td>
<td>Chlordiazepoxide (6-30 hours)</td>
</tr>
<tr>
<td>Lorazepam (12 hours)</td>
<td>Diazepam (up to 48 hours)</td>
<td></td>
</tr>
<tr>
<td>Nitrazepam (24 hours)</td>
<td>Flurazepam (3-133 hours)*</td>
<td></td>
</tr>
<tr>
<td>Temazepam (7-11 hours)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bromazepam (20 hours)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clobazam (36 hours)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(*active metabolites: approx. 3 hours for flurazepam and N1-hydroxyethyl-flurazepam & 19-133 hours for N1-desalkyl-flurazepam. Elderly subjects (66-85 years) had half-lives of between 71-289 hours.*

The British National Formulary (BNF) classifies benzodiazepines into two categories (short-acting and sustained action) with lorazepam, lormetazepam and temazepam classified as short-acting and alprazolam, chlordiazepoxide, clobazam, diazepam, flurazepam and nitrazepam classified as having a sustained action.15

The differences in the pharmacokinetic properties of the various benzodiazepines are relevant to clinical practice:

- Short-acting compounds are more suitable for older people whereas the longer-acting compounds may build up over time. This reduced drug clearance in older people may, in part, be responsible for increased susceptibility to adverse events in this patient group, the possibility of which is reduced by using shorter-acting alternatives.11
- Short-acting compounds are more likely to become habit forming or create dependency.11
- Drugs with an intermediate half-life result in fewer problems compared with short-acting alternatives when used for a short period.16
- Compounds with half-lives of more than 6 hours (e.g. nitrazepam, diazepam) may be present in the brain the following day which may result in “hangover” effects such as sedation and an increased risk of falls.17
4.2 Z-drugs
Z-drugs comprise of the non-benzodiazepine hypnotics: zolpidem and zopiclone. A third z-drug, zaleplon (Sonata®) had its marketing authorisation withdrawn in the European Union on 3 July 2015. The withdrawal was at the request of the marketing authorisation holder, Meda AB, which notified the European Commission of its decision to permanently discontinue the marketing of the product for commercial reasons.\(^\text{18}\)

Z-drugs differ structurally from benzodiazepines however they have the same pharmacological properties. Like benzodiazepines, they are GABA receptor agonists and therefore enhance GABA-mediated neuronal inhibition.\(^\text{19}\) Z-drugs were developed with the intention of overcoming some of the disadvantages of benzodiazepines e.g. next day sedation, dependence and withdrawal.\(^\text{19}\) However no clear evidence of differences in effects between z-drugs and short-acting benzodiazepines has been uncovered.\(^\text{10}\)

4.2.1 Difficulties arising from the use of z-drugs
In common with the benzodiazepines, the sedative effects of the z-drugs may persist the next day. Tolerance, dependence and withdrawal symptoms can also occur.\(^\text{20,21}\) Although benzodiazepines were the most common prescription drug implicated in poisoning deaths in Ireland (115 of deaths) in 2014, zopiclone-related deaths increased by 41%, with zopiclone implicated in 72 of the 354 poisoning deaths.\(^\text{14}\)

4.2.2 Pharmacology of z-drugs
Zolpidem, an imidazopyridine has a short half-life (mean of 2.4 hours).\(^\text{20}\) Zopiclone, a cyclopyrrolone has a longer half-life (approximately 5 hours).\(^\text{21}\) This difference in half-life is relevant to clinical practice (see section 7.3.1).

5. Legislative requirements relating to BZRA
5.1 Misuse of Drugs Regulations
A controlled drug (CD) is any substance, product or preparation specified in a Schedule of the Misuse of Drugs Act 1977.\(^\text{22}\) These substances, products or preparations, including certain medicines are either known to be, or have the potential to be, dangerous or harmful to human health, including being liable to misuse or causing social harm. Ireland is required to control substances under the Misuse of Drugs legislation, on foot of obligations as a party to the United Nations Convention on Narcotic Drugs 1961 and Psychotropic Substances 1971.
The Misuse of Drugs Regulations 2017, made under the Misuse of Drugs legislation, regulate the import, export, manufacture, production, prescribing, supply, possession and administration of CDs. A person may not possess a controlled substance unless allowed to do so under the Misuse of Drugs Regulations, or if the substance in question is exempt from such control under an Exemption Order.

The Misuse of Drugs Regulations categorise CD substances into 5 schedules (ranging from the most tightly controlled in Schedule 1 to the least tightly controlled in Schedule 5). Schedule 4 is divided into Part 1 and Part 2. The update to the Regulations (2017) had significant implications for BZRA. The benzodiazepines which were previously exempt from this legislation have been added to Schedule 4 Part 1 along with z-drugs zopiclone and zolpidem. The benzodiazepine temazepam remains in Schedule 3.

As a result of these changes the restrictions in place on the possession of CDs will apply to all BZRA. Table 2 outlines examples of medicines in each of the Schedules (1-5) of the Misuse of Drugs Regulations 2017.

Table 2: Examples of controlled drugs in Schedules 1, 2, 3, 4, or 5 of the Misuse of Drugs Regulations 2017

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Examples of medicine in this schedule*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schedule 1</td>
<td>Substances not ordinarily used as medicines e.g. Raw Opium, Coca Leaf</td>
</tr>
<tr>
<td>Schedule 2</td>
<td>Opiate substances e.g. Morphine, Fentanyl and Oxycodone</td>
</tr>
<tr>
<td></td>
<td>Some stimulants e.g. Lisdexamfetamine</td>
</tr>
<tr>
<td>Schedule 3</td>
<td>Certain benzodiazepines and painkillers</td>
</tr>
<tr>
<td></td>
<td>e.g. Temazepam, Pentazocaine, Ketamine</td>
</tr>
<tr>
<td>Schedule 4 Part 1</td>
<td>Most BZRA e.g. Diazepam, Alprazolam, Zolpidem, Zopiclone (see table 3)</td>
</tr>
<tr>
<td>Schedule 4 Part 2</td>
<td>Certain anti-epileptics e.g. Phenobarbitone &lt;100mg</td>
</tr>
<tr>
<td></td>
<td>Certain monoamine oxidase inhibitors e.g. Selegiline</td>
</tr>
<tr>
<td>Schedule 5</td>
<td>Lower strengths of painkillers e.g. Codeine (below specified concentration)</td>
</tr>
</tbody>
</table>

*This list is not exhaustive (refer to legislation for comprehensive list).

Adapted from the Medical Council and Pharmaceutical Society of Ireland Joint Guidance: Safe Prescribing and Dispensing of Controlled Drugs (2017).24
BZRA are classified in Schedule 3 and Schedule 4 Part 1. Table 3 classifies BZRA licensed for the treatment of anxiety and/or insomnia according to their CD schedule under the Misuse of Drugs Regulations 2017.

**Table 3: Controlled drug classification of BZRA licensed for the treatment of anxiety and/or insomnia**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Schedule 3</th>
<th>Schedule 4 Part 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Bromazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Clobazam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Diazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Flurazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Lorazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Lormetazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Prazepam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Temazepam</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Triazolam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Zolpidem</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Zopiclone</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

The Medical Council and Pharmaceutical Society of Ireland (PSI) developed Joint Guidance on ‘Safe Prescribing and Dispensing of Controlled Drugs’ (2017) which includes the legal requirements for **prescribing** and **dispensing** BZRA. This guidance also highlights the importance of good communication between healthcare teams involved in the prescribing and dispensing of BZRA.

Table 4 details the current prescription writing, dispensing and storage requirements for BZRA (Schedule 3 and Schedule 4 Part 1).
Table 4: Prescription writing, dispensing and storage requirements for Schedule 3 and Schedule 4 Part 1 BZRA

<table>
<thead>
<tr>
<th>Requirements</th>
<th>Schedule 3</th>
<th>Schedule 4 Part 1</th>
</tr>
</thead>
</table>
| **PRESCRIBING REQUIREMENTS**                                                 | - Name of the drug (brand or generic name)  
- Dose  
- Pharmaceutical form  
- Strength (where appropriate)  
- Total quantity in both words (e.g. five) and figures (e.g. 5)                                                                                      | - Name and address of the patient*  
- Name of the prescriber (including first name)  
- Address of the prescriber†  
- Prescriber contact number  
- Prescriber occupation  
- Prescriber registration number  
- Name of the drug (brand or generic name)  
- Dose  
- Pharmaceutical form  
- Strength (where appropriate)  
- Total quantity in both words (e.g. five) and figures (e.g. 5)                                                                                      |
| Specific criteria to be included which must be handwritten by the prescriber on the prescription | | |
| Specific criteria to be included which is not required to be handwritten on the prescription | - Name and address of the patient*  
- Name of the prescriber (including first name)  
- Address of the prescriber†  
- Prescriber contact number  
- Prescriber occupation  
- Prescriber registration number  
- Name of the drug (brand or generic name)  
- Dose  
- Pharmaceutical form  
- Strength (where appropriate)  
- Total quantity in both words (e.g. five) and figures (e.g. 5)                                                                                      | |
| Signed and dated by the prescriber                                           | Yes                                                                                                                                                                                                         | Yes                                                                                                                                               |
| Requirement for prescription to be first dispensed within 14 days of date written on prescription | Yes                                                                                                                                                                                                         | No                                                                                                                                               |
| Can prescription be repeated?                                                | No                                                                                                                                                                                                          | Yes                                                                                                                                               |
| Instalments                                                                   | Where a prescription is to be dispensed in instalments, the prescription must contain a direction specifying the number of instalments and the intervals at which the instalments may be dispensed. | Where a prescription is to be dispensed in instalments, the prescription must contain a direction specifying the number of instalments and the intervals at which the instalments may be dispensed. |
| Prescription endorsement                                                      | At the time of supply: mark on the prescription the date on which the drug is supplied.                                                                                                                   | Where the prescription has been endorsed as being repeatable i.e. where it may be dispensed on more than one occasion and where a prescription is dispensed in part, the person who dispensed the prescription shall record on the prescription:  
- Quantity of each controlled drug supplied  
- Date on which the supply was made  
- Name and address of the pharmacy where the controlled drug was supplied from.  
Where the dispensing of the drug has been completed, the person who dispensed it shall write or print prominently on the prescription the word “dispensed” and the date it was dispensed. |
| Prescription retention                                                       | The prescription shall be retained on the premises for two years.                                                                                                                                           | For a repeat prescription which is not exhausted: a copy of the prescription and any endorsements shall be retained on the premises for two years from the date of supply.  
For a prescription which is exhausted: it shall be endorsed and retained on the premises for two years. |
| Safe custody                                                                 | Required to be stored in a safe.                                                                                                                                       | Not required to be stored in a safe.                                                                                                                                                                       |

*An addressograph (sticker with patient name and address) does not fulfil the requirement for this information to be indelible; unless a Health Prescription which is a prescription issued in connection with arrangements made under section 59 of the Health Act, 1970 upon a form supplied by or on behalf of a health board i.e. GMS prescriptions. However it is best practice to always include the prescriber address.
To ensure adherence to the prescribing requirements for BZRA in the hospital setting, the patient’s name and address must be handwritten on discharge prescriptions. An addressograph (sticker with the patient’s name and address) will not fulfil the legislative requirements.

5.2 Road Traffic Act
The side-effects of BZRA include sedation, impaired concentration and alertness which can cause driving impairment. In Ireland, it is an offence to (1) drive under the influence of drugs (including prescribed drugs) where driving is impaired to such an extent that one doesn’t have proper control of the vehicle and (2) drive under the influence of three specified drugs; cannabis, cocaine and heroin (regardless of driving performance) above specified levels.²⁵

The Medical Bureau for Road Safety (MBRS) have been testing Irish drivers for the presence of drugs since 1999. Recently, the Road Traffic Act 2016 has given Gardaí new powers to conduct ‘Preliminary Drug Testing’ at the roadside or in Garda stations.²⁶ It involves testing a sample of a driver’s saliva for the presence of cannabis, cocaine, opiates and benzodiazepines. If positive, a blood specimen can be taken which will be sent to the MBRS for evidential testing. Patients are advised to follow the advice provided by their doctor and/or pharmacist when taking any medicines and to always read the patient information leaflet to check whether the medicine can affect ability to drive. The Road Safety Authority (RSA) has developed a leaflet on ‘Medicines and Driving’ which is available at www.rsa.ie/Documents/Campaigns/Anti%20Drug%20Driving/Medicines%20and%20Driving.pdf. ²⁵

Practice Point
• Counsel patients that their ability to drive safely may be reduced by BZRA.
• Refer patients to the Road Safety Authority leaflet ‘Medicines and driving’.
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. The National Institute for Health and Care Excellence (NICE) recommend 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

<table>
<thead>
<tr>
<th>Focus of intervention</th>
<th>Nature of intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STEP 1</strong>: All known and suspected presentations of GAD</td>
<td>Identification and assessment; education about GAD and treatment options; active monitoring</td>
</tr>
<tr>
<td><strong>STEP 2</strong>: Diagnosed GAD that has not improved after education and active monitoring in primary care</td>
<td>Low-intensity psychological interventions: individual non-facilitated self-help*, individual guided self-help and psychoeducational groups</td>
</tr>
<tr>
<td><strong>STEP 3</strong>: GAD with an inadequate response to step 2 interventions or marked functional impairment</td>
<td>Choice of a high-intensity psychological intervention (Cognitive Behaviour Therapy/ applied relaxation) or a drug treatment</td>
</tr>
<tr>
<td><strong>STEP 4</strong>: Complex treatment-refractory GAD and very marked functional impairment, such as self-neglect or a high risk of self-harm</td>
<td>Highly specialist treatment, such as complex drug and/or psychological treatment regimens; input from multi-agency teams, crisis services, day hospitals or inpatient care</td>
</tr>
</tbody>
</table>

*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 5 minutes.
GAD: generalised anxiety disorder
Low intensity psychological interventions which include individual non-facilitated self-help, individual guided self-help and psychoeducational groups are recommended as first-line interventions prior to drug treatment.

Step 2 may be facilitated by provision of self-help supports and information. A resource list including books, online programmes and useful websites for prescribers to disseminate to patients is available in Appendix A. Guidance for the encouragement of relaxation is available in Appendix C.

Step 3 mentions cognitive behavioural therapy (CBT) as a treatment option. CBT is a type of talking therapy that focuses on how a persons’ thoughts, beliefs and attitudes affect their feelings and behaviours, and teaches coping skills for dealing with different problems. It combines cognitive therapy (examining thoughts) and behaviour therapy (examining actions).

6.1.1 Counselling in Primary Care Service
The HSE National Counselling Service (NCS) has developed a Counselling in Primary Care (CIPC) service. CIPC is the provision of short-term counselling in primary care settings to medical card holders aged 18 years and over by professionally qualified and accredited Counsellors/Therapists who work under the supervision of the HSE-NCS. This counselling service is suitable for people with mild to moderate psychological problems and for those experiencing difficulties such as:

- Depression,
- Anxiety,
- Panic reactions,
- Relationship problems,
- Loss issues,
- Stress.

Contact details for CIPC counselling co-ordinators is available on the HSE website www.hse.ie/eng/services/list/4/Mental_Health_Services/counsellingpc/.

GPs or other members of the primary care team with the GP’s awareness can refer patients. Information for referrers and patients along with a referral form are also available on the above link.

6.2 Pharmacological treatments for anxiety
NICE guidance (2011) 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. The Irish College of General Practitioners (ICGP) guidelines for the management of Depression and Anxiety Disorders in Primary Care published in 2006 recommended SSRIs or SNRIs as first-line treatment for GAD. The SSRIs escitalopram and paroxetine, and the SNRIs duloxetine and venlafaxine are currently licensed in Ireland to treat GAD.

**Practice Point**
MMP recommends selective serotonin reuptake inhibitors (SSRIs) as first-line pharmacological treatment for generalised anxiety disorder (GAD).

* See individual Summary of Product Characteristics (SmPC) of SSRIs licensed for 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. Studies suggest that the associated dependency issues do not make them appropriate first-line pharmacological options.

The 2006 ICGP guidelines recommended benzodiazepines only as short-term adjunctive therapy in severe anxiety. A consensus paper by the CPI on the use of benzodiazepines in specialist mental health services (2012) recommended that benzodiazepines should not be used as first-line treatment but reserved as an option for treatment resistant cases.

### 6.2.2 Benzodiazepines licensed to treat anxiety
The benzodiazepines licensed to treat anxiety are:

- Alprazolam
- Bromazepam
- Chlordiazepoxide
- Clobazam
- Diazepam
- Lorazepam
- Prazepam

Licensed doses and maximum treatment durations for benzodiazepines in the treatment of anxiety as per SmPC are detailed in Appendix D.
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.\textsuperscript{43} The 2006 ICGP guidelines recommend benzodiazepines as adjunctive therapy for a maximum of two weeks.\textsuperscript{27} Similarly the consensus paper by the CPI (2012) recommends a short-term treatment duration (2-4 weeks) to reduce the risks of dependence and tolerance.\textsuperscript{11} Patients should be assessed regularly and the need for continued treatment should be evaluated.\textsuperscript{36-42} The 2015 Royal Australian College of General Practitioners (RACGP) guidance on prescribing drugs of dependence in general practice, recommends that patients being prescribed benzodiazepines should obtain all prescriptions from the same doctor so their risk of dependence can be monitored.\textsuperscript{44}

\begin{quote}
\textbf{Practice Point}

MMP recommends benzodiazepines should be prescribed for the shortest possible duration and to a maximum period of \textbf{two to four weeks} for the treatment of anxiety.
\end{quote}

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.\textsuperscript{9}

7.1 Types of Insomnia
\textbf{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.\textsuperscript{15}

\textbf{Short-term insomnia} is usually related to an emotional issue or medical illness. It may last for a few weeks (from one to four weeks) and may recur whereas \textbf{chronic insomnia} can develop due to psychiatric disorders such as anxiety, depression and abuse of drugs and alcohol.\textsuperscript{15}

Sleep onset insomnia is characterised as difficulty initiating asleep while \textbf{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.\textsuperscript{15,19} The American College of Physicians (ACP) recommends that all adult patients receive CBT for insomnia as the initial treatment for chronic insomnia disorder.\textsuperscript{45} CBT for insomnia consists of a combination of treatments that include cognitive therapy around sleep, education (e.g. sleep hygiene) and behavioural interventions (e.g. sleep restriction and stimulus control). These non-pharmacological measures should be trialled before prescribing hypnotics (see table 6).\textsuperscript{19}

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Intended effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep hygiene</td>
<td>Reduce behaviours that interfere with sleep drive or that increase arousal</td>
</tr>
<tr>
<td>Sleep restriction</td>
<td>Increase sleep drive and stabilise circadian rhythm</td>
</tr>
<tr>
<td>Stimulus control</td>
<td>Reduce arousal in sleep environment and promote the association between bed and sleep</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>Restructure maladaptive beliefs regarding health and daytime consequences of insomnia</td>
</tr>
<tr>
<td>Relaxation therapy</td>
<td>Reduce physical and psychological arousal in sleep environment</td>
</tr>
</tbody>
</table>

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.\textsuperscript{47} 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.

\textbf{Practice Point}

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). It concluded there was a lack of compelling evidence to distinguish between z-drugs (zaleplon, zolpidem, zolpiclone) or the shorter-acting benzodiazepine hypnotics. NICE recommend only switching from one z-drug to another if a patient experiences side-effects which 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.

If long-acting benzodiazepines (e.g. diazepam, flurazepam and nitrazepam) are used as hypnotics, they tend to have next day residual effects causing psychomotor impairment and affecting mental function. Zolpidem should only be prescribed to patients with sleep onset insomnia as it is not effective at maintaining sleep due to its short half-life. Zopiclone may be prescribed for patients with continuous sleep disturbances during the night. However, zopiclone may have noticeable hangover effects the following day.

Practice Point

- Avoid long-acting benzodiazepine hypnotics.
- Zolpidem should only be prescribed for patients with sleep onset insomnia.
- Zopiclone is suitable for continuous sleep disturbance.
7.3.2 BZRA licensed to treat insomnia

BZRA licensed for the treatment of insomnia are listed in table 7.

**Table 7: BZRA licensed for the treatment of insomnia**\(^{20,21,40,41,48-52}\)

<table>
<thead>
<tr>
<th>Benzodiazepines</th>
<th>Flurazepam</th>
<th>Diazepam*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lorazepam*</td>
<td>Lormetazepam</td>
</tr>
<tr>
<td></td>
<td>Nitrazepam</td>
<td>Temazepam</td>
</tr>
<tr>
<td></td>
<td>Triazolam</td>
<td>Zolpidem</td>
</tr>
<tr>
<td>Z-drugs</td>
<td>Zopiclone</td>
<td></td>
</tr>
</tbody>
</table>

*Insomnia associated with anxiety

Licensed doses and maximum treatment durations for BZRA in the treatment of insomnia as per SmPC are detailed in **Appendix D**.

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.\(^{15}\) The Department of Health (DoH) Good Practice Guidelines for prescribing benzodiazepines (2002) recommend that hypnotic benzodiazepine prescriptions be limited to between 2 and 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 (see **Appendix D**).

The SmPC for zolpidem and zopiclone state that long-term use is not recommended\(^{20}\) and treatment should be as short as possible.\(^{21}\) The duration of treatment should usually vary from a few days to two weeks with a maximum of four weeks including tapering off where clinically appropriate.\(^{20,21}\)

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.\(^{20,21,40,41,48-52}\) It may be useful to inform the patient when treatment is initiated that it will be of a limited duration.
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, longer-term use of BZRA is associated with problems such as tolerance, dependence and withdrawal symptoms.\textsuperscript{15,20,21,36-42,48-52} Patients should be made aware of the possibility of rebound phenomena to minimise anxiety should such symptoms develop when the BZRA is discontinued.\textsuperscript{10} 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,\textsuperscript{53}
- Impairment in judgement and dexterity,\textsuperscript{16}
- Forgetfulness, confusion, irritability, aggression and paradoxical disinhibition.\textsuperscript{16,21}

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.\textsuperscript{11}

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.\textsuperscript{16} Tolerance to BZRA progressively reduces their effectiveness for the treatment of insomnia or anxiety.\textsuperscript{16} 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.\textsuperscript{4} Long-term efficacy of benzodiazepines is unreliable, particularly the hypnotics where tolerance to their effects can develop in 3-14 days of continuous use.\textsuperscript{15}
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.54

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.5 Psychological and physical dependence can develop within a few weeks or months of regular or repeated use.55

Benzodiazepine dependence can present in a number of different ways including:16,54
- 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
In Ireland, 63 per 1000 older people receive long-term prescriptions for benzodiazepines and related drugs compared to an average of 29 per 1000 across the Organisation for Economic Co-operation and Development (OECD) countries.56

- 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.7,8,9,15
- 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.57
- 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.58
- Benzodiazepine use has also been associated with an increased risk of Alzheimer’s disease in older people.59 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

- Seek specialist advice 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).
  - 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

- BZRAs are not indicated in patients with severe hepatic insufficiency as they may precipitate encephalopathy.
- In patients with hepatic impairment reduced doses of a BZRA should be used.
- Use of benzodiazepines can precipitate coma and if treatment is deemed necessary then benzodiazepines with shorter half-lives are considered safer.
- There is increased cerebral sensitivity to benzodiazepines in patients with renal impairment.
- Z-drugs should be used with caution in renal impairment.

---

**Practice Point**

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 issued by the DoH in 2002 in response to the Report of the Royal College of Psychiatrists ‘Benzodiazepines: Risks, Benefits or Dependence’ (1997) stressed the significant risk of dependence in patients receiving treatment for longer than one month.⁶

The report recommended that every clinician examine the benefit:risk ratio in each individual case early in treatment and recommended that benzodiazepines should not be prescribed for longer than one month in the treatment of anxiety and should be limited to between two and four weeks in the treatment of insomnia or sleep disturbance.⁴³

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.⁴³

The guideline outlines good practice for prescribers when prescribing for the first time and when prescribing for dependent patients (see table 8).

<table>
<thead>
<tr>
<th>Table 8: Good practice guidelines for prescribing benzodiazepines⁴³</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prescribing for the first time</strong></td>
</tr>
<tr>
<td>Initiate with the lowest dose and adjust according to response</td>
</tr>
<tr>
<td>Do not prescribe for longer than four weeks</td>
</tr>
<tr>
<td>Use phased dispensing where appropriate</td>
</tr>
<tr>
<td>Record all details of medication prescribed and duration of treatment</td>
</tr>
</tbody>
</table>

9.1 Practice audit

Good practice guidelines on benzodiazepine prescribing from the CPI recommend conducting regular audits of practice.¹¹ Standards of practice should ensure short-term use of benzodiazepines and reasons for continuing prescribing beyond this term should be documented.¹¹ The ICGP have developed an audit tool for the prescribing of benzodiazepines which is available at: www.icgp.ie/go/library/catalogue/item/C2481151-D7E5-FDDE-F887EF0B2A49C554.⁶²

The HSE-PCRS provides regular prescribing reports to GPs based on dispensed drug data for BZRA on the General Medical Services (GMS) scheme. While this data is not a comprehensive analysis of all
prescribing (private and Drug Payment scheme prescriptions are not included) it can be used as a useful tool to monitor practices compared to national norms and to track changes over time.

<table>
<thead>
<tr>
<th>1: Benzodiazepines and Z drugs Prescribing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>0 - 4</td>
</tr>
<tr>
<td>5 - 11</td>
</tr>
<tr>
<td>12 - 15</td>
</tr>
<tr>
<td>16 - 24</td>
</tr>
<tr>
<td>25 - 34</td>
</tr>
<tr>
<td>35 - 44</td>
</tr>
<tr>
<td>45 - 54</td>
</tr>
<tr>
<td>55 - 64</td>
</tr>
<tr>
<td>65 - 69</td>
</tr>
<tr>
<td>70 - 74</td>
</tr>
<tr>
<td>75 - over</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2: Prolonged Use Prescribing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Duration</strong></td>
</tr>
<tr>
<td>0 months</td>
</tr>
<tr>
<td>1 - 3 months</td>
</tr>
<tr>
<td>4 - 6 months</td>
</tr>
<tr>
<td>7 - 9 months</td>
</tr>
<tr>
<td>10 - 12 months</td>
</tr>
<tr>
<td>13 months +</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3: Your Prescribing Compared to National Norm</th>
</tr>
</thead>
</table>

Figure 1: Sample BZRA prescribing analysis report – PCRS

Figure 1 explanatory notes:

Prescribing frequency is outlined in the first table where:

**Panel** is the number of patients on your panel in the age group presented

# is the number of unique patients to whom a BZRA has been dispensed

**Qty** is the total quantity of BZRA i.e. the actual number of tablets/capsules dispensed

% is the percentage of patients in the age category who have received a BZRA

The traffic light column in the first table highlights your prescribing rate compared to the national mean prescribing rate (represented by standard deviation) at an age group level. **Standard deviation is a measure of dispersion or variation in a set of data from its mean.** Green represents prescribing that is lower than or within one standard deviation higher than the national mean prescribing rate. Yellow represents a prescribing rate between one and two standard deviations higher than the national mean prescribing rate. Red represents a prescribing rate that is more than two standard deviations higher than the national mean prescribing rate.
Prolonged use prescribing is outlined in the second table where:

# is the number of unique patients on your panel to whom a BZRA have been dispensed for various periods of time. The first row presents the number of patients to whom a BZRA has not been dispensed.

% is the percentage of patients on your panel who have been dispensed a BZRA for each duration category. The first row ‘0 months’ presents the percentage of patients on your panel to whom a BZRA has not been dispensed at all. In the example, there are 79.06% of patients on the panel in the reported year to whom a BZRA has not been dispensed at all.

Your prescribing compared to the national norm is outlined in third section (bell curve)
The presentation of your overall prescribing rate on this chart is on the basis of the number of standard deviations your prescribing rate is away from the national mean. The position of your prescribing rate is highlighted with the purple marker bar on the chart.

Practice Point

The MMP recommends that prescribers:

1. Carry out a documented review of BZRA prescriptions regularly.
2. Inform patients of the risk of dependency with long-term use of BZRA (record in notes).
10. Prescribing trends of BZRA in Ireland
Analyses of the PCRS pharmacy claims were performed by the MMP to determine prescribing trends for BZRA in Ireland. The results highlighted that the four most commonly prescribed BZRA on the GMS scheme in 2016 were zopiclone, zolpidem, diazepam and alprazolam (see figure 2).

![Figure 2: Total number of BZRA prescriptions on the GMS scheme in 2016](image)

In relation to benzodiazepine utilisation, diazepam and alprazolam were by far the most commonly prescribed benzodiazepines on the GMS scheme in 2016. Zopiclone and zolpidem were the most frequently prescribed medicines of all BZRA on the GMS scheme in 2016. The PCRS annual statistical report for 2015 outlines similar figures for the previous year with the z-drugs zopiclone and zolpidem listed as the 18th and 24th most commonly prescribed products on the GMS scheme with diazepam and alprazolam listed as 27th and 30th respectively.

In 2016, total expenditure on BZRA on the GMS scheme was approximately €21.7 million which was similar to the 2015 figures with zopiclone alone accounting for €5.7 million of these figures each year (see figure 3).
Further analysis of the duration of use of BZRA for the 12 months of 2015 demonstrated that 43% of benzodiazepines and 54% of z-drugs dispensed on the GMS scheme were for greater than three months in this 12 month period (see figure 4).

Despite z-drugs being licensed for a maximum duration of four weeks in the treatment of insomnia, 42% of patients received these drugs for between 6-12 months in this 12 month period.

The analysis of all benzodiazepine use on the GMS scheme showed that 27% of patients were in receipt of a benzodiazepine for between 6-12 months in this 12 month period. While some indications for benzodiazepine use (e.g. epilepsy) may require longer-term treatment, use in anxiety and insomnia should be limited to the shortest possible duration.
11. Deprescribing of BZRA

Deprescribing is an active review process that prompts prescribers to identify medications which are not performing effectively in the risk-benefit trade-off and may in fact be causing harm to the patient. The development of dependence can pose significant challenges when discontinuation of treatment with a BZRA is attempted as withdrawal symptoms often develop. Both prescribers and patients have a role to play in the deprescribing process. Decisions about dose and reduction should be made between the prescriber and patient in a collaborative and flexible manner.

Treatment withdrawal is possible in many patients once the issues relating to prolonged drug use are explained and discussed. Minimal interventions such as a letter from the prescriber to targeted patients on BZRA can be effective in reducing or stopping use without adverse effects. The letter can explain the problems associated with long-term BZRA use and invite patients to try and reduce their use and eventually stop. A sample letter to patients is included in Appendix E.

11.1 Approaches to deprescribing

Withdrawal can be achieved by a number of methods. It is important, however, that it is managed correctly, with tapering of doses carried out gradually under the guidance of the prescriber. Abrupt withdrawal of a benzodiazepine may produce confusion, toxic psychosis, convulsions, or a condition
resembling delirium tremens. Short-term users of benzodiazepines (2-4 weeks) can usually taper off within 2-4 weeks. However long-term users should be withdrawn over a much longer period of several months or more. There are two approaches to facilitate dose reduction:

i. Patients may be slowly withdrawn from their current BZRA or

ii. Patients may be switched to an equivalent dose of a long-acting slowly-metabolised benzodiazepine which is slowly tapered down such as diazepam.

Diazepam, which has a long half-life (up to 48 hours; table 1), is often the long-acting benzodiazepine of choice to facilitate withdrawal as the availability of different strengths allows for small decremental changes in dosage. This avoids large fluctuations in plasma levels.

Switching is often recommended when patients experience severe withdrawal symptoms. Switching to diazepam is best carried out gradually, usually in a step wise manner (see section 12.2). Dose withdrawal may be commenced when switching to diazepam is complete. The first switch should be to the night time dose to avoid sedation during the daytime. Tables 9 and 10 below are examples of equivalence tables if switching from a BZRA to diazepam to facilitate deprescribing.

Table 9: Equivalence table if switching from current benzodiazepine to diazepam

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose equivalent to diazepam 5mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>250 micrograms</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>12.5 mg</td>
</tr>
<tr>
<td>Clobazam</td>
<td>10 mg</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>250 micrograms</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>7.5-15 mg</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>500 micrograms</td>
</tr>
<tr>
<td>Lorimetazepam</td>
<td>0.5-1 mg</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>5 mg</td>
</tr>
<tr>
<td>Temazepam</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

Table 10: Equivalence table if switching from current z-drug to diazepam

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose equivalent to diazepam 5mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zopiclone</td>
<td>7.5mg</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

11.2 Community detoxification
A shared care approach with substance misuse services may be required for more complex cases. Community Benzodiazepine Detoxification Guidelines have been developed by the Ana Liffey Drug Project for patients in a non-residential setting (2011) and updated in 2015. The Ana Liffey Drug Project is a national addiction service charity organisation. The organisation’s mission is to work with
people affected by problem substance use and the organisations that assist them. The aim is to reduce harm to service users and society, and to provide opportunities for development of those service users and organisations. These guidelines recommend that a Community Detoxification programme should include (1) a named key worker or health care professional who will provide psychological support and (2) a prescribing GP who delivers a physical and mental health assessment, medical support and detoxification to the patient. The guideline sets out how GPs and key workers should interact to provide effective supports while managing the risk of relapse and overdose. A patient’s suitability to participate in this structured detoxification programme is determined by the GP involved. The guidelines are available at www.drugs.ie/downloadDocs/2017/Community-Detox-Guidelines-Benzodiazepines-2017.pdf.

In the next section the MMP have incorporated educational resource material developed by the All Wales Medicines Strategy Group (2016) and guidance available in the BNF and in the NICE Clinical Knowledge Summary for the purpose of providing deprescribing support to prescribers.
12. Resources to support deprescribing of BRZA

12.1 Initial consultation

*Adapted with kind permission of the All Wales Medicines Strategy Group Educational Pack*\(^\text{16}\)

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 Managing patients who want to stop BZRA

*Summarised from NICE Clinical Knowledge Summaries*\(^\text{10,69}\)

- Decide if the patient can reduce the dose and stop their current BZRA without switching to diazepam. Withdrawal may be undertaken with or without switching to diazepam.
- Switching to diazepam is recommended for:
  - Patients on short-acting potent benzodiazepines (alprazolam and lorazepam).
  - Patients using preparations that do not easily allow for small reductions in dose.
Patients experiencing difficulty or who are likely to experience difficulty withdrawing directly from their current BZRA due to a high degree of dependency (associated with long duration of treatment, high doses, and a history of anxiety problems).

- If switching patient to diazepam, equivalence tables are set out in tables 9 & 10.
- Seek specialist advice before switching to diazepam in patients with hepatic dysfunction as diazepam may accumulate to toxic levels.
- 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.
  - Titrate dose according to severity of withdrawal symptoms.
  - Review frequently.

12.2.2 A suggested protocol for withdrawal following long-term benzodiazepine use
* From the BNF15

- 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.

Make available to the patient “Stopping your benzodiazepine and z-drug: A guide for patients” (Appendix F).

Examples of BZRA conversions to diazepam and withdrawal schedules for GPs are available at www.drugs.ie/downloadDocs/2017/Community-Detox-Guidelines-Benzodiazepines-2017.pdf.58
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 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.
- 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 which is slowly tapered down (e.g. diazepam).
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 drugs 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.
✓ 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.
14. References


17. Wilson S, Nutt D, Alford C et al. British Association for Psychopharmacology consensus


Appendix A: Suggested non-pharmacological resources for prescribers and patients

1. Cognitive Behavioural Therapy Resource List

Online Resources (free of charge)

- **Aware: Life Skills** [www.aware.ie/life-skills](http://www.aware.ie/life-skills) or Aware: Beat the Blues (age 15-18)
- **Lust for Life** [www.alustforlife.com/section/mental-health/cbt-online-course](http://www.alustforlife.com/section/mental-health/cbt-online-course)
- **Well-Being** [www.wellbeing-glasgow.org.uk](http://www.wellbeing-glasgow.org.uk)
  Well-Being includes CBT audio booklet version for people with literacy challenges.
- **Self Help Booklets** [http://web.ntw.nhs.uk/selfhelp/](http://web.ntw.nhs.uk/selfhelp/)

Overcoming Books: A self-help guide using Cognitive Behavioural Techniques (available from local libraries)

- 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 DEPERSONALIZATION 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 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

Other Resources

- **Song for Relaxation**: Marconi Union – ‘Weightless’ (caution: not whilst driving)
- **CBT App**: [www.thinkpacifica.com](http://www.thinkpacifica.com)
- **Relaxation App**: [www.calm.com](http://www.calm.com)

This list offering some suggestions was kindly compiled by Marie Carey (Clinical Nurse Specialist in CBT/Registered Nurse Prescriber) HSE West Tipperary Adult Mental Health Services. This list is not exhaustive, see overleaf for other available supports for patients.
2. Other Online Cognitive Behavioural Therapy Resources (not free of charge)

- Beating the Blues® ([www.beatingtheblues.co.uk](http://www.beatingtheblues.co.uk)) is an online CBT treatment programme for depression and/or anxiety in primary care.
- FearFighter® ([fearfighter.cbtprogram.com](http://fearfighter.cbtprogram.com)) is an evidence-based online program for panic disorder and phobia.

Both treatment programmes are endorsed by NICE.

3. Other Useful Websites

- **Mental Health Ireland** [www.mentalhealthireland.ie](http://www.mentalhealthireland.ie)

Mental Health Ireland (MHI) is a national voluntary organisation which was established in 1966 as the Mental Health Association of Ireland. Mental Health Ireland’s aim is to promote positive mental health and wellbeing to all individuals and communities in Ireland. The website provides publications free to download including:

  - MHI Guide to living with anxiety booklet
  - MHI Manage and reduce stress booklet

- **Your Mental Health** [www.yourmentalhealth.ie](http://www.yourmentalhealth.ie)

Your Mental Health is a website for patients to learn about mental health in Ireland, and how to support yourself and the people you love. It is developed by the HSE, the National Office for Suicide Prevention and partner organisations.

4. Support Guides for Patients*

- ‘The Good Sleep Guide’ (see appendix B)
- ‘The Good Relaxation Guide’ (see appendix C)
- ‘Stopping your medicine: benzodiazepines and z-drugs. A guide for patients’ – (see appendix F)

*Adapted with the kind permission of the All Wales Medicines Strategy Group Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales.
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.

*Adapted with the kind permission of the All Wales Medicines Strategy Group Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales.

Other Practical Tips
- Avoid using smart phones or other devices which emit ‘blue light’ late in the evening/night as this can disrupt normal sleep schedules.
- Do not use your phone as an alarm clock; use a separate alarm clock.
- If you need to use your phone as an alarm clock, place your phone away from sight or at the other end of the room during the night.
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.

*Adapted with the kind permission of the All Wales Medicines Strategy Group Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales.\textsuperscript{16}
Appendix D: BZRA licensed for the treatment of **anxiety and insomnia** - licensed dosage and duration as per SmPC

### Anxiety

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>Dose in adults</th>
<th>Dose in older people</th>
<th>Licensed duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam(^{36})</td>
<td>Initially <strong>0.5 mg to 1 mg daily</strong> 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.</td>
<td>Initially 0.25 mg twice daily</td>
<td>Maximum <strong>eight to twelve weeks</strong> including a tapering off process</td>
</tr>
<tr>
<td>Bromazepam(^{37})</td>
<td><strong>3 to 18 mg daily</strong> in divided doses</td>
<td>Half the adult dose</td>
<td>Maximum <strong>eight to twelve weeks</strong> including a tapering off process</td>
</tr>
<tr>
<td>Chlordiazepoxide(^{38})</td>
<td><strong>30 mg daily</strong> in divided doses</td>
<td>Half the adult dose</td>
<td>Maximum <strong>four weeks</strong> including a tapering off process</td>
</tr>
<tr>
<td>Clobazam(^{39})</td>
<td><strong>20 to 30 mg daily</strong> in divided doses or as a single dose given at night</td>
<td>10 to 20 mg daily</td>
<td>Maximum <strong>eight to twelve weeks</strong> including a tapering off process</td>
</tr>
<tr>
<td>Diazepam(^{40})</td>
<td><strong>2 mg three times daily</strong></td>
<td>Half the adult dose</td>
<td>Maximum <strong>eight to twelve weeks</strong> including a tapering off process. Treatment should not be continued at the full dose beyond four weeks</td>
</tr>
<tr>
<td>Lorazepam(^{41})</td>
<td><strong>1 to 4 mg daily</strong> in divided doses</td>
<td>Half the adult dose or less</td>
<td><strong>A few days to four weeks</strong> including the tapering off process</td>
</tr>
<tr>
<td>Prazepam(^{42})</td>
<td><strong>30 mg daily</strong> in single or divided doses</td>
<td>Half the adult dose</td>
<td>Maximum <strong>four to six weeks</strong> including a tapering off process</td>
</tr>
<tr>
<td>BZRA</td>
<td>Drug Class</td>
<td>Dose in adults*</td>
<td>Dose in older people*</td>
</tr>
<tr>
<td>------------</td>
<td>------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Benzodiazepine</td>
<td>Insomnia associated with anxiety: 5 to 15 mg</td>
<td>Insomnia associated with anxiety: 2.5 to 7.5 mg</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Benzodiazepine</td>
<td>15 to 30 mg</td>
<td>15 mg</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Benzodiazepine</td>
<td>Insomnia associated with anxiety: 1 to 2 mg</td>
<td>Insomnia associated with anxiety: 0.5 to 1 mg</td>
</tr>
<tr>
<td>Lormetazepam</td>
<td>Benzodiazepine</td>
<td>1 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>Benzodiazepine</td>
<td>5 to 10 mg</td>
<td>2.5 to 5 mg</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Benzodiazepine</td>
<td>10 to 20 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Benzodiazepine</td>
<td>0.25 mg in patients previously untreated with hypnotics</td>
<td>0.125 mg</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Z-drug</td>
<td>10 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>Z-drug</td>
<td>7.5 mg</td>
<td>3.75 mg</td>
</tr>
</tbody>
</table>

*Hypnotic BZRA should be taken at night. See individual SmPCs for more information on times these medicines should be taken in relation to bedtime.
Appendix E: Sample letters to patients on BZRA

*Taken from the ICGP Benzodiazepine Prescribing Sample Audit - Adapted from Sample letters Mercer’s Medical Centre)*

Practice Name and Address

Dear Patient,

We are currently undertaking a review of prescriptions for medications collectively known as Benzodiazepines and sleeping tablets. I am writing to you because our records show that you have received a number of prescriptions for one or more of these types of medications in the past 12 months.

Recent studies have shown that if these medications are used for long periods of time, they can have harmful side effects, including anxiety symptoms, memory and sleep problems and they can also be addictive. Long term use is therefore no longer recommended.

We are writing to ask you to consider cutting down your dose of tablets and perhaps stopping them completely at some time in the future. As each person is different, we would like to discuss this with you in person within the next 3 months.

The best way to cut down your tablets is to take them only when you feel they are absolutely necessary. It is best to cut down gradually; otherwise you may have some withdrawal side effects. You should not stop your tablets suddenly. Once you start to reduce your dose you may start to notice that you feel a lot better and you may be able to think about stopping altogether.

Please make an appointment with your GP to discuss this further. If you have not attended to discuss this within the next 3 months, we may not be able to continue to prescribe this medicine for you. If you have already discussed this with your doctor, or have stopped your medications, this letter does not apply to you.

Yours sincerely,

Dr.
Dear Patient,

Our records show that you have been prescribed benzodiazepines and/or sleeping tablets on a regular basis over the past number of months. We wrote to you on___________ asking you to make an appointment with your GP to discuss these prescriptions.

From our records I note that you have not attended for review and therefore we are no longer able to prescribe this medication for you.

If you would like to discuss this matter or if our records are incorrect, please make an appointment with your GP to discuss.

Yours sincerely

_______________________________

Dr.
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 andlorazepam 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!*

---

*Adapted with the kind permission of the All Wales Medicines Strategy Group Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales.*