



**Guidelines for the Prescribing of Benzodiazepines and Z-Drugs**

**Key points:**

- Benzodiazepines/Z drugs should only be prescribed as a last resort when alternatives have been explored.<sup>1,2</sup>
- They should only be prescribed at the lowest effective dose for the shortest time possible (2 to 4 weeks) as per licensing.<sup>1</sup>
- Only issue acute prescriptions for these drugs. These drugs should not be put onto a patient's repeat.
- Inform patients that further prescriptions will not usually be issued.<sup>2</sup>
- Existing long-term patients should be gradually withdrawn from these drugs.
- Complex patients on long term benzodiazepines/Z drugs, especially those with a history of previous dependencies, should be referred to Turning Point (see below for contact details).

**Mechanism of action**

**Benzodiazepines** work by increasing the efficiency of a natural brain chemical, gamma aminobutyric acid (GABA), to decrease the excitability of neurons. This reduces the communication between neurons and has a calming effect on many of the functions of the brain.

**Z-drugs** are short-acting non benzodiazepine hypnotics that potentiate GABA. They are thought to bind to the benzodiazepine receptor component of the GABA receptor complex<sup>2</sup>, enhancing GABA mediated inhibition of neurons.

**Comparison of Benzodiazepines and Z-drugs**<sup>1,2,4</sup>

Drug	Duration of action	Approximate equivalent dose to diazepam 5mg	Licensed Indications	Price (Drug Tariff November 2016)
<b>Benzodiazepines:</b>				
Nitrazepam	Long acting	5mg	Insomnia (short term use)	28 x 5mg tablets £1.26
Loprazolam	Intermediate acting	0.5 – 1mg	Insomnia (short term use)	28 x 1mg tablets £18.00
Lormetazepam	Intermediate acting	0.5 – 1mg	Insomnia (short term use)	30 x 0.5mg tablets £15.25 30 x 1mg tablets £11.16
Temazepam	Intermediate acting	10mg	Insomnia (short term use)	28 x 10mg tablets £3.80 28 x 20mg tablets £4.04
Diazepam	Long acting	5mg	Insomnia & anxiety (short term use)	28 x 2mg tablets £0.76 28 x 5mg tablets £0.79 28 x 10mg tablets £0.91
Chlordiazepoxide	Long acting	12.5mg	Anxiety (short term use) Treatment of alcohol withdrawal	100 x 10mg capsules £17.80
Lorazepam	Intermediate acting	0.5mg	Insomnia & anxiety (short term use)	28 x 1mg tablets £2.02 28 x 2.5mg tablets £2.90
Oxazepam	Short acting	10mg	Anxiety (short term use) and Insomnia associated with anxiety	28 x 10mg tablets £1.20 28 x 15mg tablets £1.23
Clonazepam	Long acting	0.25mg	Epilepsy and status epilepticus. NOT licenced in anxiety or insomnia	100 x 2mg tablets £27.69 100 x 0.5mg tablets £24.95
Clobazam	Long acting	10mg	Anxiety (short term use – not on NHS) Epilepsy (not under 6 years old)	30x 10mg tablets £3.29
<b>Z-Drugs:</b>				



Zaleplon	Short acting	10mg	Insomnia (short term use)	14 x 5mg capsules £3.12 14 x 10mg capsules £3.76
Zolpidem	Short acting	10mg	Insomnia (short term use)	28 x 5mg tablets £1.24 28 x 10mg tablets £1.16
Zopiclone	Short acting	7.5mg	Insomnia (short term use)	28 x 3.75mg tablets £1.17 28 x 7.5mg tablets £1.18

### **Cautions and contraindications of benzodiazepines and Z-drugs**

- Tolerance and dependence to the effects of hypnotics and z-drugs are likely to develop after no more than a few weeks of treatment<sup>1,4</sup>.
- Prolonged high level use of benzodiazepines may be associated with adverse effects e.g. memory loss and confusion, accidents and falls, low mood and insomnia. They should also be avoided in elderly patients due to these effects<sup>2</sup>.
- Avoid all benzodiazepines and z-drugs in patients with pulmonary insufficiency, significant respiratory depression, obstructive sleep apnoea or severe hepatic impairment.
- A paradoxical increase in anxiety, hostility and aggression may occur in patients taking benzodiazepines<sup>1</sup>.
- Benzodiazepines should be avoided in those with a history of substance abuse or with personality disorders<sup>4</sup>.
- Hypnotics and anxiolytics may impair judgement and increase reaction time, and so affect ability to drive or operate machinery. This effect will be increased when taken with alcohol<sup>1</sup>. Hangover effects of a night dose may impair driving on the next day.
- Benzodiazepines are now also subject to drug-driving laws which may rule them inappropriate for some patients<sup>7</sup>.
- Avoid in pregnant and lactating women<sup>1</sup>.
- Avoid concurrent prescribing with: other hypnotics, sedative tricyclic anti-depressants, antihistamines, opioids and some antifungal drugs (e.g. fluconazole)<sup>1</sup>.
- Do not prescribe to unfamiliar patients (e.g. temporary residents), without checks.

**Always check the summary of product characteristics for a particular drug for the full list of cautions and contraindications. <http://www.medicines.org.uk/emc/>**

### **Anxiety**

- Benzodiazepines should only be used for the short term management of a specific, one off circumstance e.g. air travel, pre-procedural use, prescribing the minimum appropriate quantity.
- Benzodiazepines should not be used for the treatment of generalised anxiety disorder (GAD) in primary or secondary care except as a short-term measure during crises<sup>5</sup>, and should never be used to manage long term anxiety.
- Z-drugs (sleeping tablets) are also not appropriate to prescribe for patients with anxiety<sup>1</sup>.
- For mild to moderate anxiety consider referral to Suffolk Wellbeing Service (0300 123 1781).
- For patients with severe anxiety refer to the Community Mental Health Team (CMHT).
- Drug treatment can be considered if psychological treatment fails or the patient has severe functional daytime impairment<sup>6</sup>. Follow NICE guidance for further information on drug treatment<sup>5</sup>.

### **Short term insomnia (<4 weeks)**

- Identify and address any underlying cause of insomnia or associated comorbidities<sup>1</sup>.
- Review patient's sleep expectations<sup>1</sup>; five to six hours sleep a night is normal for older people, especially if the patient naps during the day.
- Advise good sleep hygiene – see sleep guide page five.
- Only initiate benzodiazepines for short term insomnia that is severe, with disabling daytime impairment or is causing the patient extreme distress – see benzodiazepine and Z-drug prescribing guidance below.



- Review after 2 weeks and consider referral for cognitive behavioural therapy if symptoms persist<sup>2</sup>
- Consider referral to Suffolk Wellbeing Service (0300 123 1781)

### **Long-term insomnia (> 4 weeks)**

- Manage any underlying cause of insomnia or associated comorbidities.
- Review patient's sleep expectations<sup>1</sup>; five to six hours sleep a night is normal for older people, especially if the patient naps during the day.
- Advise good sleep hygiene (see sleep guide page five) and regular exercise in addition to cognitive and behavioural interventions (e.g. relaxation training). For access to these services refer to Suffolk Wellbeing Service (0300 123 1781).
- Refer to Sleep Station for advice and help in managing insomnia ([www.sleepstation.org.uk](http://www.sleepstation.org.uk))
- Hypnotics are not generally recommended for the management of long-term insomnia. A short course (up to 2 weeks) of a hypnotic drug may be considered for immediate relief or to manage an acute exacerbation of persistent insomnia – see benzodiazepine and Z-drug prescribing guidance below<sup>2</sup>.

Refer to a sleep clinic or specialist if insomnia persists ([www.sleepsociety.org.uk](http://www.sleepsociety.org.uk)).

### **Benzodiazepine and Z-drug prescribing guidance**

- Only initiate benzodiazepines for anxiety or insomnia that is **severe, disabling in daytime hours or causing the patient extreme distress**<sup>1,6</sup>.
- Only licensed for **short-term use** (2 to 4 weeks maximum)<sup>1</sup>, the first prescription should be for no longer than 7 to 14 days. Patients should be informed that treatment is only to be continued for a short duration<sup>2</sup>.
- Issue acute prescriptions only for these drugs with a need to see the patient before any further issues (not for repeat dispensing or repeat prescribing)<sup>2</sup>.
- Consider the pharmacokinetic differences between the benzodiazepines for different patient groups, e.g. avoid long-acting benzodiazepines in the elderly (e.g. diazepam) as risk of hangover, confusion, ataxia and falls<sup>1</sup>.
- Prescribe the lowest effective dose for the shortest possible time<sup>2</sup>. Treatment should not be continued beyond 4 weeks<sup>6</sup>.
- There is no compelling evidence to distinguish between zaleplon, zolpidem, zopiclone or the shorter acting benzodiazepines (e.g. temazepam, loperazolam and lormetazepam) therefore the drug with the lowest purchase cost should be prescribed<sup>7</sup>.
- Patients who have not responded to one hypnotic should not be prescribed another<sup>2</sup>.
- Encourage intermittent dosing to help prevent tolerance, e.g. only use every other night<sup>1,6</sup>.
- Suggest a time period when an 'as required' dose may be administered e.g. allow 30 minutes for natural sleep to occur before taking sleeping tablet.
- Agree short-term goals with the patient which will be specific measures of treatment progress.
- Review achievement of goals regularly (every one to two weeks), stop treatment if not effective.
- Record accurately in the patient's notes.

### **Withdrawal**

- Encourage all those prescribed benzodiazepines long term to consider reducing or tapering off their dose.
- Many patients prescribed these medications long-term will experience withdrawal symptoms. Problems are less likely if withdrawal is slow, patient led and well supported.
- A benzodiazepine can be withdrawn in steps of about one-tenth of the daily dose every one to two weeks. Some long term benzodiazepine patients may benefit from transferring to an equivalent dose of diazepam in order to taper down their dose reducing by 1-2mg every 2-4 weeks. A suggested withdrawal protocol for patients who have difficulty is described in the BNF<sup>1</sup>.
- **Consider seeking specialist advice from Turning Point for people with:**
  - A history of drug use or dependence.



- A history of drug withdrawal seizures — these generally occur in people who suddenly stop high doses of the drugs. Slow tapering is recommended for these individuals<sup>2</sup>.

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### **Education Resources for Clinicians**

- The MHRA benzodiazepine training module  
<http://www.mhra.gov.uk/ConferencesLearningCentre/LearningCentre/Medicineslearningmodules/Reducingmedicinerisk/Benzodiazepineslearningmodule/index.htm>
- Clinical Knowledge Summaries - Information on how to manage patients on benzodiazepines including managing withdrawal  
<http://cks.nice.org.uk/benzodiazepine-and-z-drug-withdrawal>
- National Prescribing Centre - Summary of benzodiazepines and new hypnotics  
[http://filesdown.esecure.co.uk/NorthLancsPCT/MeRec\\_Bull\\_15\\_5\\_.pdf\\_07012011-1137-24.pdf](http://filesdown.esecure.co.uk/NorthLancsPCT/MeRec_Bull_15_5_.pdf_07012011-1137-24.pdf)
- Information from the Royal College of Psychiatrists on anxiety, insomnia etc for patients that may be useful in practice  
<http://www.rcpsych.ac.uk/expertadvice/problemsdisorders.aspx>
- Training module from BMJ – Benzodiazepine dependence: an update on management  
<http://n3.learning.bmj.com/learning/search-result.html?moduleId=6059529>

### **References:**

1. British Medical Association and Royal Pharmaceutical Society. British National Formulary (BNF) 70, September 2015.
2. NICE clinical knowledge summaries. Insomnia and Benzodiazepine and z-drug withdrawal. Both topics last revised April 2015.
3. NICE TA77: Insomnia – newer hypnotic drugs. December 2005 (2)
4. Medicines and Healthcare products Regulatory Agency. Benzodiazepine learning module. April 2013
5. NICE CG113: Anxiety. January 2011
6. Committee on safety of medicines. Benzodiazepines, dependence and withdrawal symptoms. January 1988
7. Department of Transport, UK Government. Drugs and Driving, the law <https://www.gov.uk/drug-driving-law> Updated 4/8/2015 Accessed 15/3/201



## Good Sleep Guide

- ✓ Sleep duration varies from day to day. Try not to worry about sleeping.
- ✓ Establish fixed times for going to bed and waking up; avoid sleeping in after a poor night's sleep and avoid daytime naps.
- ✓ Try to relax before going to bed and avoid anything mentally demanding within 30 minutes of bedtime.
- ✓ Do not watch television or use any back lit device e.g. tablets and phones for an hour before trying to go to sleep. The use of non-backlit e-readers and paper books is not thought to adversely affect sleep.
- ✓ Take regular exercise throughout the day but avoid strenuous exercise within four hours of bedtime.
- ✓ Avoid caffeine, nicotine, and alcohol within 6 hours of going to bed (consider complete elimination of caffeine from the diet). Caffeine and nicotine are stimulants which could keep you awake.
- ✓ Do not eat a heavy meal before bedtime.
- ✓ Create a bedtime routine to help set your body up for a restful night (take a warm bath, read a book, listen to soft music).
- ✓ If you have problems getting off to sleep have a mug of warm milk, Horlicks, Ovaltine or herbal tea.
- ✓ The bedroom should be dark, quiet and a relaxing place. The room should be not too hot or cold<sup>2</sup>.
- ✓ Refrain from using the bedroom to eat or perform any work related activities, using it only for sleep.
- ✓ If after 30 minutes you cannot get to sleep, get up and go into another room and try to do something else (light reading or listening to relaxing music) until you feel sleepy, then go back to bed.
- ✓ Avoid taking over the counter sleep aids, as although they may help in short term use, they do not help the underlying problem causing disturbed sleep.
- ✓ A good sleep pattern may take weeks to establish, but it can be achieved.





## Information leaflet for patients on benzodiazepines and Z-drugs

### **What are benzodiazepines and Z drugs?**

#### Benzodiazepines

- Benzodiazepines are a group of medicines that are sometimes prescribed for anxiety, sleeping problems and other disorders. Examples include: diazepam, lorazepam, chlordiazepoxide, oxazepam, temazepam, nitrazepam, loprazolam, lormetazepam, clobazam and clonazepam.

#### Z drugs

- The medicines zaleplon, zolpidem and zopiclone are commonly called Z drugs. Z drugs act in a similar way to benzodiazepines. They are sometimes prescribed short term for insomnia.

### **How do benzodiazepines and Z-drugs work?**

- Benzodiazepines and Z-drugs work by decreasing the excitability of brain cells. This has a calming effect on various functions of the brain.

### **How long should these drugs be taken for?**

- Benzodiazepines and Z-drugs should only be taken for a short period of time (2 – 4 weeks). If taken for longer than a few weeks, various problems and side effects may occur.
- Your doctor will need to review you on a weekly basis and will only give you a very short supply of these drugs.

### **What are the side effects of benzodiazepines and Z-drugs**

- Tolerance – if taken for longer than a few weeks, the body and brain become used to the benzodiazepine or Z drug. The medicine then gradually loses its effect. You then need a higher dose for it to work. In time, the higher dose does not work and you need an even higher dose and so on until the risks outweigh the benefit of taking the medicine.
- Dependence (addiction) – there is a good chance that you will become dependent on a benzodiazepine or Z drug if you take it for more than four weeks. This means that withdrawal symptoms occur if the tablets are stopped suddenly. In effect, you need the medicine to feel normal. Common withdrawal symptoms include insomnia, anxiety, irritability, restlessness, agitation, depression, and tremor. Some symptoms may be similar to the initial problem so it is important they are not taken for long periods of time to avoid confusion.
- Other side effects include drowsiness and lightheadness the next day; confusion; accidents and falls; memory loss; low mood and insomnia.

### **What should you do if you have been taking a benzodiazepine or Z drug for a long time?**

- Some people who have been taking a benzodiazepine or Z drug for a long time believe that the medicine is still helping to ease anxiety or sleeping problems. However, in fact, in many people the medicine is just preventing withdrawal symptoms.
- If you have been taking a benzodiazepine or Z drug for over four weeks and want to come off it, you should discuss it with your GP. You should not stop taking your benzodiazepine or Z-drug without first seeking advice from your GP.
- Some people can stop taking benzodiazepines or Z drugs with little difficulty. However, some people develop withdrawal symptoms if they suddenly stop taking a benzodiazepine or Z drug. To keep withdrawal effects to a minimum, it is best to reduce the dose of the medicine gradually over a number of weeks or months before finally stopping it. Your doctor will advise on dosages and time scale, as this will be individual to each patient.



You can find more information on these medicines at:

<http://www.choiceandmedication.org/nsft/pages/drugslistedbycategory/>  
<http://www.rcpsych.ac.uk/expertadvice/treatmentwellbeing/benzodiazepines.aspx>  
<http://www.nhs.uk/Conditions/Insomnia/Pages/Prevention.aspx>  
<http://www.nhs.uk/Conditions/Anxiety/Pages/Treatment.aspx>