East London NHS Foundation Trust

# Benzodiazepine and Hypnotic Guidelines

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# Benzodiazepine and Hypnotics Guidelines

## Contents

# Benzodiazepine and Hypnotics Guidelines

## 1. Introduction

**1.1** Benzodiazepines are used to treat a wide variety of disorders, including sleep disorders, anxiety disorders, epilepsy, manic episodes, and symptoms of alcohol withdrawal, rapid tranquilisation and depression. Both benzodiazepines and hypnotics are useful pharmacological agents to alleviate the accompanied symptoms. However, in most cases, they are indicated for short term use only (two to four weeks) in the management of anxiety and insomnia and when used appropriately, do not present any problems to the patient. Nevertheless, use is not always appropriate and when used for longer duration it may lead to the development of physical and psychological dependence. There may be occasions, however, where, long term use is justified. For example, in patients whose quality of life is much improved with a benzodiazepine, where withdrawal causes severe distress and in patients with epilepsy or spasticity.

**1.2** The Committee on Safety of Medicines (CSM) completed a review and published guidance in 1988 for the appropriate use of benzodiazepines as anxiolytics or hypnotics because of concerns over dependence and tolerance. This was followed up by various other national drivers to promote best practice in the use of these drugs.

Refer to appendix 1 for the summary of national guidance for prescribing benzodiazepines and Z drugs.

## 2. Purpose

2.1 This guideline has been produced to help promote best practice on the use of benzodiazepines and z-drugs. Long term users should also be reviewed in accordance with their individual needs with help and social support provided to those who may want to discontinue benzodiazepines or the z-drugs. When patients are discharged on benzodiazepines and hypnotics, documentation should be made in the medical notes to that effect and General Practitioners (GPs) should be informed about this decision inclusive of a management care plan for individual patients. This guideline is not addressing the use of benzodiazepines for the management of alcohol withdrawal.

## 3. Duties

### *3.1 Prescribers*

3.1.1 Ensure that all benzodiazepines and z-drugs are prescribed appropriately and reviewed in line with this guideline.
3.1.2 All benzodiazepines and hypnotics should be reviewed on a weekly basis with clear documentation in the medical notes.
3.1.3 At discharge if benzodiazepines or hypnotics are continued, a clear management plan should be in place for GPs.
3.1.4 Appropriate monitoring should be in place when patients are prescribed high doses of benzodiazepines and when such patients have a respiratory illness (e.g. asthma). Use with caution in those with liver impairment and those with alcohol dependence or illicit drug use.
3.1.6 If duty doctor is called for prescription of a hypnotic then it should be prescribed on the 'Once Only Medication Section' of the prescription chart with endorsement 'For Review by Ward Doctor' as soon as possible and nursing staff made aware of this.
3.1.7 As with all new prescriptions of medicines, please note any consent to treatment directions.

### *3.2 Pharmacists*

3.2.1 Ensure that all benzodiazepine and z-drugs prescriptions are appropriate and they are reviewed in line with this guideline.
3.2.2 Ensure that there is a management and review plan for any benzodiazepines and z hypnotics prescribed on discharge.

### *3.3 Nurses*

3.3.1 Ensure that prescribed benzodiazepines and z-drugs are administered in accordance with this guideline.
3.3.2 Patients are encouraged to use relaxation techniques and to avoid stimulants before administration of hypnotics.
3.3.3 A sleep chart is considered and completed for all patients complaining of sleep difficulties and this should be discussed with the ward doctor and at ward rounds.
3.3.4 Physical health should be monitored when patients suffer from a respiratory illness; respiratory rate and signs of excess sedation.
3.3.5 The ward doctor should be informed at the earliest opportunity if the duty doctor was called to prescribe a benzodiazepine or Z-drug.

## 4 Benzodiazepine and Z Hypnotic Withdrawal

**4.1** Withdrawal of benzodiazepines after long term use should be approached cautiously, especially in patients with the following diagnoses;

- Patients with long standing sleep disorder
- Patients suffering from psychosis or mood disorder
- Patients with epilepsy who may be at greater risk of suffering from withdrawal seizures
- Elderly patients with physical problems

**4.2** The patient should be fully involved in the benzodiazepine withdrawal programme with appropriate provision of information and clear explanation about the withdrawal syndrome and, expectations as failures are more likely if inadequate information is provided with a fast reduction regime.

**4.3** Patients who have taken benzodiazepines for a long time may require a longer period during which doses are reduced. These patients should be carefully assessed as in some cases underlying symptoms may emerge which would require appropriate intervention.

**4.4** Those patients with more complex problems who have benzodiazepine dependence should be considered for referral to the local Special Substance Misuse Team for more specialist advice and support. Benzodiazepines may be used when necessary and for short periods of time in opiate withdrawal to relieve anxiety and agitation. If a hypnotic is required during the detoxification stage then a non benzodiazepine agent should be used on an 'as required basis' for a short period of time.

**4.5** Reassurance and relaxation advice should be offered to help with withdrawal symptoms. It is worth considering alternative interventions which might be helpful such as anxiety management, cognitive treatments or group therapy. It may also be helpful to provide information about appropriate support groups or alternative therapies such as aromatherapy, meditation and yoga or massage. The basic principles of sleep hygiene should be promoted.

**4.6** Benzodiazepines should never be stopped abruptly but should be reduced gradually over time depending on individual requirements because it may cause confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens. Note that barbiturates have no place in current usual practice, although rarely patients on long term barbiturates may be admitted/be in contact with services and like long term benzodiazepines this should not be suddenly stopped.

**4.7** 40% of patients on a benzodiazepine withdrawal programme will experience physical withdrawal symptoms and it is difficult to establish which patients will be affected. The withdrawal syndrome may occur within a few hours in the case of short acting ones and can develop at any time up to 3 weeks after stopping a long acting benzodiazepine. Sometimes withdrawal symptoms may not appear until several reductions have been made in which case it might be wise to adopt a slower withdrawal programme. Refer to Appendix 3 for withdrawal symptoms.

**4.8** Some patients may increase their alcohol consumption during a period of withdrawal and this should be monitored during the benzodiazepine reduction period. Depression is also common during the withdrawal programme and such patients should be assessed for depressive symptoms, with an antidepressant being prescribed if necessary.

### 4.9 Suggested Reduction Programme for those on long term Benzodiazepines

- Transfer the dose of the specific benzodiazepine to an approximate equivalent dose of diazepam, preferably at night, which is then gradually reduced according to the individual's needs, dependent on duration of use of the benzodiazepine.

Refer to Appendix 2 for benzodiazepine approximate equivalent doses.

- Reduce the dose by one-eighth (range one-tenth to one quarter) of the dose every 2 weeks and preferably give as divided doses.

- If withdrawal symptoms occur consider maintaining the patient on the same dose and adopt a slower pace of reduction.

- Reduce the dose further in smaller fortnightly steps, preferably to reduce more slowly than too quickly.

- Stop completely: this may vary from 4 weeks to a year or more, after initiating the reduction, again depending on individuals.

Refer to Appendix 3 for withdrawal symptoms.

## 5 Withdrawal from Long Term Hypnotics

5.1 Reduce medication using weekly steps of smallest dose i.e zopiclone reduce by 3.75mg per week.

5.2 Monitor individual patient response, and if not tolerated reduce the dose slowly.

5.3 For some patients immediate withdrawal may be appropriate.

## 6 Recommendations for in-patient use of benzodiazepines

6.1.1 New benzodiazepine should only be prescribed for short term relief (and reviewed within four weeks) of severe anxiety, insomnia and aggression.

6.1.2 Use should be documented in the notes with a clear management plan for review and duration of therapy.

6.1.3 For 'as required benzodiazepines', the prescriber must endorse the following;

- indication for use

- clarify when to use
- state a maximum dose

6.1.4 Documentation should be made in the notes that the patient has been informed about advice on non-drug therapies for anxiety or insomnia.

6.1.5 Records should show that the patient has been given appropriate advice

- about the risks of benzodiazepine use i.e. potential risks of sedation
- and decreased ability to drive safely,
- including the potential for dependence.

6.1.6 All prescriptions whether regular or when required should be regularly reviewed at weekly ward rounds and continued use should be clearly documented in notes.

6.1.7 All 'as required' prescriptions should be cancelled if not used in the past weeks except PICU patients where needs are different. Pharmacists can cancel such prescriptions after discussion with the ward doctor.

6.1.8 In those who are over 65, the benzodiazepine of choice is lorazepam due to fewer incidents of hangover effects, ataxia and falls associated with its use compared to diazepam. However, the dose should be reduced compared to the adult dose. Diazepam may be indicated in some patients.

6.1.9 Patients should be issued with leaflets regarding the specific benzodiazepine or hypnotic and the minimum effective dose should be prescribed.

6.2.1 Prior to discharge, prescriptions of benzodiazepines initiated by the hospital should be reviewed and cancelled where possible, and GPs informed about the plan supported by the consultant psychiatrist if patients are discharged on benzodiazepines. This should also be recorded in the discharge liaison form.

6.2.2 For those patients admitted on benzodiazepines, withdrawal should be considered after discussion with the patient. This should be done in a planned, stepwise manner under supervision with mental state examination and advice provided to the GP about the withdrawal programme put in place.

6.2.3 In patients with a diagnosis of Borderline Personality Disorder, caution should be used with benzodiazepines which, if essential, can be used for a short period of time as supported by Marsha Linehans DBT protocol for borderline patients in crisis with severe agitation/anxiety.

6.2.4 Administer with caution to elderly or debilitated patients and those with liver disease. Also when taken in combination with other drugs with CNS effects as excessive sedation can cause confusion and disorientation specially in the over 65 years old.

6.2.5 In case of benzodiazepine high dose adverse effects (respiratory depression, excess sedation) manage with flumazenil injection (a benzodiazepine antagonist) which reverses the hypnotic/sedative effects of benzodiazepines. This may have to be repeated due to the short duration action of flumazenil.

## 7 Inpatient Treatment of Insomnia

7.1 Insomnia is a distressing symptom which, if untreated can lead to sleep deficit problems such as memory problems, lack of concentration and can affect normal function and quality of life. Short term use of hypnotics is useful and can help restore sleep and normal functioning. However, tolerance and dependence is likely if patients continue treatment with hypnotics for longer than a few weeks. Non-pharmacological measures should be tried in the first instance;

- Advice on good sleep hygiene,
- Relaxation techniques,
- Avoidance of day time naps,
- Avoidance of caffeine drinks, nicotine, alcohol, heavy exercise and heavy meals in the evenings,
- Reassurance should be given about sleep, i.e. in elderly people the need for sleep decreases with age.

7.2 Hypnotics for short term insomnia should not be given for more than three weeks: intermittent use is advisable with omission of some doses. There is now evidence to suggest that the use of zopiclone and anxiolytic benzodiazepines are associated with an increased risk of road traffic accidents.

7.3 The Z drugs were developed to avoid the disadvantages associated with benzodiazepines (e.g. hangover effect the next day, sedation, dependence, withdrawal) although these benefits have not been clearly shown. Zopiclone, and zolpidem are available for use with zopiclone being the most widely prescribed hypnotic within the Trust.

7.4 Temazepam and nitrazepam are also licensed as hypnotics but are now rarely used. Temazepam is a controlled drug and increases nurses' administration documentation. Refer to the Medicines Policy on administration of Controlled Drugs.

7.5 Sedative antihistamines can sometimes be used on a short term basis only i.e. promethazine, but this can cause hangover drowsiness the next day.

## 8 Recommendations for Inpatient Hypnotic Prescribing

8.1 Patients should not be routinely prescribed a hypnotic on admission this should only be done if considered essential.

8.2 The lowest possible dose should be prescribed in the 'as required' prescription with a clear indication for use and this should be limited to a short time (7 days) and not exceed 4 weeks due to the potential of dependence and tolerance.

8.3 Alternate night dosing can be considered as patients tend to sleep better. It is advisable to endorse the prescription with this statement.

8.4 Those admitted on hypnotics should continue on them as abrupt cessation can lead to withdrawal problems, but reviewed as soon as possible. The prescription should be endorsed to state 'Long Term Use'.

8.5 Patients who do not respond to one hypnotic, should not be prescribed any of the others unless an adverse effect has occurred that is directly related to a specific hypnotic.

8.6 All hypnotics should be used within their licensed therapeutic indications and doses. Doses above the BNF recommended dose would be queried by pharmacy staff and authorised by Consultants.

8.7 Antipsychotics should not be routinely prescribed as alternatives to hypnotics as this is an off label use.

8.8 The reason for prescribing a hypnotic should be documented in the notes and hypnotics should not be given routinely at 22.00hrs together with other sedative medication. The patient should be allowed to fall asleep as naturally as possible and if unable to sleep then a hypnotic can be given.

8.9 Hypnotics should be regularly reviewed at weekly ward rounds with a view to stop as soon as possible. If no doses are administered in the past week, the prescription can be cancelled by the pharmacist after consultation with ward doctor. Principles of good sleep hygiene should be discussed at the earliest opportunity. See the link below for patient information on sleep problems.
If the duty doctor is called out to prescribe a hypnotic, this should be done on the '***Once Only Medication Section'*** and this should be reviewed by the ward doctor as soon as possible.
http://www.rcpsych.ac.uk/mentalhealthinfoforall/problems/sleepproblems/sleepingwell.aspx

## 9 Hypnotic Prescribing at Discharge

9.1 Hypnotic use should be reviewed prior to discharge and no patients should be discharged on it unless

- The patient is on it long term or
- The consultant psychiatrist supports such use with documentation in the notes with justification for long term use and
- With clear instructions for the GP to continue/discontinue over a planned period of time.

9.2 The cheapest hypnotic should be prescribed as there does not seem to be any compelling evidence to suggest any clinically useful difference between the Z drugs in line with NICE guidelines 2004 on use of hypnotics.

**Table 2 Monthly cost of Hypnotics**

| **Drug** | **Pack Size** | **Monthly Cost (BNF No 59-March 2010)** |
|---|---|---|
| Zopiclone 7.5mg | 28 | £1.52 |
| Zopiclone 3.75mg | 28 | £1.52 |
| Zolpidem 5mg (Elderly dose) | 28 | £1.63 |
| Zolpidem 10mg | 28 | £1.72 |
| Nitrazepam 5mg | 28 | £1.00 |
| Temazepam 10mg | 28 | £4.88 |
| Temazepam 20mg | 28 | £2.77 |

9.3 The prescriber should endorse the prescription with the indication for use i.e. insomnia.

9.4 The duration of the treatment should be specified.

9.5 A dose range should not be specified, if a dose range is specified then the minimum number of dose units will be supplied by pharmacy team in line with inpatient use.

## 10 Benzodiazepines in Pregnancy

10.1 Benzodiazepines and metabolites freely cross the placenta and accumulate in fetal circulation.

10.2 It is advisable to avoid use in the first trimester because of risks of teratogenicity (association with incidence of cleft palate).

10.3 High doses or prolonged use by the mother in the third trimester may precipitate fetal benzodiazepine syndrome including floppy infant syndrome, impaired temperature regulation and withdrawal symptoms in the newborn.

10.4 In cases of severe anxiety, low-dose chlorpromazine may be considered as an alternative to benzodiazepine, for which it is advisable to seek specialist advice.

## 11 Benzodiazepines in Lactation

11.1 Benzodiazepines are excreted in breast milk in levels sufficient to produce effects in the newborn, including sedation, lethargy, and poor temperature regulation.

11.2 Metabolism in infants is slower especially during the first 6 weeks and long acting benzodiazepines can accumulate.

11.3 Use involves a risk benefit ratio and it would be advisable to contact specialist centres for advice. For further information contact the Medicine Information Department for the Trust on 0207 510 8295 or by email at medicinesinformation@eastlondon.nhs.uk

## 12. Hypnotics in Pregnancy and Lactation

12.1 The z-drugs should not be prescribed during pregnancy. General advice about sleep hygiene measures should be discussed. If a sedative drug is necessary to aid sleep then a sedating antihistamine (e.g. promethazine), a benzodiazepine or low dose chlorpromazine may be considered on a short term basis at the lowest possible dose.

12.2 Z-drugs are not recommended by manufacturers in lactation as small amounts are excreted in breast milk and use involves a risk benefit outcome.

## References:


1. BNF No 59, March 2010.
2. Benzodiazepines and newer hypnotics, MeReC Bulletin, No 5, Vol 15, April 2005.
3. National Institute for Clinical Excellence. Guidance on the use of zaleplon, zolpidem, and zopiclone for the short term management of insomnia. Technology Appraisal 77; April 2004.
4. National Service Framework Medicines and older people: implementing medicines related aspects of the NSF for older people. London: Department of Health, 2001.
5. Committee on Safety of Medicines. Benzodiazepines, dependence and withdrawal symptoms. Current Problems 1988;21:1-2.

6. Royal College of Psychiatrists. Benzodiazepines: risks, benefits or dependence: a re-evaluation. Council Report CR 59. London: Royal College of Psychiatrists; 1997.
7. Taylor D. et al. Maudsley Prescribing Guidelines 2009.
8. Schafaer C. et al. Drugs During Pregnancy and Lactation, Second Edition 2007.
9. Bezchlibnyk-Butler et al. Clinical Handbook of Psychotropic Drugs, 16th Edition 2006.
10. S.R.Onyett. The benzodiazepine withdrawal syndrome and its management. J of the Royal College of Practitioners, April 1989.
11. National Institute for Clinical Excellence. Guidelines on Antenatal and Postnatal Mental Health, April 2007.

Appendix 1

**Summary of Guidance for Prescribing Benzodiazepines and Z Drugs**

**1988 CSM Advice on Benzodiazepines**

***As Anxiolytics***

1. Benzodiazepines are indicated for the short- term relief (two to four weeks only) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short term psychosomatic, organic or psychotic illness.
2. The use of benzodiazepines to treat short term 'mild' anxiety is inappropriate and unsuitable.

***As Hypnotics***

1. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or subjecting the individual to extreme distress.

**1999 Mental Health NSF Guidance on Benzodiazepines**

1. Reinforced CSM advice recommending that benzodiazepines should be used for no more than two to four weeks for severe and disabling anxiety.
2. It also recommended for health authorities to have systems in place to monitor and review prescribing rates of benzodiazepines within the local clinical audit programme and PCT managers to implement this recommendation. Implementation of the CSM advice for benzodiazepines and NICE guidance relating to z drugs should remain a priority.

**2001 The NSF for Older People**

Advised on reducing prescribing for older people by encouraging them to discontinue benzodiazepines by provision of psychoeducation and support.

**2004 NICE Guidance on the use of Z Drugs**

1. It is recommended that hypnotics be prescribed for short periods of time only in accordance with their licensed indications after trials of non-pharmacological measures that have proved unsuccessful.
2. It is recommended that the drug with the lowest cost be used due to lack of compelling evidence to distinguish between zopiclone, zaleplon and zolpidem. This also applies to the shorter-acting benzodiazepine hypnotics; temazepam, lormetazepam and loprazolam.

3. It is recommended that switching from one of these hypnotics to another should only occur in the presence of adverse effects related directly to a specific agent.

**Appendix 2**

**Approximate Equivalent doses and General properties of most commonly used Benzodiazepines**

Approximate equivalent doses, Diazepam 5mg

| | |
|---|---|
| Lorazepam | 500 micrograms |
| Temazepam | 10mg |
| Chlordiazepoxide | 15mg |
| Nitrazepam | 5mg |
| Oxazepam | 15mg |
| Clonazepam | 250 micrograms |

BNF No 59
March 2010.

| | | Anxiolytic | Sedative/Hypnotic | Potency |
|---|---|---|---|---|
| **Short Acting** | Midazolam | + | +++ | |
| | Lorazepam | +++ | ++ | High |
| | Oxazepam | ++ | + | Low |
| | Temazepam | + | +++ | Low |
| **Long-Acting** | Chlordiazepoxide | ++ | | Low |
| | Nitrazepam | + | +++ | - |
| | Clonazepam | ++ | + | High |

**Activity:**

Weak: +
Moderate: ++
Strong: +++

Bezchlibnyk-Butler et al. Clinical Handbook of Psychotropic Drugs, 16th Edition 2006.

**Appendix 3**

**Benzodiazepines with Anxiolytic and Hypnotic Properties/ Z Drugs**

| | Benzodiazepines | Z Drugs |
|---|---|---|
| Hypnotics | Nitrazepam<br>Temazepam<br>Loprazolam<br>Lormetazepam<br>Flurazepam | Zopiclone<br>Zolpidem<br>Zaleplon |
| Anxiolytics | Diazepam<br>Lorazepam<br>Alprazolam<br>Chlordiazepoxide<br>Oxazepam | |

BNF No 59, 2010

**Benzodiazepine Withdrawal Symptoms**

| | |
|---|---|
| Anxiety Symptoms | Anxiety<br>Apprehension<br>Tremor<br>Sweating<br>Insomnia |
| Psychological Symptoms | Depersonalisation<br>Depression<br>Perceptual distortions<br>Abnormal body sensations (i.e. crawling in the skin)<br>Abnormal sensations of movement<br>Hypersensitivity to stimuli ( i.e. photophobia |
| Somatic Symptoms | Ataxia ( unsteady gait)<br>Pain (headache)<br>Paraesthesia, i.e. pins and needles<br>Flu-like symptoms<br>Gastro-intestinal symptoms |
| Major Complications | Seizures<br>Psychosis<br>Delirium<br>Confusional States |

Onyett S.R. The Benzodiazepine withdrawal syndrome and its management. J of the Royal College of GPs, April 1989.

# Appendix 4

# Patient Information Leaflet

# Non Drug Methods to Help You Sleep:

1. The duration of sleep varies from day to day. Do not worry as you are bound to feel anxious the more you worry and this will make it harder for you to fall asleep.

2. If you have problems getting to sleep, try and relax, have a cup of warm milk or herbal tea, read a book, or listen to soothing music.

3. Avoid strenuous exercise just before you go to bed. Instead try relaxation techniques i.e. muscle relaxation exercises or yoga which can be helpful to reduce anxiety and to promote sleep.

4. Avoid caffeine-containing drinks (tea and coffee) or foods i.e. chocolates late in the evening, and heavy meals just before bedtime.

5. Avoid cigarette smoking late in the evening or if you are in bed and cannot sleep as this will make it more difficult for you to sleep because nicotine interferes with sleep as it is a stimulant.

6. Your bedroom should be comfortable, not too hot or cold, and you should not have a television in the bedroom as this can stimulate your brain and keep you awake.

7. Keep the bedroom as dark as possible if external light disturbs your sleep, and turn lights off before sleep.

8. Ensure you have a routine for sleeping and waking up.

9. Avoid sleeping during the day as this will make it difficult for you to sleep at night except when you are not too well i.e. suffering from flu or cold.

## Appendix 5

### Guidance on use of ‘As required Benzodiazepines and Hypnotics’ for Nursing Staff

1. The ‘As Required’ section is a very useful aspect of patient care, however this is open to inappropriate drug administration.

2. Do not routinely offer night sedation to all patients, allow patients to fall asleep naturally.

3. Advise on good sleep hygiene before resorting to use of hypnotics.

4. If patient has already been prescribed a benzodiazepine on the regular section at night, this would aid sleep, do not offer a hypnotic at the same time even it this is prescribed on the ‘as necessary section’.

5. Discourage patients to have caffeine drinks or cigarettes late in the evening.

6. Talk to patients about addictive potential of hypnotics and benzodiazepines.

7. Consider completing a sleep chart for each patient having sleep difficulties.