### Benzodiazepine and z-drug withdrawal

Last revised in September 2018Next planned review by December 2023 Back to top

### Scenario: Benzodiazepine and z-drug withdrawal

From age 16 years onwards.

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How do I assess someone on long-term benzodiazepines or z-drugs?

Discuss with the person the potential <u>complications</u> of long-term benzodiazepine or z-drug use/benefits of stopping and enquire about their willingness to withdraw from the drug. If the person is willing:

- Assess whether this is a suitable time to stop taking the drugs.
  - The chances of success are improved when a person's physical and psychological health and personal circumstances are stable. In some circumstances it may be more appropriate to wait until other problems are resolved or improved before starting drug withdrawal.
  - Enquire about:
    - Symptoms of depression. Withdrawing these drugs can worsen symptoms
      of clinical depression. The priority is to manage depression first, before
      attempting drug withdrawal. For more information, see the CKS topic
      on <u>Depression</u>.
    - Symptoms of anxiety. Withdrawing treatment when significant symptoms of anxiety are present is likely to make symptoms worse and is therefore unlikely to succeed. However, when symptoms are reasonably well controlled and stable it may be possible to attempt careful drug withdrawal. For more information, see the CKS topic on Generalized anxiety disorder.
    - Symptoms of long-term insomnia. If insomnia is severe, consider addressing
      this with non-drug treatments prior to starting withdrawal of a
      benzodiazepine or z-drug. For more information, see the CKS topic
      on Insomnia.
    - Any medical problems and whether these are well controlled and stable. If problems are causing significant distress, consider managing these first, prior to starting withdrawal of benzodiazepines or z-drugs.
- Consider whether the withdrawal of the benzodiazepine or z-drug can be appropriately managed in primary care.
  - People are considered suitable if they:
    - Are willing, committed, and compliant, and have adequate social support.
    - Have no previous history of complicated drug withdrawal.
    - Can be reviewed regularly.

- Consider seeking specialist advice, or referral to an appropriate specialist for people with:
  - A history of alcohol or other drug use or dependence be aware that heavy users of alcohol may use it as a substitute for the drug being withdrawn.
  - Concurrent, severe medical or psychiatric disorder or personality disorder.
  - A history of drug withdrawal seizures these generally occur in people who suddenly stop high doses of the drugs. Slow tapering is recommended for these individuals.

### If the person is unwilling to stop taking a benzodiazepine or z-drug:

- Do not pressurize them to stop if they are not motivated to do so.
- Listen to the person, and address any concerns they have about stopping.
  - Explain that for most people who withdraw from treatment slowly, symptoms are mild and can usually be effectively managed by other means.
  - Reassure the person that they will be in control of the drug withdrawal and that they
    can proceed at a rate that suits them.
- Reiterate the benefits of stopping the drug.
  - The discussion should include an explanation of tolerance, adverse effects, and the risks of continuing the drug.
- Review at a later date if appropriate, and reassess the person's motivation to stop.
- In people who remain concerned about stopping treatment despite explanation and reassurance, persuading them to try a small reduction in dose may help them realize that their concerns are unfounded.

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#### **Basis for recommendation**

The recommendations on assessement of a person on long-term treatment with a benzodiazepine or z-drug are based on expert opinion contained within published reviews and guidelines on managing benzodiazepine and z-drug dependence [Lader and Russell, 1993; Mant and Walsh, 1997; Ashton, 2002a; Taylor et al, 2012; Ashton, 2013a; Ford and Law, 2014; All Wales Medicines Strategy Group, 2016] (Note: CKS has included this chronology of publications rather than replacing the older references, as the earlier original guidelines continue to form the basis of current guidance).

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#### How do I manage someone who wants to stop benzodiazepines or z-drugs?

For all people undergoing assisted withdrawal, provide resources such as patient
information leaflets, for example from the <u>Royal College of Psychiatrists</u> for
benzodiazepines, and <u>MIND</u> for z-drugs, in addition to information about local and
national support groups, a list of which can be found in the <u>Ashton Manual</u>.

- Note: the two potential approaches for withdrawal are slow dose reduction of the person's current benzodiazepine or z-drug, or switching to an approximately equivalent dose of diazepam, which is then tapered down.
- Switching to diazepam should be considered for:
  - People using the short-acting potent benzodiazepines (that is, alprazolam and lorazepam).
  - People using preparations that do not easily allow for small reductions in dose (that is alprazolam, flurazepam, loprazolam and lormetazepam).
  - People experiencing difficulty or who are likely to experience difficulty withdrawing directly from temazepam, nitrazepam, or z-drugs, due to a high degree of dependency (associated with long duration of treatment, high doses, and a history of anxiety problems).
  - Seek specialist advice (preferably from a hepatologist) before switching to diazepam in people with hepatic dysfunction as diazepam may accumulate to a toxic level in these individuals. An alternative benzodiazepine without active metabolites (such as oxazepam) may be preferred.
    - For information on switching to diazepam, including dose equivalences, see the section on <u>Switching to diazepam</u>.
- Upon dose reduction of the person's existing drug or diazepam, negotiate a
  flexible withdrawal schedule (dose tapering). Be guided by the person in making
  adjustments, so that they remain comfortable with the withdrawal.
  - Advise the person that:
    - Drug withdrawal should be gradual to minimize the risk of withdrawal effects.
    - With slow tapering, many people experience few or no withdrawal symptoms. If withdrawal symptoms are present, some users will have lost all their symptoms by the end of the drug withdrawal schedule. For most people, symptoms will disappear within a few months. Only a very small number of people will suffer from protracted withdrawal symptoms which will gradually improve over a year or longer. For more information, see the section on Prognosis.
    - Nearly all of the acute symptoms of withdrawal are those of anxiety.
    - Some of the withdrawal symptoms may be similar to the original complaint but do not indicate a return of this.
    - It is not possible to estimate the severity and duration of withdrawal symptoms as these will depend on a number of factors (such as severity of dependence and speed of withdrawal).
  - Offer reassurance that the person will be in control of the drug withdrawal and can proceed at a rate that suits them. Drug withdrawal may take 3 months to a year, or longer if necessary. Some people may be able to withdraw in less time.

- The rate of reduction should take into account the drug, dose and duration of treatment, as well as personal circumstances.
- Titrate the drug withdrawal according to the severity of withdrawal symptoms. If the person experiences difficulties with a dose reduction, encourage them to persevere and suggest delaying the next step down. Do not revert to a higher dosage. Make future dose reductions in smaller steps if necessary.
- Where available, and if considered necessary and appropriate, cognitive behavioural therapy (CBT) may be offered to help ameliorate withdrawal symptoms.
- Advise the person against taking extra tablets in times of stress and compensating for benzodiazepines or z-drugs by increasing the intake of alcohol or other drugs (prescription, non-prescription, or illicit drugs) or smoking.
- For information on specific withdrawal schedules, see the section on <u>Withdrawing</u>
   a benzodiazepine or z-drug.
- Remind the person of the DVLA regulations relating to benzodiazepine use and driving (note: use of a supratherapeutic dosage outside BNF guidelines constitutes persistent misuse or dependence for licensing purposes, whether in a programme of substance withdrawal or maintenance, or otherwise). The following advice should be given to people who take benzodiazepines:
  - You should not drive if you feel drowsy, dizzy, unable to concentrate or make decisions.
  - It is an offence to drive if you have more than a specified amount of benzodiazepine in your body whether your driving is impaired or not.
  - Roadside drug screening tests are in place in the UK. These test the saliva for drugs that impair driving. If you have a positive roadside drug test for benzodiazepines, the police may ask you to provide a blood sample to measure the amount of benzodiazepine in your body.
  - If you are found to have more than the specified amount of benzodiazepine, as long as your driving is not impaired, you are taking your medicine on the advice of your GP, or your pharmacist, you will be able to raise a 'statutory defence' and the police may not prosecute you.
  - It may be helpful to keep evidence with you while you are driving, that you are taking a benzodiazepine in accordance with medical advice. Suitable evidence may include: your medication box with the pharmacy label on, or the other half of your prescription with the list of medicines prescribed by your doctor.
- The DVLA provides no advice for people taking z-drugs.
- For more information, see <u>Assessing fitness to drive: a guide for medical</u> professionals available on the <u>DVLA website</u>.

 During the withdrawal process, review the person frequently (with exact intervals determined by clinical judgement) to detect and manage problems, and to provide advice and encouragement. At review:

### If anxiety is present:

- Explain that anxiety is the most common acute withdrawal symptom.
- Reassure that anxiety is likely to be temporary.
- Consider slowing or suspending withdrawal until symptoms become manageable.
- Consider recommending non-drug treatments including relaxation techniques (such as progressive muscular relaxation and controlled breathing techniques), or CBT if symptoms are severe or protracted. For more information, see the CKS topic on Generalized anxiety disorder.
- Adjunct drug therapy should not be routinely prescribed, but may be considered.
- Propranolol: for severe, physical symptoms of anxiety (such as palpitations, tremor, and sweating) only if other measures fail.
- Antidepressants: only if depression or panic disorder coexist or emerge during drug withdrawal.
- Do not prescribe antipsychotics which may aggravate withdrawal symptoms.
- Seek specialist advice if symptoms are severe and/or difficult to manage.

### o If depression emerges or coexists with withdrawal symptoms:

- See the CKS topic on <u>Depression</u> for further information on management.
- Consider suspending drug withdrawal until the depression resolves.

### If insomnia is present.

- Provide information on good sleep hygeine.
- For more information on management, see the CKS topic on Insomnia.

### . Be aware that stopping the last few milligrams is often seen as being particularly difficult:

- Reassure the person that this is usually an unfounded fear derived from long-term psychological dependence.
- Warn the person not to be tempted to prolong the drug withdrawal to an extremely slow rate towards the end (such as reducing by 0.25 mg diazepam each month).
   Advise the person to consider stopping completely when they reach an appropriate low dose (such as diazepam 1 mg daily).
- If the person did not succeed on their first attempt, encourage them to try again.
  - Remind the person that reducing benzodiazepine dosage, even if this falls short of complete drug withdrawal, can still be beneficial.

 If another attempt is considered, <u>reassess</u> the person, and treat any underlying problems (such as depression) before trying again.

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### How should I withdraw a benzodiazepine?

**Withdrawal should be gradual** (dose tapering, such as 5–10% reduction every 1–2 weeks, or an eighth of the dose fortnightly, with a slower reduction at lower doses), and titrated according to the severity of withdrawal symptoms.

These schedules are adapted from the Ashton Manual [Ashton, 2002b].

• Diazepam is available in a variety of strengths (2 mg, 5 mg, and 10 mg) and formulations (scored tablets or liquid) to facilitate dose reduction, particularly at lower doses.

#### Suggested withdrawal schedule for diazepam

- From diazepam 40 mg per day or less:
  - Reduce dose by 2–4 mg every 1–2 weeks until reaching 20 mg per day, then
  - o Reduce dose by 1–2 mg every 1–2 weeks until reaching 10 mg per day, then
  - o Reduce dose by 1 mg every 1–2 weeks until reaching 5 mg per day, then
  - o Reduce dose by 0.5–1 mg every 1–2 weeks until completely stopped.
- Estimated total withdrawal time:
  - o From diazepam 40 mg per day: 30–60 weeks.
  - o From diazepam 20 mg per day: 20–40 weeks.

# Suggested withdrawal schedules for temazepam, nitrazepam, and zopiclone without diazepam conversion

- From temazepam 20 mg daily or less:
  - o Reduce daily dose by a quarter of a 10 mg tablet (2.5 mg) every 2 weeks.
  - The target dose for when to stop is when the person is taking only a quarter of a 10 mg tablet as a daily dose.
  - If stopping is not possible at the target dose, offer temazepam liquid (10 mg/5 mL) and an oral syringe to achieve further reductions.
  - Estimated total withdrawal time: 16–20 weeks or longer.

### From nitrazepam 10 mg daily or less:

- o Reduce the daily dose by a quarter of a 5 mg tablet (1.25 mg) every 2 weeks.
- The target dose for when to stop is when the person is taking only a quarter of a
   5 mg tablet as a daily dose.
- o If stopping is not possible at the target dose, offer nitrazepam (2.5 mg/5 mL) liquid and an oral syringe to achieve further reductions.

o Estimated total withdrawal time: 16–20 weeks or longer.

### • From zopiclone 7.5 mg per day or less:

- o Reduce the daily dose by half of a 3.75 mg tablet (1.875 mg) every 2 weeks.
- The target dose for when to stop is when the person is taking only half of a 3.75 mg tablet.
- If stopping is not possible at the target dose, one option is to convert to diazepam to complete the withdrawal, although this is controversial.
- Estimated total withdrawal time: 16–20 weeks or longer.

For more information on withdrawal schedules for other benzodiazepines and z-drugs, see the <u>Ashton Manual</u> (available online at <u>www.benzo.org.uk</u>).

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#### **Basis for recommendation**

The recommendations on management of a person who wishes to withdraw from a benzodiazepine or z-drug are based on expert opinion contained within published reviews and guidelines on managing benzodiazepine and z-drug dependence [CSM, 1988; Lader and Russell, 1993; Mant and Walsh, 1997; Ashton, 2002a; Australian Government Department of Health and Ageing, 2004; Lader et al, 2009; Ashton, 2013b; Lingford-Hughes et al, 2012; Taylor et al, 2012; Ashton, 2013a; Ford and Law, 2014; All Wales Medicines Strategy Group, 2016; BNF 76, 2018] (Note: CKS has included this chronology of publications rather than replacing the older references, as the earlier guidelines continue to form the basis of current guidance).

### Gradual withdrawal of benzodiazepines and z-drugs

- Withdrawing benzodiazepines slowly is recommended to allow a smooth, gradual fall in the level of drugs in the blood, thus minimizing withdrawal symptoms [Ashton, 2005; Lader et al, 2009; Lingford-Hughes et al, 2012; BNF 75, 2018].
- Abrupt drug withdrawal (particularly following the use of high doses) can produce confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens [<u>Lader et al, 2009</u>;
   <u>Ford and Law, 2014</u>; All Wales Medicines Strategy Group, 2016; BNF 76, 2018].
- Gradual drug withdrawal is also recommended for people dependent on z-drugs as the
  manufacturers of these drugs warn that abrupt termination of treatment can lead to
  withdrawal symptoms, particularly in people taking high doses [ABPI, 2018a; ABPI, 2018b].
  Given that they work similarly to benzodiazepines, the same approaches have therefore
  been recommended for z-drug withdrawal [Ashton, 2002b].

### Switching to diazepam

- Switching to diazepam is recommended for some people particularly if they have difficulty withdrawing or if they are on short-acting, potent benzodiazepines [Ashton, 2002a; Ashton, 2005; Taylor et al, 2012; BNF 76, 2018].
- Diazepam is preferred because:

- It possesses a long half-life (20–100 hours), thus avoiding sharp fluctuations in plasma level.
- It is available in a variety of strengths and formulations. This facilitates stepwise
  dose substitution from other benzodiazepines or z-drugs and allows for small
  incremental reductions in dosage (especially at low doses).

### Time required for drug withdrawal

- Although some experts have recommended drug withdrawal over 8–12 weeks, or longer (such as 6 months) if the person has tried to stop before but failed [<u>Lader et al, 2009</u>], the time needed for drug withdrawal can vary from 4 weeks to a year or longer [<u>Ashton, 2002a</u>; <u>Ashton, 2005</u>; <u>BNF 76, 2018</u>].
- Consequently, no specific time frame has been recommended as drug withdrawal should be
  titrated according to the severity of withdrawal symptoms and individual preference.
   However, it is recommended that the person should be encouraged not to prolong the drug
  withdrawal to a slower rate towards the end [Ashton, 2002a; Lader et al, 2009].

### **Examples of drug withdrawal schedules**

- These are adapted from the Aston Manual [Ashton, 2002b]. This widely published manual was developed on the basis of clinical experience of managing people withdrawing from benzodiazepines and z-drugs in an English specialist clinic over a 12-year period.
- The drug withdrawal schedules are comparable to that recommended by the British National Formulary which suggests withdrawing in steps of about one-eighth (range one-tenth to one-quarter) of the daily dose every fortnight [BNF 76, 2018].

# Hypnotics and anxiolytics

## **Overview**

Most anxiolytics ('sedatives') will induce sleep when given at night and most hypnotics will sedate when given during the day. Prescribing of these drugs is widespread but dependence (both physical and psychological) and tolerance occur. This may lead to difficulty in withdrawing the drug after the patient has been taking it regularly for more than a few weeks. Hypnotics and anxiolytics should therefore be reserved for short courses to alleviate acute conditions after causal factors have been established.

Benzodiazepines are the most commonly used anxiolytics and hypnotics; they act at benzodiazepine receptors which are associated with gamma-aminobutyric acid (GABA) receptors. Older drugs such as <a href="mailto:meprobamate">meprobamate</a> and barbiturates are **not** recommended—they have more side-effects and interactions than benzodiazepines and are much more dangerous in overdosage.

## Benzodiazepine indications

- Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling, or causing the patient unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness.
- 2. The use of benzodiazepines to treat short-term 'mild' anxiety is inappropriate.
- 3. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or causing the patient extreme distress.

# Dependence and withdrawal

Withdrawal of a benzodiazepine should be gradual because abrupt withdrawal may produce confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens.

The benzodiazepine withdrawal syndrome may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine, but may occur within a day in the case of a short-acting one. It is characterised by insomnia, anxiety, loss of appetite and of body-weight, tremor, perspiration, tinnitus, and perceptual disturbances. Some symptoms may be similar to the original complaint and encourage further prescribing; some symptoms may continue for weeks or months after stopping benzodiazepines.

Benzodiazepine withdrawal should be flexible and carried out at a reduction rate that is tolerable for the patient. The rate should depend on the initial dose of benzodiazepine, duration of use, and the patient's clinical response. Short-term users of benzodiazepines (2–4 weeks only) 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.

A suggested protocol for withdrawal for prescribed long-term benzodiazepine patients is as follows:

- 1. Transfer patient stepwise, one dose at a time over about a week, to an equivalent daily dose of diazepam preferably taken at night.
- 2. Reduce diazepam dose, usually by 1–2 mg every 2–4 weeks (in patients taking high doses of benzodiazepines, initially it may be 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.
- 3. Reduce diazepam dose further, if necessary in smaller steps; steps of 500 micrograms may be appropriate towards the end of withdrawal. Then stop completely.
- 4. For long-term patients, the period needed for complete withdrawal may vary from several months to a year or more.

Approximate equivalent doses, diazepam 5 mg

- ≡ alprazolam 250 micrograms
- ≡ clobazam 10 mg
- ≡ clonazepam 250 micrograms
- $\equiv$  flurazepam 7.5–15 mg
- $\equiv$  chlordiazepoxide 12.5 mg
- $\equiv$  loprazolam 0.5–1 mg
- ≡ lorazepam 500 micrograms
- $\equiv$  lormetazepam 0.5–1 mg
- $\equiv$  nitrazepam 5 mg
- $\equiv$  oxazepam 10 mg
- $\equiv$  temazepam 10 mg

Withdrawal symptoms for long-term users usually resolve within 6–18 months of the last dose. Some patients will recover more quickly, others may take longer. 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.

# **Hypnotics**

Before a hypnotic is prescribed the cause of the insomnia should be established and, where possible, underlying factors should be treated. However, it should be noted that some patients have unrealistic sleep expectations, and others understate their alcohol consumption which is

often the cause of the insomnia. Short-acting hypnotics are preferable in patients with sleep onset insomnia, when sedation the following day is undesirable, or when prescribing for elderly patients. Long-acting hypnotics are indicated in patients with poor sleep maintenance (e.g. early morning waking) that causes daytime effects, when an anxiolytic effect is needed during the day, or when sedation the following day is acceptable.

*Transient insomnia* may occur in those who normally sleep well and may be due to extraneous factors such as noise, shift work, and jet lag. If a hypnotic is indicated one that is rapidly eliminated should be chosen, and only one or two doses should be given.

Short-term insomnia is usually related to an emotional problem or serious medical illness. It may last for a few weeks and may recur; a hypnotic can be useful but should not be given for more than three weeks (preferably only one week). Intermittent use is desirable with omission of some doses. A short-acting drug is usually appropriate.

Chronic insomnia is rarely benefited by hypnotics and is sometimes due to mild dependence caused by injudicious prescribing of hypnotics. Psychiatric disorders such as anxiety, depression, and abuse of drugs and alcohol are common causes. Sleep disturbance is very common in depressive illness and early wakening is often a useful pointer. The underlying psychiatric complaint should be treated, adapting the drug regimen to alleviate insomnia. For example, clomipramine hydrochloride or mirtazapine prescribed for depression will also help to promote sleep if taken at night. Other causes of insomnia include daytime cat-napping and physical causes such as pain, pruritus, and dyspnoea.

Hypnotics should **not** be prescribed indiscriminately and routine prescribing is undesirable. They should be reserved for short courses in the acutely distressed. Tolerance to their effects develops within 3 to 14 days of continuous use and long-term efficacy cannot be assured. A major drawback of long-term use is that withdrawal can cause rebound insomnia and a withdrawal syndrome.

Where prolonged administration is unavoidable hypnotics should be discontinued as soon as feasible and the patient warned that sleep may be disturbed for a few days before normal rhythm is re-established; broken sleep with vivid dreams may persist for several weeks.

## **Elderly**

Benzodiazepines and the Z-drugs should be avoided in the elderly, because the elderly are at greater risk of becoming ataxic and confused, leading to falls and injury.

## **Dental patients**

Some anxious patients may benefit from the use of hypnotics during dental procedures such as <u>temazepam</u> or <u>diazepam</u>. <u>Temazepam</u> is preferred when it is important to minimise any residual effect the following day.

## Benzodiazepines

Benzodiazepines used as hypnotics include <u>nitrazepam</u> and <u>flurazepam</u> which have a prolonged action and may give rise to residual effects on the following day; repeated doses tend to be cumulative.

<u>Loprazolam</u>, <u>lormetazepam</u>, and <u>temazepam</u> act for a shorter time and they have little or no hangover effect. Withdrawal phenomena are more common with the short-acting benzodiazepines.

If insomnia is associated with daytime anxiety then the use of a long-acting benzodiazepine anxiolytic such as <u>diazepam</u> given as a single dose at night may effectively treat both symptoms.

## Zolpidem, and zopiclone

Zolpidem tartrate and zopiclone are non-benzodiazepine hypnotics (sometimes referred to as Z-drugs), but they act at the benzodiazepine receptor. They are not licensed for long-term use; dependence has been reported in a small number of patients. Both zolpidem tartrate and zopiclone have a short duration of action.

### Chloral and derivatives

There is no convincing evidence that they are particularly useful in the elderly and their role as hypnotics is now very limited.

### Clomethiazole

<u>Clomethiazole</u> may be a useful hypnotic for elderly patients because of its freedom from hangover but, as with all hypnotics, routine administration is undesirable and dependence occurs.

### **Antihistamines**

Some **antihistamines** such as <u>promethazine hydrochloride</u> are on sale to the public for occasional insomnia; their prolonged duration of action can often cause drowsiness the following day. The sedative effect of antihistamines may diminish after a few days of continued treatment; antihistamines are associated with headache, psychomotor impairment and antimuscarinic effects.

### Alcohol

**Alcohol** is a poor hypnotic because the diuretic action interferes with sleep during the latter part of the night. Alcohol also disturbs sleep patterns, and so can worsen sleep disorders.

### Melatonin

<u>Melatonin</u> is a pineal hormone; it is licensed for the short-term treatment of insomnia in adults over 55 years.

# **Anxiolytics**

Benzodiazepine anxiolytics can be effective in alleviating anxiety states. Although these drugs are sometimes prescribed for stress-related symptoms, unhappiness, or minor physical disease, their use in such conditions is inappropriate. Benzodiazepine anxiolytics should not be used as sole treatment for chronic anxiety, and they are not appropriate for treating depression or chronic psychosis. In bereavement, psychological adjustment may be inhibited by benzodiazepines.

Anxiolytic benzodiazepine treatment should be limited to the lowest possible dose for the shortest possible time. Dependence is particularly likely in patients with a history of alcohol or drug abuse and in patients with marked personality disorders.

Some antidepressant drugs are licensed for use in anxiety and related disorders. Some antipsychotic drugs, in low doses, are also sometimes used in severe anxiety for their sedative action, but long-term use should be avoided because of the risk of adverse effects. The use of antihistamines (e.g. <a href="https://hydroxyzine.hydrochloride">hydroxyzine.hydrochloride</a>) for their sedative effect in anxiety is not appropriate.

**Beta-adrenoceptor blocking drugs** do not affect psychological symptoms of anxiety, such as worry, tension, and fear, but they do reduce autonomic symptoms, such as palpitation and tremor; they do not reduce non-autonomic symptoms, such as muscle tension. Beta-blockers are therefore indicated for patients with predominantly somatic symptoms; this, in turn, may prevent the onset of worry and fear.

## Benzodiazepines

**Benzodiazepines** are indicated for the *short-term relief of severe anxiety*; long-term use should be avoided. <u>Diazepam</u>, <u>alprazolam</u>, <u>chlordiazepoxide hydrochloride</u>, and <u>clobazam</u> have a sustained action. Shorter-acting compounds such as <u>lorazepam</u> and <u>oxazepam</u> may be preferred in patients with hepatic impairment but they carry a greater risk of withdrawal symptoms.

In *panic disorders* (with or without agoraphobia) resistant to antidepressant therapy, a benzodiazepine may be used; alternatively, a benzodiazepine may be used as short-term adjunctive therapy at the start of antidepressant treatment to prevent the initial worsening of symptoms.

<u>Diazepam</u> or <u>lorazepam</u> are very occasionally administered intravenously for the *control of panic attacks*. This route is the most rapid but the procedure is not without risk and should be used only when alternative measures have failed. The intramuscular route has no advantage over the oral route.

## **Buspirone**

<u>Buspirone hydrochloride</u> is thought to act at specific serotonin (5HT<sub>1A</sub>) receptors. Response to treatment may take up to 2 weeks. It does not alleviate the symptoms of benzodiazepine withdrawal. Therefore a patient taking a benzodiazepine still needs to have the

benzodiazepine withdrawn gradually; it is advisable to do this before starting <u>buspirone</u> <u>hydrochloride</u>. The dependence and abuse potential of <u>buspirone hydrochloride</u> is low; it is, however, licensed for short-term use only (but specialists occasionally use it for several months).

## Meprobamate

<u>Meprobamate</u> is **less effective** than the benzodiazepines, more hazardous in overdosage, and can also induce dependence. It is **not** recommended.

## **Barbiturates**

The intermediate-acting **barbiturates** have a place only in the treatment of severe intractable insomnia in patients **already taking** barbiturates; they should be **avoided** in the elderly. Intermediate-acting barbiturate preparations containing amobarbital sodium, butobarbital, and secobarbital sodium are available on a named patient basis.

The long-acting barbiturate phenobarbital is still sometimes of value in epilepsy but its use as a sedative is unjustified.

The very short-acting barbiturate thiopental sodium is used in anaesthesia.

Increased hostility and aggression after barbiturates and alcohol usually indicates intoxication.

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### Related drugs

- ALPRAZOLAM
- BUSPIRONE HYDROCHLORIDE
- CHLORDIAZEPOXIDE HYDROCHLORIDE
- CLOBAZAM
- CLOMETHIAZOLE
- CLOMIPRAMINE HYDROCHLORIDE
- DIAZEPAM
- FLURAZEPAM
- HYDROXYZINE HYDROCHLORIDE
- LOPRAZOLAM
- LORAZEPAM
- <u>LORMETAZEPAM</u>
- MELATONIN
- MEPROBAMATE
- MIRTAZAPINE
- <u>NITRAZEPAM</u>
- OXAZEPAM
- PROMETHAZINE HYDROCHLORIDE
- TEMAZEPAM

- THIOPENTAL SODIUM
- ZOLPIDEM TARTRATE
- ZOPICLONE