https://cks.nice.org.uk/benzodiazepine-and-z-drug-withdrawal#!scenario

Benzodiazepine and z-drug withdrawal

Last revised in January 2019 Next planned review by December 2023

Scenario: Benzodiazepine and z-drug withdrawal
From age 16 years onwards.

How do I assess someone on long-term benzodiazepines or z-drugs?
Discuss with the person the potential complications 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 Depression.
    - **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.

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).

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 Royal College of Psychiatrists for benzodiazepines, and MIND for z-drugs, in addition to information about local and national support groups, a list of which can be found in the Ashton Manual.
- 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 Switching to diazepam.
- 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 Withdrawing 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 Assessing fitness to drive: a guide for medical professionals available on the DVLA website.
- 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.
    - If depression emerges or coexists with withdrawal symptoms:
        - See the CKS topic on Depression 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, reassess the person, and treat any underlying problems (such as depression) before trying again.

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

    - Estimated total withdrawal time: 16–20 weeks or longer.
- From zopiclone 7.5 mg per day or less:
    - 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 Ashton Manual (available online at www.benzo.org.uk).

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 [Lader et al, 2009; Ford and Law, 2014; 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 [Lader et al, 2009], the time needed for drug withdrawal can vary from 4 weeks to a year or longer [Ashton, 2002a; Ashton, 2005; BNF 76, 2018].
- 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].
- The drug manufacturer advises that treatment should not exceed 4 weeks including the period of tapering off [ABPI, 2019].

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].