



PATIENTS TAKING HYPNOTIC AND ANXIOLYTIC DRUGS

Top tips for MURs

- Advise patients with anxiety or insomnia that benzodiazepine treatment should usually only be used for two to four weeks
- Advise patients that benzodiazepines and z-drugs may cause tolerance and dependence
- Advise patients with insomnia to consider keeping a sleep diary and those with anxiety an anxiety diary
- Advise patients that alcohol and caffeine may keep them awake at night
- Counsel patient on signs and symptoms of complications that need referral (**see red flags overleaf**) and common side effects (**see overleaf**)
- Check that patients on beta blockers have annual heart rate and blood pressure checks
- Advise patients on benzodiazepines that they should not stop taking them without first seeking the advice of their doctor due to the risk of withdrawal symptoms
- Check that patients have had liver function tests
- Counsel patients taking Zaleplon that if they wake during the night they should not take a second dose
- Counsel patient that hypnotics and anxiolytics affect performance of skilled tasks (e.g. driving). Hangover effects of a night dose may persist the following day.
- Advise that alcohol can increase the sedative effects of benzodiazepines and z-drugs and should be avoided
- Report any relevant adverse drug reactions to the Yellow Card Scheme

What are hypnotics and anxiolytics used for?

Anxiolytics are used to treat generalised anxiety disorder (GAD), panic disorders (with or without agoraphobia), post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, specific phobias and acute stress disorder. Anxiety disorders can exist in isolation but more commonly occur with other anxiety and depressive disorders. Hypnotics are used to treat insomnia which is characterised by difficulty initiating or maintaining sleep. Benzodiazepine anxiolytics are only indicated for the short-term (2-4 weeks) treatment of severe anxiety; benzodiazepine and z-drug hypnotics are only indicated for the short-term (2-4 weeks) treatment of insomnia.

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patients on healthy eating, exercise & weight loss (if BMI > 25kg/m²) - reduce saturated fat and salt intake, avoid salt substitutes, increase oily fish intake, complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Counsel patient on good sleep hygiene techniques. Recommend 7 to 9 hours sleep each night
- Advise patients who smoke of the benefits of stopping smoking and refer to Stop Smoking Wales or Pharmacy Stop Smoking services if willing to stop

How do hypnotic and anxiolytic drugs work?

Benzodiazepines	Potentiate the effect of the inhibitory neurotransmitter GABA at the GABA _A receptor, therefore improving sleep and relieving anxiety. Benzodiazepines are differentiated by their durations of action. Long acting hypnotics e.g nitrazepam can cause next day drowsiness. Short acting drugs e.g lorazepam are associated with greater problems during withdrawal.
Z-drugs (Zaleplon, Zopiclone & Zolpidem)	Modulate the GABA _A – benzodiazepine receptor complex, to improve sleep. Zolpidem and zaleplon have some selectivity for the type 1 receptor.
Melatonin	A hormone secreted by the pineal gland involved in regulating circadian rhythms in humans.
Antihistamines (e.g promethazine)	Antagonise histamine H ₁ -receptors resulting in sedation. May also antagonise dopaminergic, muscarinic and α-adrenergic receptors.
Beta blockers (usually propranolol)	Antagonism of beta adrenergic receptors reduces autonomic symptoms of anxiety, such as palpitation, sweating and tremor.
Buspirone	A 5-HT _{1A} receptor partial agonist used in the treatment of anxiety. Has a short half-life and active metabolite (a noradrenergic α ₂ receptor antagonist).
Antidepressants	See the WCPPE MUR guide for antidepressants.
Chloral Hydrate (limited role in treating insomnia)	Alcohol type hypnotic with active hypnotic metabolite trichlorethanol. Precise mechanism of action unknown.





Red flags that need referral

- Any symptoms of benzodiazepine withdrawal (insomnia, anxiety, loss of appetite and weight-loss, tremor, perspiration, tinnitus and perceptual disturbances) which may continue for months after stopping
- Treatment of anxiety or insomnia with a benzodiazepine for longer than 4 weeks (see CSM guidelines)
- Hypnopombic hallucinations (dream images persisting into waking state) and disinhibition syndrome
- Pregnancy – use of benzodiazepines in late pregnancy has been associated with neonatal withdrawal
- Breastfeeding – benzodiazepines are present in milk with a risk of toxicity in the infant
- Elderly - increased memory impairment or confusion

What are the common side effects to look out for?

Drug	Common side effects	Recommendation
Benzodiazepines	Paradoxical disinhibition (rare but potentially serious). Effects range from talkativeness and excitement to aggressive and antisocial acts	Refer to prescriber for review.
	Confusion, ataxia, amnesia, loss of balance and 'pseudodementia' (particularly in elderly patients)	Refer to prescriber for review. Benzodiazepines should be avoided in the elderly; if prescribed, half normal dose should be recommended
	Drowsiness, dizziness, psychomotor impairment	Advise that this may affect the performance of skilled tasks (e.g. driving): the effect of alcohol is enhanced. Refer to prescriber for potential switch to less sedating drug.
	Muscle weakness	Refer to prescriber for review.
B-Blockers	Cold extremities, hypotension	Refer to prescriber for review and possible medication switch.
	Sleep disturbances	Refer to prescriber for review and possible medication switch.
Chloral Hydrate	Gastric irritation, bloating, flatulence, headache, excitement, delirium, ketonuria and rash	Refer to prescriber for review and possible medication switch.
Zaleplon	Parosethesia, confusion, drowsiness, fatigue, dysmenorrhoea (women)	Refer to prescriber for review.
Zopiclone & Zolpidem	Drowsiness (may persist the next day)	Advise that this may affect the performance of skilled tasks (e.g. driving): the effect of alcohol is enhanced.
	Taste disturbance and dry mouth (zopiclone)	If not tolerated refer to prescriber.
	Nausea, vomiting, headache, dizziness, sleep-walking, hallucination, nightmares	Refer to prescriber for review.
Melatonin	Headache, abnormal dreams, dizziness, nausea	Usually wears off within a few weeks, if persistent refer to prescriber.

Potential serious drug interactions?

Drugs used to treat anxiety and insomnia interact with many other medications - **See BNF Appendix1: Interactions for more details.**

- An increased sedative effect with alcohol and an increased hypotensive effect with alpha-blockers (also enhanced sedative effect); angiotensin-II receptor antagonists and diuretics
- A change in plasma concentration is seen with concomitant use with certain antibacterials (clarithromycin, erythromycin, telithromycin and rifampicin); cimetidine; antiepileptic and antifungal drugs
- Other interactions include melatonin (avoid concomitant use with fluvoxamine); St John's Wort (reduced plasma concentration with midazolam); antivirals (avoid concomitant use); disulfiram (increased risk of temazepam toxicity) and lithium (increased risk of neurotoxicity with clonazepam)

Where can you find more information?

- Distance learning pack "Introduction to Pharmaceutical Care in Mental Health" found on the WCPPE website (www.wcppe.org.uk)
- The National Centre for Mental Health (NCMH) website has downloadable patient information leaflets written by specialist mental health pharmacists and other information (<http://ncmh.info>)
- NICE guidance: Zaleplon, zolpidem and zopiclone for the short term management of insomnia TAG 77: Generalised anxiety disorder (with or without agoraphobia) in adults: Management in primary, secondary and community care CG 113 can be found on NICE website (www.nice.org.uk)
- British Association for Psychopharmacology consensus statement: Benzodiazepines: risks and benefits. A reconsideration available at (www.bap.org.uk)
- Clinical Knowledge Summaries - Benzodiazepine and z-drug withdrawal: Insomnia and Sleep disorders can be found on CKS website (<http://cks.nice.org.uk>)
- Mind website (www.mind.org.uk/)
- Benzodiazepines: How they work and how to withdraw ([The Ashton Manual](http://www.theashtonmanual.com/))www.benzo.org.uk)

