Nottinghamshire Area Prescribing Committee

Benzodiazepines and Z-Hypnotics Guidance on Prescribing and Deprescribing

For the Management of Insomnia and Anxiety Disorders in Adults

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Benzodiazepines and Z-Hypnotics Guidance on Prescribing and Deprescribing		
V1.0	Last reviewed: August 2021	Review date: August 2024

NHS
Nottinghamshire Area Prescribing Committee

Key messages

- Benzodiazepines and z-hypnotics are classed as Dependence Forming Medications (DFMs)[1].
- Benzodiazepines are effective and indicated for the short-term 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].
- Z-hypnotics are effective for the short-term treatment of insomnia; when the insomnia is severe, disabling or causing the patient extreme distress.
- The long term use of benzodiazepines and z-hypnotics for insomnia and anxiety are of limited benefit and have well documented harms including tolerance, dependence, risk of falls and cognitive impairment[2,3].
- The risk of harms is increased in patients co-prescribed other sedative medicines and/or in patients taking alcohol or illicit substances.
- Before prescribing a benzodiazepine or z-hypnotic, explain the risks and have an agreed plan with the individual about how to stop treatment.
- Non-pharmacological treatments including sleep hygiene and psychological approaches should be continued alongside prescribing.
- Established long term use of benzodiazepines and z-hypnotics should be proactively reviewed.

Scope

- Inclusions: The use of benzodiazepines for anxiety and/or insomnia and the use of z-hypnotics for insomnia
- Exclusions: The use of benzodiazepines for rapid tranquillisation, alcohol detoxification, end of life care, movement disorders, spasticity management, IV sedation for procedures, epilepsy and children and young people (<18 years of age)

Non pharmacological management of insomnia

Sleep hygiene

- Always the first-line approach to managing insomnia and should be continued alongside any hypnotic prescription
- A patient leaflet on sleep hygiene is available from the Choice and Medication website.
- Sleep diaries can be helpful for identifying sleeping patterns and lifestyle factors that may exacerbate or maintain insomnia. The diary should be kept for at least two weeks. Sleep diary templates are available on the NHS live well website and the Sleep Council Website.
- See Appendix 1 for sleep hygiene advice specific to inpatient units.

Optimising treatment for co-morbidities

- Consider other triggers or factors associated with the insomnia (e.g. physical illness, other stressors, substance misuse).
- If there is an underlying physical health condition such as pain, respiratory or cardiac disease, sleep problems are likely to improve when the condition has been adequately treated.
- Optimise any other medicines the person is taking that may be causing insomnia

Psychological Therapies

- Recommended first line for the treatment of chronic sleep problems. The benefits of psychological interventions for chronic insomnia often last well beyond the termination of active treatment[4].
- Consider sign posting to Sleepio™ - https://www.sleepio.com/ - a six week digital (online) sleep improvement program that uses Cognitive Behavioral Therapy (CBT) techniques.
- Improving Access to Psychological Therapy (IAPT) providers in Nottinghamshire offer various higher intensity psychological interventions for the treatment of chronic sleep problems. The interventions on offer depend on the provider but include therapist-led digital interventions as well as face to face therapy for more complex cases.

Other medicines

- Always check whether the patient takes any other prescribed or over the counter medicines to aid sleep (these may interact with benzodiazepines and z-hypnotics to cause additive side effects, present an increased risk of overdose and potential for misuse when used concomitantly).
- Sedating antihistamines such as promethazine (Phenergan®, Sominex®) are only licensed for temporary sleeping difficulties (1-2 weeks); not appropriate for the management of chronic insomnia.
- Sedating antidepressants are not licensed for the treatment of insomnia and are not recommended to be prescribed unless treating an appropriate co-morbidity.

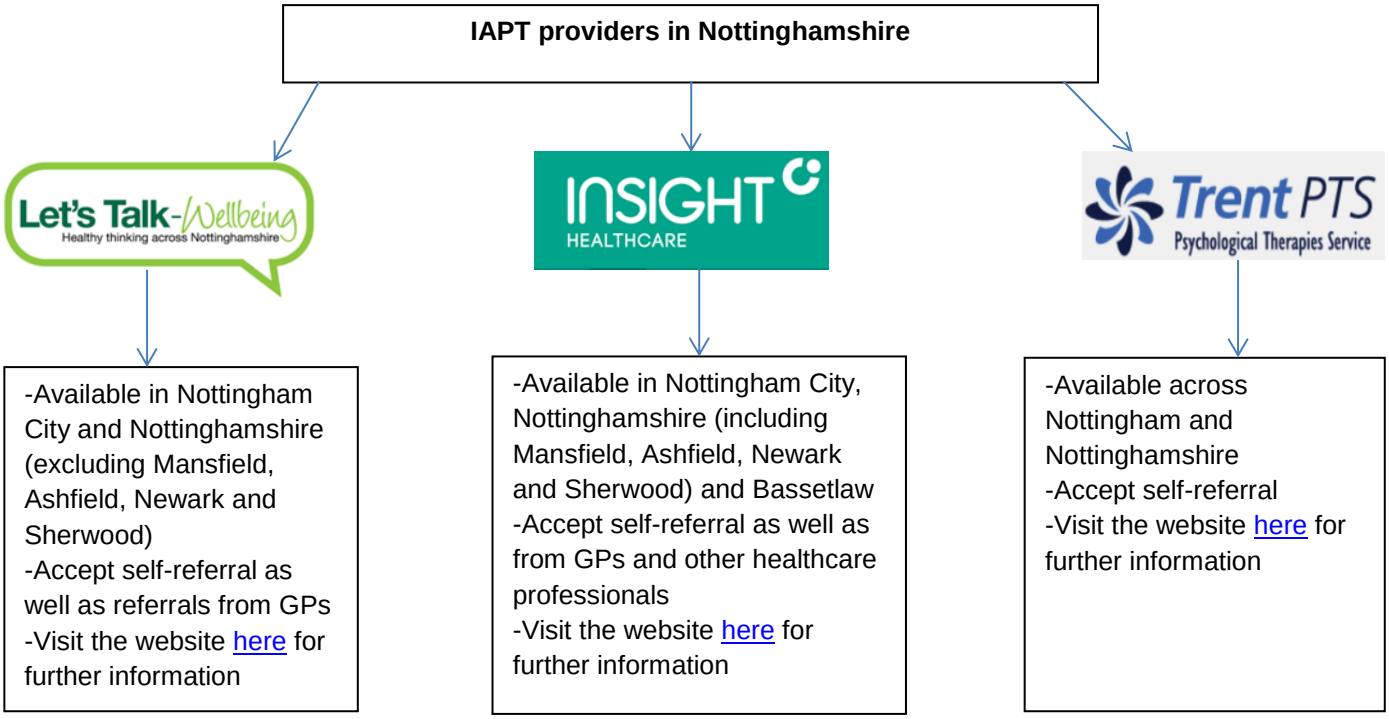
Non pharmacological management of anxiety

Optimise treatment for co-morbidities

- Consider other triggers or factors associated with the anxiety (e.g. physical illness, other stressors, substance misuse).
- Review and optimise treatment for underlying mental health conditions such depression and panic disorder.

Psychological Therapies

- Low intensity psychological interventions (individual and facilitated self-help therapies) are recommended first line for the management of anxiety. See NHS information on self-help for anxiety and NHS information on self-help therapies.
- Consider a referral to Improving Access to Psychological Therapy (IAPT) providers in Nottinghamshire. They offer various higher intensity psychological interventions for the treatment of anxiety. The interventions on offer depend on the provider but include therapist led digital interventions as well as face to face therapy for more complex cases.



Prescribing Principles – Primary Care

- Reserve benzodiazepine and z-hypnotic prescribing for short courses to alleviate severe, disabling symptoms.
- If a prescription is required it should be limited to a short time period (no longer than two weeks, preferably less than one week).
- Use the lowest effective dose for the shortest possible period.
- Inform the patient that further prescriptions for z-hypnotics and benzodiazepines will not usually be given, ensure the reasons for this are understood and document this in the patient's notes.
- Do not issue further prescriptions without seeing the patient.
- Switching from one z-hypnotic to another should only occur if a patient experiences adverse effects considered to be directly related to the specific agent.
- Patients who have not responded to one z-hypnotic should not be prescribed any of the others.
- See Appendix 2 for a comparison of different benzodiazepines and z-hypnotics
- Ensure discharge communication for benzodiazepine and z-hypnotic prescriptions is reviewed and action taken in a timely manner; new prescriptions not containing information on course duration/review should be queried with the discharging service.

Prescribing Principles – Secondary Care

On admission

- Determine whether the patient takes one or more of these medicines, regularly or intermittently for anxiety, insomnia or both.
- Review the patient's use of benzodiazepines and z-hypnotics to decide whether their continued use is indicated. This may involve speaking to the patient or carer, checking their online records e.g. Summary Care Record (SCR), SystmOne, or speaking to their GP.
- Patients who have taken these medicines ***for longer than four weeks*** should not have this treatment stopped abruptly due to the risk of precipitating withdrawal symptoms, unless risks outweigh benefits e.g. the patient is severely intoxicated.
- Discontinuation should be planned and gradual over at least 4-6 weeks (longer in most cases).
- If there are concerns about the length of time a patient has been taking one of these medicines this should be referred to in any correspondence to the usual prescriber (e.g. GP, Community Mental Health Team).

New prescriptions

- Ensure non-pharmacological interventions are continued (see Appendix 2 – Practical Sleep Hygiene for Hospital Inpatients).
- Reserve for short prescribing duration to alleviate severe, disabling symptoms.
- If a prescription is required it should be limited to a short time period (up to 7 days initially) and then reviewed.
- Start with the lowest licensed dose.
- A review/stop date should be stated clearly on the prescription.
- Ensure repeated PRN (as required) doses are recognized and reviewed in planned ward rounds and multidisciplinary team meetings.
- Out of hours doctors should not be expected to make decisions about continuation or prescription for discharge.
- Nursing and pharmacy staff should check with the prescriber if a benzodiazepine or z-hypnotic continues to be administered/requested after the stated review period.
- Intermittent use of z-hypnotics (every 2nd/3rd night) can help prevent tolerance developing. Explain to the patient the limitations of sleeping tablets. On initiation, consider a verbal 'contract' with the patient to manage expectations.
- Ideally, z-hypnotics should not be given/taken before midnight (to give the patient an opportunity to get to sleep without them).
- See Appendix 2 for a comparison of different benzodiazepines and z-hypnotics

Discharge (TTO) and temporary leave prescriptions

- Review and aim to reduce or stop short-term benzodiazepine or z-hypnotics prior to discharge.
- Carefully consider if PRN benzodiazepines or z-hypnotics are still necessary for periods of leave or on discharge.
- The decision to prescribe benzodiazepines or z-hypnotics for periods of leave or discharge should only be made by a senior clinician in the treating team.
- If prescribed, the exact quantity to be supplied should be stated based on recent and likely usage.
- The minimum possible quantity should always be prescribed.
- If patients are discharged back to primary care on z-hypnotics or benzodiazepines then the discharge summary should clearly state the likely duration of treatment and when this should be reviewed and stopped by the GP.
- Pharmacy will aim to confirm with the prescriber all discharge prescriptions for benzodiazepines and z-hypnotics where it is known that the patient was not taking these medicines prior to their hospital admission.

Outpatient prescriptions

- Exceptionally, there may be occasions where patients with severely disabling symptoms are prescribed longer courses under the supervision of a Consultant Psychiatrist.
- All out-patient repeat prescriptions (FP10s, community cards) should be reviewed regularly by the prescribing team to assess continuing need.
- Ensure no more than one prescriber is supplying z-hypnotics or benzodiazepines.
- All those involved in a patient's care (e.g. carers, care co-ordinators, community pharmacists) can play a valuable role in identifying chronic use of these medicines and bringing this to the attention of the prescribing team.

Management and Review of Long Term Benzodiazepines and Z-hypnotics

Discussion with the patient

- Reiterate benefits of stopping (tolerance to these medicines reduces effectiveness, dependence develops and continuing treatment may only serve to prevent withdrawal symptoms, risk of withdrawal increases with higher doses and length of use, avoid adverse effects, reduce risk of accidents and minimize risk of interactions with alcohol/illicit substances/other sedative medicines).
- Explain the risks associated with the long term use of benzodiazepines and z-hypnotics (cognitive impairment, anxiety, depression, reduced coping skills, emotional blunting and reduced social functioning)[5].
- Explanation that withdrawal symptoms may occur following each reduction but these symptoms tend to settle within a few days.
- It is not possible to estimate the severity of withdrawal; this will depend on a number of individual factors.
- Stress that benzodiazepines and z-hypnotics should not be stopped suddenly and that the reduction will take time (months not weeks).
- Stress that abrupt withdrawal of benzodiazepines may produce confusion, toxic psychosis, convulsions or a condition resembling delirium[2]
- Assess whether this is a suitable time for withdrawal (consider physical and mental health)
- Consider whether the withdrawal can be appropriately managed in primary care (is the patient committed and willing with adequate social support? Can they be reviewed regularly?
- Seek specialist advice if there is a history of alcohol or other drug dependence, concurrent severe physical or mental health disorder or a history of drug withdrawal seizures.

If the patient is engaged and willing to taper

- Decide whether the patient can withdraw their current medicine without switching to diazepam first (see deprescribing algorithm below).
- Agree a reduction schedule with the patient; they should guide adjustments so they remain comfortable and feel in control of the withdrawal.
- When considering frequency of reductions consider your capacity for follow up and review.
- Patients may experience withdrawal symptoms for several days after reduction so weekly reductions may be too quick.
- Withdrawal can take 4 weeks to 1 year (or longer)
- If symptoms relapse consider maintaining current dose for 1-2 weeks, then taper at a slower rate
- The reduction becomes a larger proportion of the dose as the dose reduces. This is why patients may run into difficulty as they reach lower doses. Consider smaller dose reductions as the dose becomes lower.
- If a person does not succeed on their first attempt, encourage them to try again.

What if the patient is not keen?

- Address any concerns the patient has
- Show empathy; this can be a very sensitive topic
- Explain that we now have better ways of working out how helpful medicines really are and we know that a lot of things that we thought were helpful in the past have proved to be disappointing
- Reassure that if a tapering trial does not work we can think again
- Allow time to reflect on information and arrange a further appointment if necessary.
- If, after reflection, the patient is still not keen then do not pressurize to stop and review again in 3 to 6 months

Withdrawal symptoms

- The risk of withdrawal symptoms increases with longer use, higher dosage and higher potency medicines.
- May mimic the original condition being treated.
- **Benzodiazepines** – sweating, insomnia, loss of appetite, palpitations, perceptual disturbances, tremor, anxiety, depression, panic attacks, headache and nausea[5]
- A protracted withdrawal syndrome may occur in a minority of people (up to 15%); usually those who have taken benzodiazepines for many years.
- Established benzodiazepine dependence can be very difficult to treat. This may result in prolonged withdrawal symptoms and may even become a long term state.
- **Z-hypnotics** – Rebound insomnia (with broken sleep and vivid dreams), impaired concentration, abdominal cramps, palpitations, perceptual disturbances, anxiety and depression[5]

Managing withdrawal symptoms

- Provide reassurance – with slow tapering many people experience few or no withdrawal symptoms.
- If withdrawal symptoms are present, they will disappear in a few months for most people.
- Advise patient not to compensate by increasing intake of alcohol/illicit substances/other sedatives.

Anxiety

- Consider slower or suspending withdrawal until symptoms become manageable.
- Consider non pharmacological management
- Adjunct medications should not be routinely prescribed (but may be considered)

Depression

- Consider suspending withdrawal until the depression resolves
- Treat as per NICE CG90[6]

Insomnia

- See information above on sleep hygiene and psychological therapies

Benzodiazepine (BZD) or Z-hypnotic on repeat prescription (>4 weeks) Dependence Forming Medicines deprescribing algorithm.
Algorithm for use locally in Nottinghamshire with permission from PrescQIPP CIC.

Include: patients suitable for managed withdrawal with

- **Insomnia on its own**
- **Anxiety**

Consider if:

- Willing
- Committed
- Compliant
- Have adequate social support
- Ensure that can be reviewed regularly

Exclude (ensure regular review of therapy):

- Specialist/CMHT/substance misuse initiated
- Potential substance misusers
- Patients who may be diverting some or all of their supply
- Suicide risk
- People with epilepsy
- Terminal illness
- Alcohol withdrawal
- Restless legs
- Dementia
- History of complicated drug withdrawal
- Short term use e.g. prior to flying, muscle relaxant, unmanaged anxiety, depression, physical or mental condition that may be causing or aggravating insomnia

Continue BZD or Z-drug

Ensure directed communication: Review patient in clinic. Aim to ensure that the same HCP is seen.

- Reiterate benefits of stopping
- Explain tolerance, adverse effects and risks of continuing
- Discuss potential risks, benefits, withdrawal plan, symptoms and duration

See PrescQIPP Bulletin 175 attachments 4 and 5. See MIND for Z-drugs)

- Agree on treatment regimen (written plan)
- Arrange follow up appointments
- Ensure practice staff are briefed on reducing regimen

If unwilling to stop BZD or Z-drug:
Do not pressurise to stop if not motivated
Address any concerns about stopping

Review at a later date and reassess the persons motivation to stop

Refer to sleep clinic or specialist with expertise in sleep medicine

Insomnia[1]
Use sleep diaries, sleeping health leaflets and self-help strategies (see NHS sleeping habits information) to manage insomnia. See attachment 1 on self care resources

Anxiety[2]
Low intensity psychological interventions:
Individual non-facilitated self-help – written or electronic
Individual guided self-help
Psychoeducational groups
High intensity psychological intervention (CBT or applied relaxation). See attachment 1 on self care resources

Taper and then stop BZD or Z-drug

Withdrawal of BZD or Z-drug Table 1

Short-acting BZD Table 2

Monitor every 1-2 weeks for duration of tapering. Estimated time of withdrawal 8–12 weeks or longer. Be guided by the patient; if previously tried but failed, withdrawal can take 4 weeks to 1 year or longer

If symptoms relapse consider maintaining current BZD or Z-drug dose for 1-2 weeks, then taper at a slower rate

Benzodiazepine (BZD) or Z-hypnotic on repeat prescription (>4 weeks) Dependence Forming Medicines (DFM) deprescribing algorithm
Algorithm for use locally in Nottinghamshire with permission from PrescQIPP CIC

Table 1. Tapering BZD or Z-drug[5]
Taper slowly in collaboration with the patient, for example ~5-10% every two weeks, or 1/8th of dose fortnightly titrated according to the severity of withdrawal syndromes

Benzodiazepines	Reduction
Temazepam ≤ 20mg	Reduce daily dose by a quarter of a 10 mg tablet (2.5 mg) every 2 weeks Consider temazepam 10mg/5ml liquid to achieve further reductions if needed
Nitrazepam ≤ 10mg	Reduce daily dose by a quarter of a 5 mg tablet (1.25 mg) every 2 weeks Consider nitrazepam 2.5mg/5ml liquid to achieve further reductions if needed
Zopiclone ≤ 7.5mg	Reduce daily dose by a half of a 3.75 mg tablet (1.875 mg) every 2 weeks Consider conversion to diazepam 2mg/5ml to achieve further reductions if needed

Table 2. For short acting BZD switch to diazepam[5]
For example, alprazolam, loprazolam, lormetazepam. This regimen may also be considered for people likely to experience difficulty in withdrawal due to dependency.

Transfer patient stepwise to an equivalent daily dose of diazepam preferably taken at night.

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.

- Reduce diazepam dose further, if necessary, in smaller steps; steps of 500 micrograms may be appropriate towards the end of withdrawal. Then stop completely.

For long-term patients, the period needed for complete withdrawal may vary from several months to a year or more

Diazepam 5 mg equivalent doses[3,5]
≡ alprazolam 250 micrograms
≡ clobazam 10 mg
≡ clonazepam 250 micrograms
≡ flurazepam 7.5–15 mg
≡ chlordiazepoxide 12.5 mg
≡ loprazolam 0.5–1 mg
≡ lorazepam 500 micrograms
≡ lormetazepam 0.5–1 mg
≡ nitrazepam 5 mg
≡ oxazepam 10 mg
≡ temazepam 10 mg
≡ zolpidem 10 mg
≡ zopiclone 7.5 mg

Table 3: Evidence[4]

Benzodiazepine Dependence: Gradual withdrawal
Evidence High

Use of several BZD: Switch to diazepam
Evidence: Good

Psychotherapy: Cognitive behavioural therapy and other approaches
Evidence: Good

Table 4. Resources

PrescQIPP Benzo reduction programme (2016)
PrescQIPP Bulletin 175 Hypnotics
PrescQIPP Bulletin 184 Behavioural change strategies
Canadian deprescribing benzodiazepine receptor agonist algorithms and guidelines
Ashton CH. Slow withdrawal schedules.
RGCP Top ten Tips: Dependence forming medications
NHS Wales Hypnotics and anxiolytics practice guide

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Driving

- Department of Health driving legislation is available at https://www.gov.uk/drug-driving-law
- There are DVLA regulations around benzodiazepine use and driving (note that doses outside of BNF guidance constitutes persistent misuse or dependence for licensing purposes whether in a programme of withdrawal or not).
- Advise patients not to drive if they feel drowsy, dizzy or unable to concentrate.
- Counsel patients about the risks of impaired reaction times and injury even if they feel well.
- Remind that it is an offence to drive with more than a specified amount of benzodiazepine in your body, whether driving is impaired or not.
- Advise patients to keep evidence they are taking a benzodiazepine in accordance with medical advice (e.g. medication box with pharmacy label, evidence of repeat prescription).
- The DVLA provides no advice for people taking z-hypnotics

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Appendix One
Sleep hygiene in hospital

Sleep in hospital may be disrupted for a number of reasons[1,2]:

- Disruption to normal sleep patterns (usual wake / sleep times).
- Proximity of other people.
- Noise (from other patients, staff, machines).
- Lighting – too dark during the during the day, too light at night.
- Worries (about diagnosis, care, treatment, concerns outside the hospital).
- Being in an unusual environment.
- Physical symptoms (such as pain, nausea or breathlessness).
- Being woken for medical or nursing care during the night.
- Some medication may affect sleep patterns.

Rest and sleep are an important part of recovery and healing. Studies have suggested that sleep loss in hospital is associated with worse health outcomes, including cardio-metabolic derangements and increased risk of delirium in older patients[1].
In an acute care setting some common strategies to prevent insomnia may be more challenging to implement, however a thoughtful approach may allow integration of some of these into routine care.

At night:

- Avoid medical or nursing intervention unless necessary. Consider amending timing of medicine administration, blood tests and observations if safe to do so.
- If possible try to avoid diuretics and CNS stimulant medicines at bedtime (including steroids, nicotine, decongestants, and medicines for ADHD or narcolepsy).
- Encourage avoidance of caffeine (ensure decaffeinated options are available on the ward)
- Encourage toileting before bedtime.
- Actively address pain (one study suggested toileting and pain are the biggest causes of insomnia reported by patients in the hospital setting)[1]
- Ensure a comfortable temperature – encourage patients to remove or request blankets.
- Ensure your patient is comfortable – assist with positioning, wearing own nightclothes if suitable.
- Avoid turning on lights, ensure conversations are at low volume and away from patient areas where possible. Minimise unnecessary phone calls (staff and patients).
- Patients may wish to bring ear plugs or eye masks in to hospital (this is included in the NUH Packing for Hospital checklist for patients[4]).
- Encourage avoidance of screen time within 1 hour of bedtime.
- Encourage relaxation strategies. Offering a milky or non-caffeinated drink (avoiding large volumes of liquid at bedtime), soft music / spoken word (via headphones) and breathing techniques have all been shown to aid relaxation[2,6].

During the day:

- Encourage natural light (open blinds, curtains).
- Encourage gentle exercise if appropriate (eg sitting out, use of day room).
- Encourage avoidance of napping in the afternoon. If needed, naps are better taken earlier in the day and limited to 30 mins.

Hypnotics / sleeping tablets
New prescriptions of hypnotics for sleep alone should be avoided unless absolutely necessary, and only used for the shortest possible time.

There can be a useful short term window for hypnotics to encourage sleep / wake cycle if non-pharmacologic options are insufficient e.g. after surgery or in times of distress. Discuss this with your patient *before* prescribing and have a clear plan for stopping before discharge.

Remember:

- Sleeping tablets do not just affect our sleep – they can also affect day time alertness, memory and coordination; they may increase harm from falls and reduce engagement in rehabilitation (eg therapy interventions.)
- Although many people assume that sleep medication will help them to function adequately the next day, there is little scientific evidence to support this.
- Effects on memory may also be at night – patients may report more sustained sleep due to not remembering waking episodes the following day[5].

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Other local patient resources on sleep hygiene

- Adult self-help resource: *Managing Insomnia and Sleep Problems*. Nottinghamshire Healthcare NHS Trust, Loughborough University. Available at www.nuh.nhs.uk
- Nottingham Children's Hospital guidance: *A behavioural approach to managing sleep difficulties*. Community Paediatric Department. Available at www.nuh.nhs.uk

Appendix Two
Comparison of Benzodiazepines and Z-hypnotics

Medicine	Usual adult dose for anxiety (per day)[2]	Usual adult dose for insomnia (per day)[2]	Approximate half-life**	Other information
Clonazepam	0.5mg – 1mg up to two or three times a day*	N/A	20-60hours (mean = 30hours)	Off-label indication
Diazepam	2mg three times a day, increased if necessary to 15mg – 30mg daily in divided doses*	*Insomnia associated with anxiety* 5mg – 15mg daily at bedtime*	24-48 hours (2-5 days for active metabolite)	In frail or older people consider very low starting dose
Lorazepam	1-4mg daily in divided doses*	*Insomnia associated with anxiety* 1-2mg daily at bedtime*	12 hours	In frail or older people consider very low starting dose
Nitrazepam	N/A	5mg – 10mg before bedtime	24 hours	Avoid use in the elderly. **Non-formulary in Nottinghamshire**
Temazepam	N/A	10mg – 20mg before bedtime*	8-15 hours	Schedule 3 controlled drug
Zopiclone	N/A	7.5mg before bedtime*	4-6 hours	Slower onset than zolpidem but longer duration of action
Zolpidem	N/A	10mg before bedtime*	Mean = 2.4 hours	Potent and quick acting (usually works within 15 minutes)

*For debilitated patients or older patients lower doses (e.g. half adult doses) are recommended. See the medication's Summary of Product Characteristics (SPC) for further information.

**Half-life does vary between patients and can be longer in certain patient groups (e.g. renal impairment, older individual.