SECTION 5: TREATMENT OF INSOMNIA

Formulary and Prescribing Guidelines
5.1 Approved Drugs for the treatment of Short term Insomnia in ADULTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zopiclone</td>
<td>Tabs 3.75mg, 7.5mg</td>
<td>'Z-drug'. 1st line.</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Tabs 5mg, 10mg</td>
<td>'Z-drug'. Alternative 1st line.</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Tabs 10mg, 20mg</td>
<td>Benzodiazepine. 2nd line Controlled drug</td>
</tr>
<tr>
<td></td>
<td>Liquid 10mg/5ml</td>
<td></td>
</tr>
<tr>
<td>Promethazine</td>
<td>Tabs 10mg, 25mg</td>
<td>Antihistamine. 3rd line</td>
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<tr>
<td></td>
<td>Elixir 5mg/5ml</td>
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</table>

Treatment of insomnia in children is discussed in section 12, whilst further information is provided in section 11 in relation to drug use in older adults.

The Z-drugs are believed to have greater selectivity for the omega 1- benzodiazepine receptor (resulting in lesser anxiolytic, anticonvulsant and muscle relaxant effects, with purported lower potential for dependence and tolerance). Additionally, zopiclone is reported not to cause REM rebound upon discontinuation, due to aforementioned (relative to BDZs) receptor selectivity. Onset of activity for zopiclone is 30-45 minutes, and duration of action is quoted as ‘short’ (or 6 hours). It is metabolised by the CYP3A4 system and thus, is subject to interactions with inhibitors such as erythromycin. Temazepam is a non-selective benzodiazepine, and consequently has some anxiolytic (and muscle-relaxant) activity in addition to the hypnotic action. It possesses an intermediate duration of activity (8-10 hours) and an onset of action of approximately 1 hour. It is not associated with the same degree of accumulation as seen with flurazepam or nitrazepam on chronic administration. It is not oxidized in the liver (it is conjugated and then excreted) and, thus, does not compete with other hepatically metabolized drugs.

As a benzodiazepine, temazepam normally increases stage 2 sleep, at the expense of REM, and stages 3 and 4 – resulting in REM rebound (manifested as vivid dreams) upon discontinuation. As with all benzodiazepines, the risk of dependence and withdrawal syndrome should be considered when prescribing. See the BNF for further information and guidance relating to minimising such risks. Prescribers should be conscious of the risk of diversion when prescribing for leave/discharge or in an outpatient setting as benzodiazepines have abuse potential. The FDA has warned of a serious risk of death when benzodiazepines are used in combination with opioid analgesic or cough preparations.

People with borderline or antisocial personality disorders should only be prescribed sedative medication for short-term crisis management or treatment of comorbid conditions.

**MELATONIN M/R tabs 2mg**

Melatonin M/R is licensed for the short-term treatment of primary insomnia (characterised by poor quality of sleep) but only in patients who are aged 55 years old or over. Its licence permits use for up to 13 weeks. The British Association of Psychopharmacology (BAP) recommend the use of melatonin prolonged release therapy as first-line medication in the elderly for sleep problems (with endorsement of CBT as first-line treatment).

**Circadin** is the only melatonin product in the UK that is licensed. The MHRA have produced guidance indicating that where melatonin is needed, the licensed product should...
be used wherever possible – including off-label use where deemed suitable by the clinician.

Circadin tablets may be crushed, but in doing so the product loses its controlled release profile and becomes identical to an immediate release product; near maximal release of melatonin is reached within the first hour. Crushed tablets may be administered to children in small portions of food, water, juice, yoghurt or jam. Using Circadin either crushed (to obtain an immediate release profile) or halved (to obtain alternative M/R doses) offers a more cost effective method of obtaining specific doses/release profiles compared to using expensive ‘special’ formulations.

The table below indicates how patients stabilised on melatonin capsules, tablets or liquid which are not Circadin M/R can be switched to or initiated onto the relevant Circadin M/R dose and how the desired profile

It should be noted that the prescription of Circadin is subject to a “Non-Formulary” request approval.

<table>
<thead>
<tr>
<th>Switch Melatonin capsules, tablets or liquid to Circadin as follow:</th>
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<tbody>
<tr>
<td>• Melatonin 1mg caps or tabs immediate release – half a tablet crushed</td>
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<tr>
<td>• Melatonin 1mg/1ml or 5mg/5ml – half a tablet crushed and amend dose</td>
</tr>
<tr>
<td>• Melatonin 2mg immediate release caps or tablet-one tablet crushed</td>
</tr>
<tr>
<td>• Melatonin 3mg immediate release caps or tablets-one tablet &amp; a half crushed</td>
</tr>
<tr>
<td>• Melatonin 3mg CR tabs or caps-one tablet &amp; a half (do not crush)</td>
</tr>
<tr>
<td>• Melatonin 5mg immediate release-2 tablets and a half crushed</td>
</tr>
</tbody>
</table>

5.2 Treatment of insomnia

BAP endorse the use of CBT-based treatment packages (including sleep restriction and stimulus control) as ‘first line treatment for chronic insomnia because of efficacy (considered equivalent to prescription medications for short term treatment of chronic insomnia)’. BAP also endorses the need for increased availability of this therapy (within the UK). The ideal hypnotic has a rapid onset of effect (within 20 minutes), helps the patient sleep throughout the night, does not cause daytime impairment, and has no abuse potential. Currently, there is no such ideal hypnotic.

- Hypnotics should not be prescribed indiscriminately/routinely but only after non-pharmacological methods have failed and where the insomnia is so severe that it is interfering with normal daily life. Hypnotics should only be prescribed after consideration of non-drug therapies, including CBT.

- Use should be short-term only (2-4 weeks, as per licensed indications). Hypnotics which have been prescribed in hospital should not normally be continued on discharge.

- The lowest possible dose should be used, and, where possible, use should be intermittent.
• Longer acting benzodiazepines, such as nitrazepam (non-formulary) should be avoided.

• A patient should only be switched from one hypnotic to another if they experience adverse effects (considered directly related to a specific hypnotic)

• A patient who has not responded to zopiclone should not be prescribed zaleplon (non-formulary) or zolpidem

• Benzodiazepines and the Z-drugs\textsuperscript{12} should be avoided, as much as possible, in the elderly who are at risk of side effects such as ataxia, and confusion leading to falls and injuries. They should only be prescribed following a falls risk assessment

• Treatment should be tapered off gradually\textsuperscript{5}.

• Patients should not routinely be prescribed hypnotics on discharge without a discontinuation plan communicated to the GP.

• NICE have published an overview about hypnotics\textsuperscript{13} It includes a tool to support ‘deprescribing’ of hypnotics, produced by the Bruyère Research Institute Deprescribing Guidelines Research Team in Canada and endorsed by NICE. This can help support the optimal use of hypnotics. A copy of the tool is shown in Appendix 1.

5.3 Sleep hygiene

This term refers to ways of promoting satisfactory sleep. Sleep hygiene on its own is not considered effective, but is seen as a useful adjunct to CBT (cognitive behavioural therapy) or pharmacological therapy.

The environment should be conducive to sleep, e.g.

• Familiar setting

• Comfortable bed

• Correct temperature (not too warm and not too cold)

• Darkened, and quiet (that is, non-stimulating) room

Encourage:

• Bedtime routines

• Going to bed only when tired

• Regular daily exercise, exposure to sunlight, and general fitness

• A warm bath or hot milky drinks may promote sleep

• Reassurance to elderly patients that 5-6 hours sleep a night is normal as one gets older

Avoid
• Overexcitement near bedtime
• Late evening exercise
• Caffeine containing drinks late in the day
• Smoking and excessive alcohol
• Large meals late at night
• Thinking about problems and plans at bedtime
• Excessive or late napping during the day
• Too much time awake in bed (especially distressed)

References

4. BNF: 72nd Current edition, Sep 2017
8. BAP Consensus guidelines – insomnia
9. NICE eyes on evidence – prescriptions for anxiolytics and hypnotics and risk of death – June 2014
Appendix 1: Deprescribing tool.

**Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm**

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**Why is patient taking a BZRA?**

- Insomnia as its own or OI insomnia where underlying comorbidities managed
- For those 65 years of age: taking BZRA regardless of duration (avoid as first line therapy in older people)
- For those 65-84 years of age: taking BZRA > 4 weeks

**Engage patients**

The 4 questions to engage patients:
- What keeps you up at night?
- Do you feel drowsy during the day?
- Have your signs improved or worsened over time?
- Are you happy with your sleep?

**Recommend Deprescribing**

**Taper and then stop BZRA**

Taper slowly in collaboration with patient, for example 25% every two weeks, and if possible, 12.5% reductions near end and planned drug free days.

- For those > 65 years of age: strongly recommendation from systematic review and GRADE approach
- For those 18-64 years of age: weak recommendation from systematic review and GRADE approach

Offer behavioural sleeping advice; consider CBT if available (see reverse)

**Monitor every 1-2 weeks for duration of tapering**

Expected benefits:
- May improve sleep duration, daytime sleepiness, and reduce falls

Withdrawal symptom:
- Insomnia, anxiety, irritability, sweating, gastrointestinal symptoms

**Cessation of non-drug approaches to manage insomnia**

Use CBT and/or other (non-pharmacological) approaches according to National Institute of Health and Care Excellence (NICE) guideline for insomnia.

**BZRA Availability**

<table>
<thead>
<tr>
<th>BZRA</th>
<th>Strength</th>
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<tbody>
<tr>
<td>Alprazolam</td>
<td>0.25 mg, 0.5 mg, 1 mg, 2 mg</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>5 mg, 10 mg, 25 mg</td>
</tr>
<tr>
<td>Clobazam</td>
<td>0.25 mg, 0.5 mg, 1 mg, 2 mg</td>
</tr>
<tr>
<td>Clonazepam (Risperidone)</td>
<td>5 mg, 7.5 mg, 10 mg</td>
</tr>
<tr>
<td>Doxepin (Doxase)</td>
<td>15 mg, 30 mg</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5 mg, 1 mg, 2 mg</td>
</tr>
<tr>
<td>Midazolam (Midazolam)</td>
<td>5 mg, 10 mg</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>10 mg, 15 mg, 30 mg</td>
</tr>
<tr>
<td>Temazepam</td>
<td>25 mg, 30 mg</td>
</tr>
<tr>
<td>Tranquilizers (Haldol)</td>
<td>10 mg, 25 mg</td>
</tr>
<tr>
<td>Zopiclone (Zopiclone)</td>
<td>5 mg, 7.5 mg</td>
</tr>
<tr>
<td>Zolpidem (Zolpidem)</td>
<td>5 mg, 10 mg</td>
</tr>
</tbody>
</table>

**T = tablet, C = capsule, S = sublingual tablet**

**Patients should understand:**
- The rationale for deprescribing (associated risks of continued BZRA use, reduced long-term efficacy)
- Withdrawal symptoms (insomnia, anxiety) may occur but usually mild, transient and short-lived (days to a few weeks)
- They are part of the tapering plan, and can control tapering rate and duration

**Tapering doses**

There is no published evidence exists to suggest switching to long acting BZRA reduces incidence of withdrawal symptoms or is more effective than tapering short-acting BZRA.

- If dosage forms do not allow 25% reductions, consider reduction in nightly use rather than drug-free days during latter part of tapering, or switch to lorazepam or oxazepam for final taper steps

**Behavioural Management**

Primary care:
- 1. Do bed only when sleepy
- 2. Do not read or watch TV in bed
- 3. Avoid alcohol or sedatives
- 4. Do not nap
- 5. Avoid caffeine

Secondary care:
- 1. Encourage light exercise in the evening
- 2. Use behavioural therapies (CBT) (see reverse)

T = tablet, C = capsule, S = sublingual tablet

**Using CBT**

- CBT helps people understand their insomnia, set more realistic goals, make necessary lifestyle changes, and learn new strategies to deal with insomnia.

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Approved by Medicines Management Group June 2019