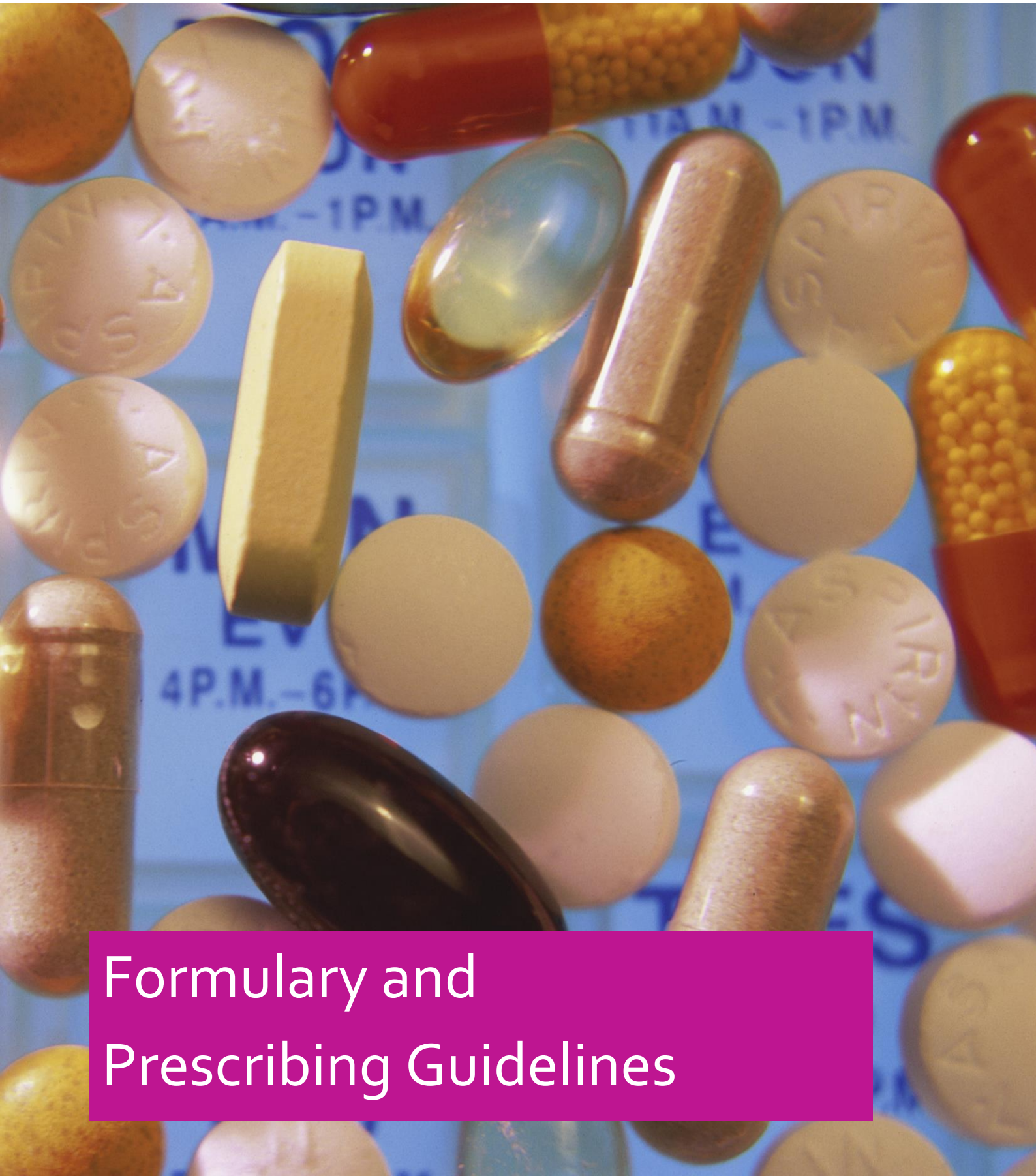
Essex Partnership University
NHS Foundation Trust

SECTION 5: TREATMENT OF INSOMNIA



Formulary and Prescribing Guidelines

5.1 Treatment of insomnia

Hypnotic medication should be avoided if possible due to potential for significant adverse effects. 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).[1] 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[2].

- 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[1]. Hypnotics should only be prescribed after consideration of non-drug therapies, including CBT.[3]

- 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[4] 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[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[6] 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.

- Guidance for the management of service users with benzodiazepine dependence can be found in the Trust Formulary and Prescribing Guidelines Section 10

5.2 Sleep hygiene

This term refers to ways of promoting satisfactory sleep. Good sleep hygiene should be considered in all people with insomnia, and information offered. This aims to make people more aware of behavioural, environmental and temporal factors that may be detrimental or beneficial to 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)

5.3 Approved Drugs for the short-term treatment of Insomnia in ADULTS

Drug	Formulations	Comments
Zopiclone	Tabs 3.75mg, 7.5mg	'Z-drug'. ***1st line***.
Zolpidem	Tabs 5mg, 10mg	'Z-drug'. **Alternative 1st line**.
Daridorexant	Tabs 25mg, 50mg	Orexin receptor Antagonist. **Alternative 1st line**.
Melatonin^	M/R tabs 2mg	Only approved for use in **Children and Adolescents and adults over 55 of age for up to 13 weeks. Alternative 1st line**
Temazepam	Tabs 10mg, 20mg Liquid 10mg/5ml	Benzodiazepine. ***2nd line*** Controlled drug
Promethazine	Tabs 10mg, 25mg Elixir 5mg/5ml	Antihistamine. ***3rd line***

^Melatonin is non-formulary for use in **adults aged between 18 and 54** and requires a non-formulary application for use in this patient group.

Treatment of insomnia in children is discussed in section 12, whilst further information is provided in section 11 and section 13 in relation to drug use in older adults and learning disabilities respectively.

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[2]). Additionally, zopiclone is reported not to cause REM rebound upon discontinuation, due to aforementioned (relative to BDZs) receptor selectivity[7]. Onset of activity for zopiclone is 30-45 minutes, and duration of action is quoted as 'short' (or 6 hours[2]). 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[8-10].

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[2]. 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.[11]

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

Both Z-drugs and benzodiazepines are associated with dependence, characterised by both tolerance and withdrawal symptoms. This possibility should be explained to patients so that a shared decision can be reached about the benefits and risks of treatment, including that missed doses or sudden cessation may lead to symptoms of withdrawal and that support will be provided at the time that withdrawal occurs.

Factors which may increase the risk of problems during withdrawal, such as long duration of use, high dose, and history of withdrawal symptoms should be considered. NICE has published guidance on safe prescribing and withdrawal of medicines associated with dependence and withdrawal symptoms, Z-drugs and benzodiazepines.[12]

Daridorexant

Daridorexant is an orexin OX1 and OX2 receptor antagonist that blocks the action of orexin and decreases wakefulness. Daridorexant is recommended by NICE (TA922: Daridorexant for treating long-term insomnia).[13] as a possible treatment for insomnia in adults:

- who have had symptoms for 3 nights or more per week for at least 3 months, and whose daytime functioning is considerably affected
- only if cognitive behavioural therapy for insomnia has not worked, or if it is unsuitable or not available.

If the insomnia does not improve enough, daridorexant should be reviewed and stopped after 3 months. If treatment is continued after 3 months, there should be regular checks to make sure it is still effective, efficacy has been shown in trials for up to 12 months, however the effectiveness of longer term treatment is unknown.

In a study where treatment was continued up to 52 weeks, no withdrawal was reported on stopping daridorexant, and currently the data suggests a low risk of dependency. It is also associated with low levels of next day sedation and falls. Caution should be used if considering prescribing in patients with serious or uncontrolled mental health conditions or those who use alcohol or other substances as patients with suicide ideation/attempt, acute/unstable psychiatric conditions or alcohol/drug abuse were excluded from clinical trials.[15]

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[8]. Its licence permits use for up to 13 weeks[8]. 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**)[1].

There are now a number of melatonin products that are licensed, melatonin M/R 2mg tablets are the preferred product and should be prescribed generically. 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.

Melatonin M/R 2mg 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

Melatonin M/R 2mg tablets 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.

A number of other licensed melatonin products are now available, including immediate release tablets/capsules in various strengths, M/R 1mg and 5mg tablet strengths and liquid formulations, but at significantly higher costs (5-40 times) than the M/R 2mg tablets. They remain non-formulary within EPUT. If there is a specific requirement for a different formulation other than the M/R 2mg tablets, this can be requested via a "Non-Formulary" request approval.

The table below indicates how patients stabilised on melatonin capsules, tablets or liquid which are not melatonin M/R 2mg tablets can be switched to or initiated onto the relevant melatonin M/R 2mg tablets dose and how to achieve the desired release profile.

Switch Melatonin capsules, tablets or liquid to melatonin M/R 2mg tablets as follow:

- Melatonin 1mg caps or tabs immediate release – half a tablet crushed
- Melatonin 1mg/1ml–half a tablet crushed per 1mg of liquid
- Melatonin 2mg immediate release caps or tablet-one tablet crushed
- Melatonin 3mg immediate release caps or tablets-one tablet & a half crushed
- Melatonin 3mg CR tabs or caps-one tablet & a half (do not crush)
- Melatonin 5mg immediate release-2 tablets and a half crushed

References

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Appendix 1: Deprescribing tool.