PrescQIPP
Funded by the NHS for the NHS

Melatonin

£17.8 million was spent on melatonin across England, Wales and Scotland. (NHSBSA (England and Wales Jul-Sept 22) and Public Health Scotland (Scotland Jun-Aug22).

This bulletin focuses on melatonin and provides information on ensuring that prescribing is appropriate, reviewing ongoing prescribing and deprescribing melatonin (as it is intended for short-term use). This includes information on regular drug holidays to determine whether any benefit continues to be maintained after stopping treatment.

Recommendations

- The risk of falls and fractures associated with melatonin should be considered before commencing treatment and at each review in patients aged 45 years or over.
- All patients prescribed melatonin for the following indications should have their treatment discontinued:
  - Jet lag - this is not recommended on the NHS due to the limited and conflicting evidence of benefit
  - Insomnia with Alzheimer's disease.
- Where melatonin is being considered and before treatment is started, all patients:
  - Under the age of 19 with autism spectrum disorder should have a consultation with a specialist paediatrician or psychiatrist with expertise in the management of autism or paediatric sleep medicine.
  - With challenging behaviour and learning disabilities should have a consultation with a psychiatrist (or a specialist paediatrician for a child or young person) with expertise in melatonin use in people with a learning disability.
- Melatonin should be used together with non-pharmacological interventions.
- Review all adults aged 55 years and over on modified-release melatonin after three weeks of treatment and only continue for a further ten weeks if a response is seen. Review and deprescribe melatonin in adults after a total of 13 weeks treatment.
- Review children on melatonin after three months and deprescribe melatonin if there is no clinically relevant treatment effect seen.
- All suitable patients should undergo a two-week drug holiday to assess their need for ongoing treatment. This should take place three months after the commencement of treatment and six-monthly thereafter. If sleep improvements are maintained without melatonin, therapy should be stopped.
- If there is a consistent correlation of sleep deterioration during a drug holiday, patients should be advised to continue melatonin without a break unless they are suspected to be a poor metaboliser of melatonin (in which case regular washout with ongoing drug holidays when the benefit wanes, is recommended).
- For patients where caution should be exercised with drug-holidays and deprescribing, refer to the patient's specialist for advice on managing this, including where melatonin is prescribed under a formal shared care arrangement.

Recommendations

- A cost-effective licensed preparation should be selected where possible.
- Review patients prescribed unlicensed melatonin specials and melatonin used "off-label" and discuss with them whether a change to a licensed alternative is suitable for them. For patients prescribed unlicensed or 'off-label' melatonin, where there is no suitable licensed alternative, they should be given sufficient information regarding this.

National guidance

Insomnia disorder

The National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summary (CKS) on insomnia includes prescribing advice for prolonged-release melatonin. They differentiate between short and long-term insomnia, defined as less than three months duration and more than three months duration, respectively.[1]

For short-term insomnia (less than three months duration), the need for adjunctive treatment with a short-term hypnotic medication (a non-benzodiazepine hypnotic medication (z-drug) or prolonged-released melatonin if over 55 years of age) should be considered if sleep hygiene measures fail, daytime impairment is severe causing significant distress, and insomnia is not likely to resolve soon. However, hypnotics should not be prescribed routinely (or on a repeat prescription) and, where indicated, should be used only for a short course (on an acute prescription).[1]

Pharmacological therapy should be avoided for long-term insomnia (more than three months duration). However, for some people with severe symptoms or an acute exacerbation, a short course of a hypnotic drug (preferably less than one week) may be considered as a temporary adjunct to behavioural and cognitive treatment. For people over 55 years of age with persistent insomnia, treatment with prolonged-release melatonin may be considered. In terms of duration of treatment, the recommended initial duration of treatment is three weeks.[1] If there is a response to treatment, it should be continued for a further ten weeks only, in accordance with the licensed indication (13 weeks total treatment length).[1,2]

In Scotland, the Scottish Medicines Consortium (SMC) made the decision that melatonin prolonged-release tablets (Circadin®) are not recommended for use within NHS Scotland as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep, in patients who are aged 55 or over. This is due to a submission from the manufacturer not being submitted.[3]

Sleep disorders and Attention Deficit Hyperactivity Disorder (ADHD)

Some immediate-release melatonin preparations are licensed for the treatment of insomnia in children and adolescents aged 6–17 years with ADHD, where sleep hygiene measures have been insufficient.[4–6] For the licensed immediate-release preparations of melatonin, treatment should only be initiated by physicians experienced in ADHD and/or paediatric sleep medicine.[4,6]

However, in 2021, NICE published an exceptional surveillance document concerning NICE guideline 87 [NG87], Attention deficit hyperactivity disorder: diagnosis and management.[7] This was in relation to evidence being identified in the development of an evidence summary for a different indication that could impact on the recommendations in NG87.[7,8]

As a result, the NICE guideline was not amended to add a recommendation about melatonin. It concluded that there is evidence that melatonin can advance sleep onset times in adults and children. However, the evidence for its effect on quality-of-life (QoL) and ADHD symptoms was either lacking or uncertain.[7]

Consequently, melatonin should not be routinely prescribed for patients with ADHD and should only be considered if other treatments are ineffective/unsuitable, in line with the manufacturer recommendations.

It is recommend that, after at least three months of treatment, the physician should evaluate the treatment effect and consider stopping treatment if no clinically relevant treatment effect is seen.[4–6] If treatment is continued, monitoring thereafter should take place at regular intervals (at least every six months) to check that melatonin is still the most appropriate treatment. During treatment, especially if the treatment effect is uncertain, discontinuation attempts should be made regularly, e.g. at least once per year.[4,6]

It is also recommended that if the sleep disorder has started during treatment with medicinal products for ADHD, dose adjustment or switching to another product should be considered.[4–6]

Prolonged-release melatonin is not licensed for this indication.[2]

Sleep disorders in adults who are blind

NICE published the evidence summary about melatonin treating sleep disorders in adults who are blind [ES38] in August 2021.[8] They found limited evidence from three very small studies which suggested that melatonin might improve total night sleep duration and reduce the amount of time spent awake after falling asleep in adults with sleep disorders who are totally blind. However, they concluded that it was not possible to say what dose should be used and how long treatment should be continued.[8]

Autism Spectrum Disorder (ASD)

The NICE clinical guideline on ASD in under 19s: support and management [CG170] recommends that a pharmacological intervention to aid sleep is only recommended for use in ASD in under 19s if sleep problems persist despite following the sleep plan and if sleep problems are having a negative impact on the child or young person and their family or carers.[9]

Melatonin can be considered in this instance. It should only be used following consultation with a specialist paediatrician or psychiatrist with expertise in the management of autism or paediatric sleep medicine and it should be used in conjunction with non-pharmacological interventions. Treatment should be regularly reviewed to evaluate the ongoing need for a pharmacological intervention and to ensure that the benefits continue to outweigh the side effects and risks.[9]

The NICE clinical guideline on ASD diagnosis and management in adults does not discuss insomnia or sleep disorders.[10]

The Scottish Intercollegiate Guidelines Network (SIGN) guideline 145 on assessment, diagnosis and interventions for autism spectrum disorders states that no evidence was identified on the use of melatonin in adults with ASD to improve sleep problems. Randomised controlled trials (RCTs) in children have shown improvements in sleep time and sleep-onset latency, particularly when used with cognitive behavioural therapy (CBT). Melatonin (3mg controlled-release) is effective in reducing sleep problems in children with ASD.[11]

The SMC rejected the melatonin prolonged-release formulation, Slenyto®, for the treatment of insomnia in children and adolescents aged 2-18 years with autism spectrum disorder and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient, due to an insufficiently robust economic analysis.[12] NHS Wales reviewed Slenyto® for the same indication and recommends it as an option. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.[13]

For adults and children with ASD who have sleep difficulties which have not resolved following behavioural interventions, SIGN states that a trial of melatonin to improve sleep onset may be considered but the use of melatonin should follow consultation with a psychiatrist (or paediatrician, if

relevant) with expertise in the management of sleep medicine and/or ASD, and the use of melatonin should be in conjunction with behavioural interventions.[11]

An adequate baseline sleep diary should be obtained before any trial of melatonin with continuation of sleep hygiene measures (bedtime and wake-up routine, avoidance of day-time sleep) and a sleep diary during any medication trial.[11] A daily sleep diary template can be obtained from https://www.nhs.uk/livewell/insomnia/documents/sleepdiary.pdf

Melatonin prescriptions should be regularly reviewed in the context of any emerging possible side effects and/or reduced therapeutic effect.[11]

Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis/encephalopathy (ME)

The NICE guideline on diagnosis and management of myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome [NG206], does not mention melatonin.[14] Full details of the evidence and the committee's discussion are available in the evidence review F: pharmacological interventions. Melatonin was included in the search for evidence. However, the only study found was excluded as it contained no usable outcome data because the results were reported as medians.[15]

Cerebral palsy in under 25s

The NICE guideline on assessment and management of cerebral palsy in under 25s [NG62], states that, if no treatable cause for sleep disturbance is found, a trial of melatonin should be considered for children and young people with cerebral palsy, particularly for problems with falling asleep.[16]

Challenging behaviour and learning disabilities

The NICE guideline on prevention and interventions for people with learning disabilities whose behaviour challenges [NG11], states that medication should not be offered to aid sleep unless the sleep problem persists after a behavioural intervention. If this is the case, then it should only be prescribed after consultation with a psychiatrist (or a specialist paediatrician for a child or young person) with expertise in its use in people with a learning disability, together with non-pharmacological interventions and regular reviews (to evaluate the continuing need and ensure that the benefits continue to outweigh the risks).[17]

If medication is needed to aid sleep, melatonin should be considered, this is an off-label use.[17]

Parkinson's disease in adults

The NICE guideline on Parkinson's disease in adults [NG71], recommends considering melatonin (or clonazepam) to treat rapid eye movement sleep behaviour disorder if a medicines review has addressed the possible pharmacological causes. This is an off-label use of melatonin.[18]

Dementia: Alzheimer's disease

NICE [NG97] states that melatonin should not be offered to manage insomnia in people living with Alzheimer's disease.[19] For people living with dementia who have sleep problems, a personalised multicomponent sleep management approach should be considered that includes sleep hygiene education, exposure to daylight, exercise and personalised activities.[19]

Jet lag

There are several preparations of melatonin licensed for jet lag.[4-6] However, melatonin is not recommended to be prescribed for jet lag in primary care on the NHS because there is limited and conflicting evidence of benefit.[20-22]

Further information on advice to give to people who experience sleep disturbance due to jet lag can be found at https://cks.nice.org.uk/topics/sleep-disorders-shift-work-jet-lag/management/jet-lag/

Melatonin-induced sleep EEG

A melatonin-induced sleep recording is an alternative way to obtain a sleep recording in children and young people with epilepsy or suspected epilepsy.[23]

This should be prescribed in secondary care.

Clinical effectiveness

Robust, large-scale evidence to support the use of melatonin for insomnia is lacking and its long-term effects are unknown. A Canadian Health Technology Review published in 2022 suggested that melatonin may be effective for some sleep-related outcomes, such as decreasing sleep onset latency, increasing total sleep time and improving overall sleep quality, but this may differ depending on how it is measured, with some studies reporting mixed results.[24]

The effects of melatonin on sleep appear to be modest and the absolute benefit of melatonin compared to placebo is smaller than for other pharmacological treatments for insomnia.[25] In addition, there is currently no evidence to evaluate the cost-effectiveness of melatonin for insomnia in comparison to other treatments.[24]

There is evidence to support the use of melatonin to improve sleep onset latency and total sleep time in children and adolescents with a variety of neurodevelopmental disorders,[26] and children with ASD or neurodevelopmental disabilities caused by Smith-Magenis syndrome who have not shown improvement in insomnia after standard behavioural intervention.[27]

Prolonged-release melatonin is licensed as monotherapy for the short-term treatment (maximum duration 13 weeks) of primary insomnia in people aged 55 years or over.[2]

The Slenyto® brand of prolonged-release melatonin is licensed for the treatment of insomnia in children and adolescents aged 2-18 with ASD and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient.[28,29]

Immediate-release melatonin (not all brands) is licensed for the treatment of insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient.[4–6]

All other indications are currently unlicensed ('off-label' use of a licensed medicine) and the prescriber should be satisfied that there is no suitably licensed medicine that will meet the patient's need. Patients, or their parents or carers, must be given sufficient information about the unlicensed medicines proposed, to allow them to make an informed decision.[30]

Safety

The Adaflex® summary of product characteristics states that melatonin causes few, and no serious, adverse reactions in the short term, up to three months.[4] Reported adverse reactions to melatonin are mainly headache, nausea and fatigue in both adults and children.[4–6] These adverse reactions are, however, also common for placebo-treated patients in the relevant clinical studies and there was no significant difference between patients who received active treatments and placebo in these studies.[4] No serious adverse reactions have been observed in the paediatric population.[4] However, the long-term effects of melatonin are poorly studied.[4,5]

A retrospective cohort study looking at data from 2008 to 2013, of patients aged 45 years and older, attending UK primary care, showed that patients who received three or more melatonin prescriptions had a significantly elevated risk of fracture. Z-drugs were also associated with a significantly increased risk of fracture.[31] The risk of falls and fractures associated with melatonin should be considered before commencing treatment and at each review in patients aged 45 years or over.

The NICE CKS on insomnia lists the adverse effects of melatonin as: arthralgia, headache, increased risk of infection, abdominal pain, dyspepsia, dry mouth, mouth ulceration, nausea, weight gain, hypertension, chest pain, malaise, dizziness, restlessness, nervousness, irritability, anxiety, abnormal

dreams, proteinuria, glycosuria, pruritus, rash, dry skin, drowsiness, sleepiness, and disorientation with a moderate influence on ability to drive and use machines. Melatonin may cause drowsiness and may decrease alertness for several hours, therefore it is not recommended prior to driving and using machines.[1]

Treatment with melatonin is not recommended during pregnancy or in women of childbearing potential not using contraceptives as there are no data from the use of melatonin in pregnant women, animal studies are incomplete and exogenous melatonin is known to readily cross the placenta. Similarly, melatonin is not recommended during breastfeeding.[4–6] High doses of melatonin and use for longer periods than indicated may compromise fertility in humans.[4,6]

Multiple interactions exist with melatonin which may alter its safety by increasing plasma melatonin levels or producing additive adverse effects. Examples of agents known to interact include alcohol, combined hormonal contraceptives, quinolones, fluvoxamine, warfarin, opioids and other drugs with CNS depressant effects.[1] Prescribers should be familiar with the current prescribing information at the time of signing each prescription.

Patient factors

In some countries, melatonin is available to buy in health food shops or online. It is sold as a complementary medicine. However, these supplements are not authorised for sale in the UK, where melatonin is a prescription-only medicine.[32]

For patients with swallowing difficulties, melatonin is available as a 1mg/ml oral solution. This oral solution is licensed for sleep onset insomnia in children and adolescents aged 6–17 years with ADHD where sleep hygiene measures have been inadequate.[6]

In addition, 1-5mg immediate-release melatonin tablets (Adaflex®) can be crushed and mixed with water directly before administration as a licensed use for insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient.[4] It is a more cost-effective choice than the oral solution (as shown in table 1).

Circadin® can also be crushed. However, while there are no safety concerns with crushing this preparation, it will affect the prolonged-release properties of the product.[33] This is an off-label use.

A cost-effective licensed preparation should be selected where possible. Review patients prescribed unlicensed melatonin specials and discuss with them whether a change to a licensed alternative is suitable for them. For patients prescribed unlicensed or 'off-label' melatonin, where there is no suitable licensed alternative, they should be given sufficient information regarding this.

Digital sleep improvement and sleep diaries

There are a number of free sleep diary apps available to patients, which may be useful as part of a sleep assessment.

Sleepio™ is a self-help sleep improvement programme for adults based on cognitive behavioural therapy for insomnia (CBT-I). It is primarily accessed through a website, but there is an app available for iOS mobile and Android devices. It is designed to be completed in six weeks. It is structured around a sleep test, weekly interactive CBT-I sessions and regular sleep diary entries. NICE Medical technologies guidance [MTG70] recommends Sleepio™ as a cost saving option for treating insomnia and insomnia symptoms in primary care for people who would otherwise be offered sleep hygiene or sleeping pills.[34] A commissioning template for Sleepio™ can be found with the attachments accompanying this bulletin.

Deprescribing and drug holidays

For persistent chronic sleep disorders in children and adults, to ascertain whether there is an ongoing need for melatonin, a 'drug holiday' should be considered three months post initiation and six-monthly thereafter. Treatment can be stopped abruptly and should be stopped for two weeks.[35]

If sleep improvements are maintained without melatonin, therapy should be stopped.[35]

However, if sleep deteriorates and continues to be an issue, the original dose where sleep improved should be re-instated and ongoing drug holidays should be considered at annual review. If there is a consistent correlation of sleep deterioration during the drug holiday, patients should be advised to continue without a break unless they are suspected to be a poor metaboliser of melatonin.[35]

Poor metabolisers of melatonin may find that melatonin efficacy reduces over time as melatonin accumulates in the plasma and this leads to an absent peak concentration at bedtime. This is identified through clinical history; patients may report an initial benefit with melatonin and then ineffectiveness. These patients may need regular two week washout periods if and when benefit wanes, in order to see a continued effect with melatonin. A drug holiday when the effect has waned will facilitate washout and patients often see a benefit after recommencement.[35]

For patients under the age of 18 years or those under active specialist review for conditions relating to their melatonin prescription (including under formal shared care), primary care clinicians should not independently deprescribe melatonin as this should be done in liaison with their specialist.[36]

Costs and savings

There is a significant cost associated with both licensed and unlicensed melatonin. Table 1 illustrates the cost differences.[37]

Please note: Preparations listed in table 1 as unlicensed are those where a basic price has been set and is listed in the Drug Tariff.[37] All other unlicensed (or special-order) melatonin strengths and formulations have a reimbursement price that is unregulated and can therefore be subject to increased costs and considerable variation and fluctuation in cost. Refer to table 2 for a list of unlicensed melatonin specials preparations. Refer to the PrescQIPP bulletins on Specials prescribing and Repatriation of Specials for further information on specials.

Table 1: NHS reimbursement cost of melatonin[37]

Melatonin product	Cost per 28 doses
Melatonin prolonged-release	
Melatonin 1mg modified-release tablets	£19.23
Melatonin 2mg modified-release tablets	£14.36
Melatonin 3mg modified-release capsules (unlicensed)	£36.70
Melatonin 5mg modified-release tablets	£96.13
Melatonin immediate-release product	
Melatonin 1mg tablets	£12.41
Melatonin 1mg capsules (unlicensed)	£16.54
Melatonin 1mg/ml oral solution sugar free	£66.37 (2mg dose)
Melatonin 2mg tablets	£14.28
Melatonin 2mg capsules	£53.67
Melatonin 2mg/5 ml oral solution (unlicensed)	£19.24 (2mg dose)
Melatonin 2mg/5 ml oral suspension (unlicensed)	£25.20 (2mg dose)
Melatonin 2.5mg capsules (unlicensed)	£60.34
Melatonin 2.5mg/5 ml oral solution (unlicensed)	£17.21 (2.5mg dose)
Melatonin 2.5mg/5 ml oral suspension (unlicensed)	£13.13 (2.5mg dose)

Melatonin product	Cost per 28 doses
Melatonin 3mg tablets	£18.49
Melatonin 3mg capsules	£58.33
Melatonin 3mg/5 ml oral solution (unlicensed)	£18.76 (3mg dose)
Melatonin 3mg/5 ml oral suspension (unlicensed)	£27.36 (3mg dose)
Melatonin 4mg tablets	£18.88
Melatonin 4mg/5 ml oral suspension (unlicensed)	£192.02 (4mg dose)
Melatonin 5mg tablets	£21.72
Melatonin 5mg capsules	£98.00
Melatonin 10mg capsules (unlicensed)	£49.06
Melatonin 10mg/5 ml oral solution (unlicensed)	£23.44 (10mg dose)
Melatonin 10mg/5 ml oral suspension (unlicensed)	£23.35 (10mg dose)

There is usually a delay in supply associated with ordering unlicensed specials.

Action plan

1. Review all patients prescribed melatonin on the NHS for jet lag and discontinue treatment.
2. Melatonin should be discontinued for insomnia in people living with Alzheimer's disease.
3. Ensure that under 19s with autism have had melatonin recommended by a specialist paediatrician or psychiatrist with expertise in the management of autism or paediatric sleep medicine, and that they are using it together with non-pharmacological interventions. Suitable arrangements for the transfer of care should be in place.
4. Ensure that patients with challenging behaviour and learning disabilities have had melatonin recommended by a psychiatrist (or a specialist paediatrician for a child or young person) with expertise in its use in people with a learning disability, and that they are using it together with non-pharmacological interventions. Suitable arrangements for the transfer of care should be in place.
5. Review all adults aged 55 years and over on modified-release melatonin after three weeks of treatment and only continue for a further ten weeks if a response is seen. Review and deprescribe melatonin in adults after a total of 13 weeks treatment.
6. Review children on melatonin after three months and deprescribe melatonin if there is no clinically relevant treatment effect seen.
7. Initiate a two-week drug holiday for all suitable patients to assess their need for ongoing treatment, three months after the commencement of treatment and six monthly thereafter. If sleep improvements are maintained without melatonin, therapy should be stopped. If there is a consistent correlation of sleep deterioration during a drug holiday, patients should be advised to continue without a break unless they are suspected to be a poor metaboliser of melatonin (in which case regular washout with ongoing drug holidays when the benefit wanes is recommended).
8. For patients where caution should be exercised with drug-holidays and deprescribing, including patients prescribed melatonin under a shared-care agreement, refer to the patient's specialist for advice on managing this.
9. Ensure that patients prescribed an unlicensed "special" formulation of melatonin or are prescribed melatonin 'off-label' are given suitable information about this and have been reviewed to determine whether there is a licensed product available that suits their needs. To identify "specials", refer to table 1 which lists unlicensed specials included in the drug tariff and also table 2 which lists melatonin unlicensed specials formulations not included in the drug tariff.

Table 2. Unlicensed melatonin specials preparations[38]

Unlicensed melatonin specials preparation
Melatonin 500microgram capsules
Melatonin 500microgram tablets
Melatonin 1mg/ml oral solution alcohol free sugar free
Melatonin 1mg/ml oral drops
Melatonin 1mg/5ml oral solution
Melatonin 1mg/5ml oral suspension
Melatonin 2mg modified-release capsules
Melatonin 2.5mg tablets
Melatonin 3mg modified-release tablets
Melatonin 3mg lozenges sugar free
Melatonin 3mg orodispersible tablets
Melatonin 4mg capsules
Melatonin 4mg/5ml oral solution
Melatonin 5mg/5ml oral solution
Melatonin 5mg/5ml oral suspension
Melatonin 6mg modified-release capsules
Melatonin 6mg capsules
Melatonin 6mg tablets
Melatonin 6mg/5ml oral solution
Melatonin 6mg/5ml oral suspension
Melatonin 7mg/5ml oral solution
Melatonin 7mg/5ml oral suspension
Melatonin 7mg capsules
Melatonin 7.5mg capsules
Melatonin 8mg capsules
Melatonin 8mg/5ml oral solution
Melatonin 9mg capsules
Melatonin 10mg tablets
Melatonin 15mg/5ml oral suspension
Melatonin 20mg capsules

Savings

Based on three months prescribing data from NHSBSA (England and Wales Jul-Sept22) and Public Health Scotland (Scotland Jun-Aug22).

£17.8 million was spent on melatonin across England, Wales and Scotland. £1.1 million was spent on unlicensed melatonin specials across England and Wales.

As melatonin is only clinically indicated for specific indications and its long-term benefit is unclear, **a 25% reduction in the prescribing of melatonin preparations** (excluding melatonin 1mg, 2mg, 3mg, 5mg capsules, and melatonin 1mg/ml oral solution sugar free preparations as these are used in other saving calculations) **could release savings of approximately £10.9 million per annum across England, Wales and Scotland. This equates to £15,402 per 100,000 patients. A 25% reduction in unlicensed melatonin specials could save £334,360 annually across England and Wales.**

As the cost of melatonin specials not included in the Drug Tariff are unknown, savings figures from switching to a licensed melatonin alternative cannot be provided. However, it is likely that savings will be achieved as melatonin specials can be seen to be more expensive than licensed preparations when looking at prescribing data.

Where immediate-release melatonin is indicated, the tablets represent a more cost-effective choice than the capsules. **Switching 80% of patients on melatonin 1mg, 2mg, 3mg, or 5mg capsules to the respective strength tablet would save £2.5 million per annum in England and Wales and £1.1 million in Scotland. This equates to £5,240 per 100,000 population.**

Melatonin 1mg/ml oral solution sugar free is expensive compared to Adaflex® tablets (melatonin immediate release) which can be crushed and mixed with water directly before administration.[4] **Switching 50% of patients from melatonin 1mg/ml oral solution sugar free to Adaflex® tablets could save £6 million per annum in England and Wales and £850,364 in Scotland. This equates to £9,586 per 100,000.**

Summary

Large-scale, high-quality evidence to demonstrate the cost-effectiveness, and long-term efficacy and safety of melatonin for insomnia is lacking. In addition, many melatonin preparations are unlicensed "specials" or their use is off-label for various conditions and age-groups, which increases both prescriber responsibility and medico-legal risk. Regular drug holidays are recommended to ensure ongoing benefit beyond three months of treatment, and treatment should be discontinued when it is no longer indicated. Where immediate-release melatonin is indicated, the licensed tablets (crushed if needed) are more cost-effective than the capsules and liquid. Where modified-release melatonin is indicated, the 2mg prolonged release tablets are the least costly. In addition, melatonin is not recommended for jet lag on the NHS due to a lack of evidence.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-318-melatonin/
Implementation tools	
Data pack	https://data.prescqipp.info/?pdata.u/#/views/B318_Melatonin/Front-Page?:iid=1

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