Guideline on the Use of Melatonin for the Management of Sleep Disorders in Children, Adolescents, and Adults

Key Points

Initiation

Melatonin is not recommended for initiation in primary care. It should only be considered for initiation by specialists, where other sleep hygiene methods alone have been unsuccessful.

- The prescribing of melatonin in **CHILDREN / ADOLESCENTS** in Kent and Medway is ONLY supported for children / adolescents with sensory deficits, learning disabilities, an autistic spectrum condition, or living with Attention Deficit Hyperactivity Disorder (ADHD); and where it has been initiated by a specialist.
- Prescribing in **ADULTS** is ONLY supported for the **short-term treatment (up to 13 weeks maximum)** of primary insomnia in patients who are aged 55 or over. Primary i.e. insomnia not attributable to an underlying cause.
- Melatonin is NOT routinely funded for the management of jet lag within Kent & Medway and in patients with insomnia with Alzheimer's disease.[PRGC PR 2021-01]
- Non-pharmaceutical treatments (e.g. sleep hygiene, CBT) need to be continued if melatonin is started.

Review and Discontinuation

- 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, if appropriate.
- 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.

Product Choice

Preferred cost-effective product:

- **Melatonin 2mg modified-release (MR) tablets** (generic version of Circadin®).
  Must be prescribed generically as 2mg MR tablets (licensed product, off-label use).
  - For patients with swallowing difficulties melatonin MR 2mg tablets can be halved or divided into four to maintain the prolonged release effect to some extent.
  - For an immediate release effect and for patients with swallowing difficulties, take crushed and mixed with 15-30ml water, orange juice or milk or soft food for example jam or yoghurt (off-label).
- 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.
- Patients prescribed unlicensed or 'off-label' melatonin should be given sufficient information regarding this.

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Contents

Aim

This guideline has been designed to support clinicians within primary and secondary care with the management of melatonin prescribing for adults and children with sleep disorders within NHS Kent and Medway.
This guideline will also provide recommendations on the cost-effective prescribing of melatonin by considering product formulations and brand, groups of patients for whom melatonin is indicated, and information around review and discontinuation. Information on drug holidays will also be included. NB: The use of other hypnotics (e.g. benzodiazepines) will not be covered within this guideline.

Background

Melatonin is a naturally-occurring hormone produced in the brain by the pineal gland. It is normally produced in a circadian manner in response to falling light levels, with production starting in the evening and peaking around 2-4am. Its primary function is to induce the physiological changes which prepare the body for sleep, including a hypnotic effect and a fall in body temperature.

Since melatonin production is affected by light exposure detected by the retina; it is thought that this rhythm is disturbed in children with brain damage, neurodevelopmental disorders such as autism or visual disturbance.

Synthetic melatonin is used to promote sleep in a variety of conditions and is considered to have a favourable side-effect profile.

Non-pharmacological Treatment

The interventions stated below should be initiated by the clinician before considering any form of medication to treat the sleep difficulties. A sleep diary (Appendix 1) is recommended before commencing a trial of melatonin in children and adults. This should be completed for at least 2 weeks prior to starting melatonin to determine the baseline sleep pattern and to assess if sleep hygiene measures are being adhered to. Sleep hygiene measures and a sleep diary should continue throughout treatment with melatonin.

Patient response to treatment and the ongoing effectiveness of melatonin should be monitored using sleep diaries and assessment of sleep hygiene measures. Melatonin should only be continued where there is clear evidence of ongoing effectiveness. Prescribing of

melatonin should be reviewed regularly and treatment breaks are recommended to assess ongoing need.

Sleep hygiene

Advice on sleep hygiene should be offered to those with insomnia. For further information refer to:

- Sleep problems - Every Mind Matters - NHS (www.nhs.uk)
- Sleep hygiene tips - Headspace
- Healthy Sleep Tips for Children: https://www.nhs.uk/live-well/sleep-and-tiredness/healthy-sleep-tips-forchildren/
- Self referral form | With You Kent eReferral | IAPT Portal

Melatonin in Children and Adolescents

Treatment with melatonin should only be initiated by a **specialist clinician**, which may include Paediatric Consultant, Child Psychiatrist or Non-Medical Prescriber with a specialist interest in paediatric sleep disorders, in-line with this prescribing guidance.

Whenever possible the patient (and their parents / guardian) should be involved in the decision making about initiating treatment and should be given information about melatonin in order to make an informed choice. Printable leaflets including information about good sleep hygiene can be found at https://www.nhs.uk/live-well/sleep-and-tiredness/healthy-sleep-tips-for-children/

The prescribing of melatonin in children/adolescents in Kent and Medway is **only** supported for children/adolescents with sensory deficits, learning disabilities, an Autism Spectrum Disorder (ASD) or those living with ADHD.

Melatonin prescribing in children is specialist initiation only – the dose should be stabilised and response to melatonin assessed before prescribing can be continued in primary care. Continued prescribing and monitoring of melatonin will usually be the responsibility of the GP. It will be expected that the specialist initiating melatonin will be responsible for providing advice for deprescribing.

Dosage

Consult the latest edition of the British National Formulary for Children: https://bnfc.nice.org.uk/

Initially 2 mg once daily, increased to 4mg once daily after 5 days if required. The dose should be taken before bedtime.

If treatment at 4mg daily remains ineffective at controlling sleep, advice of a specialist clinician should be sought as daily doses of 6mg and above are rarely required.

Patients and carers should be advised on initiation that treatment with melatonin and the need for continued use, will be reassessed every 6 months via a treatment holiday (see section on review below).

Renal impairment: The effect of any stage of renal impairment on melatonin pharmacokinetics has not been studied. Caution should be used when melatonin is administered to such patients.

Hepatic impairment: There is no experience of the use of melatonin in patients with liver impairment. Published data demonstrates markedly elevated endogenous melatonin levels

during daytime hours due to decreased clearance in patients with hepatic impairment. Therefore, melatonin is not recommended for use in patients with hepatic impairment.

Melatonin in Adults

Treatment with melatonin should only be initiated by a **specialist clinician**, which may include Consultant Psychiatrists, Secondary Care Geriatricians or Non-Medical Prescribers with a specialist interest in sleep disorders, in-line with this prescribing guidance.

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. 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).

Dose: 2 mg once daily for up to 13 weeks, dose to be taken 1–2 hours before bedtime.

Review, Drug Holiday, and Discontinuation

There is no routine ongoing monitoring required specifically for melatonin in primary care other than monitoring for possible adverse effects and continued need.

A melatonin drug holiday should be attempted every 6 months as some children/ adolescents will have settled into a regular sleep pattern and may not need to continue at the same dose or may even be able to maintain sleep with no melatonin.

This could be considered during school holidays or over an extended weekend. However, timing of a treatment holiday should be in discussion with the patient / guardian and consider individual circumstances where the impact of potential sleep disruption can be minimised.

If sleep patterns are maintained during the treatment holiday, stopping melatonin permanently should be considered. Or alternatively, if treatment with melatonin is still required, dosing can be reduced by 2mg. If the difficulties recur the original dose should be reinstated, but a further trial reduction / treatment holiday should be attempted 6 months later, and every 6 months thereafter.

Some clinical experience from the National Child and Adolescent Learning Disability Psychiatry Network suggests that the efficacy of melatonin may be lost if prescribed for longer than two years continuously. It suggests that if melatonin is withdrawn prior to this, sensitivity may be re-established, and melatonin successfully re-introduced at a lower dose if still required.

Reinforcement of good sleep hygiene should be discussed at each 6-monthly review and should be continued by the child / adolescent in conjunction with melatonin prescribing.

Individual patients may require additional monitoring based on co-morbidities or interacting medicines. It is likely these patients would remain within secondary care / community services and any primary care monitoring will be agreed on a case-by-case basis.

Children transitioning to adults

Melatonin is not currently recommended across Kent and Medway for adult patients under 55 years old. Young people who are transitioning to adult services or reach 18 years should be reviewed in conjunction with advice from the specialist services where applicable.

If sleep concerns remain, treatment should follow standard guidance for adults with sleep problems.

The expectation is for children's services to be responsible for reviewing and deprescribing melatonin prior to the child turning 18 years old.

NHS Kent and Medway do not support the prescribing of melatonin in adults under 55 years old.

Product choice

Preferred cost-effective product:

- Melatonin 2mg MR tablets (generic version of Circadin®). Must be prescribed generically as 2mg MR tablets *(licensed product, off-label use)*.

For patients with swallowing difficulties:

- Melatonin MR 2mg tablets can be halved or divided into four to maintain the prolonged release effect to some extent.
- For an immediate release effect and for patients with swallowing difficulties, melatonin 2mg MR tablets can be crushed and mixed with water, orange juice, milk, or soft food e.g. jam or yoghurt (off-label) and given immediately, or added to 15-30ml water for administration via enteral feeding tubes.

(Licensed product, off-label use/administration)

Note – the MR properties will be lost once crushed and the product will be equivalent to immediate-release (IR). The tablets are not film-coated.

Restricted use:

Alternatives (ONLY if preferred cost-effective product is not tolerated/suitable e.g. feeding tubes, and indication-specific licensed products needed):

- Adaflex® 1mg, 2mg, 3mg, 4mg, and 5mg standard release tablets. ONLY use if preferred product is not tolerated/suitable, and ONLY in children aged 6-17 years with ADHD. The tablet can be crushed and mixed with water directly before the administration. Must be prescribed by brand name *(licensed product, licensed use).*

- Slenyto® 1mg MR and 5mg MR tablets. ONLY use if preferred product is not tolerated/suitable, and ONLY in children aged 2-18 years with Autism Spectrum Disorder (ASD) and/or Smith-Magenis Syndrome (SMS). Must be prescribed by brand name *(licensed product, licensed use)*.

- Ceyesto 3mg standard release tablets. ONLY use if preferred product is not tolerated/suitable, and ONLY in children aged 6-17 years with ADHD and insomnia, where sleep hygiene measures have been insufficient. Must be prescribed by brand name *(licensed product, licensed use)*.

- Melatonin 1mg/ml oral solution (Colonis Pharma Ltd) – use is restricted only to patients for whom tablets (including crushed tablets) are not tolerated/suitable e.g. feeding tubes, due to higher cost and safety concerns with formulation containing excipients potentially harmful to children (e.g. propylene glycol, sorbitol). Melatonin 1 mg/ ml oral solution is not recommended for use in children younger than 6 years of age. But can be considered as an alternative for administration via fine bore feeding tubes or a very limited number of children who will not tolerate the crushed melatonin 2mg MR tablets

e.g. those with significant feeding difficulties who do not have a feeding tube *(licensed product/administration, off-label use).* Note: Safety concerns are dose dependent.

Patients prescribed unlicensed or 'off-label' melatonin should be given sufficient information informing them of this.

Contraindications and Cautions

For latest information on contraindications and cautions please consult the latest edition of the British National Formulary (BNF or BNFc) https://bnf.nice.org.uk/ or Summary of Product Characteristics (SPC) for individual melatonin products: http://www.medicines.org.uk/emc/

Adverse effects

For latest information on adverse effects please consult the latest edition of the British National Formulary (BNF or BNFc) https://bnf.nice.org.uk/ or Summary of Product Characteristics (SPC) for individual melatonin products: http://www.medicines.org.uk/emc/

Drug Interactions

For latest information on drug interactions please consult the latest edition of the British National Formulary (BNF or BNFc) https://bnf.nice.org.uk/ or Summary of Product Characteristics (SPC) for individual melatonin products: http://www.medicines.org.uk/emc/

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