Melatonin prescribing guidance for Adaflex®, Slenyto® and Ceyesto® in the treatment of insomnia in children and young people aged 6 to 18 with years with a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD) or Smith Magenis Syndrome (SMS)

This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Introduction

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced by the pineal gland during the dark hours of the day and night which appears to support the normal circadian rhythm and aid sleep onset. It is used as a treatment of sleep disorders in children. It is most helpful where sleep onset is a significant problem but is rarely useful to maintain sleep if a child is waking during the night. Melatonin should not be used in isolation but should be combined with a behavioural programme, involving Clinical Psychology where necessary.

Specialist assessment for melatonin treatment

Specialist prescriber should:

- Rule out other causes of insomnia (e.g. bedtime resistance, sleep disordered breathing, side effects of medication (e.g. stimulants), nocturnal enuresis, mouth breathing, presence of pets waking them up).
- Give parents and young people with insomnia written advice and guidance on good sleep habits (sleep hygiene).
- Ask carers/parents to complete a sleep diary for 7 nights where practical to do so.
- If the patient is on a stimulant medication, consider timings and release profile of formulation and seek pharmacy advice, if needed.
- Complete baseline sleep evaluation (using questionnaire such as the sleep disturbance scale for children).

Where optimising sleep hygiene measures and support mechanisms in the above steps have been unsuccessful or are not appropriate, and the insomnia is negatively affecting the patient's well-being, a trial of melatonin may be considered.

Initiation of melatonin by specialist

Specialist prescriber should:

- Outline to the patient and family/carers risks and benefits of melatonin, including side effects and aims of treatment.

- Explain that melatonin is not intended to be taken long term; it is used to support the family to re-establish a good sleep pattern.
- Explain the treatment plan and dosing schedule.
- Explain the recommended treatment breaks to assess whether melatonin is still required. See the deprescribing section for details.
- Document the target symptoms for melatonin treatment (e.g. sleep onset, sleep duration, sleep quality).
- Optimise the dose of melatonin over at least twelve weeks before requesting primary care to take over prescribing under an individual management plan.
- Review the effectiveness of melatonin at 12 weeks.
- The management plan should include:
  - The outcome of the assessment.
  - Any sleep hygiene methods to be continued.
  - Brand of melatonin and dose to be prescribed.
  - Outcome of three-month review.
  - Prescribing team's contact details.
  - Parents understanding of treatment breaks and commitment to carry out every six months. (Leaflet available in appendix 1)

Melatonin (Adaflex®) for the treatment of insomnia in patients with ADHD

Prescribing status: Amber 2 (initiation by specialist and stabilisation for 12 weeks then continuation in primary care).

Adaflex® is licensed for Insomnia in children and adolescents aged 6 to17 years with ADHD, where sleep hygiene measures have been insufficient.

- In ADHD, sleep onset is the primary issue as, once asleep, the children tend to remain asleep. Therefore, an immediate release preparation is preferable to minimise hangover effect which may occur with a modified release product.
- First line is melatonin (Adaflex®) tablets (available as immediate release 1mg, 2mg, 3mg, 4mg and 5mg). Prescribers should prescribe by brand.
- Starting dose 1 milligram to 2 milligrams administered 30 to 60 minutes before bedtime.
- If an inadequate response has been observed, the dose should be increased by 1 milligram every week until up to a maximum 5 milligrams per day, independent of age. The lowest effective dose should be used.
- The tablet is licensed to be crushed and mixed with water directly before the administration. Guidance on how to mix.
- Specialist to review after first 3 months before requesting that prescribing is transferred to primary care.
- In primary care the child/young person should have a 2-week break from medication every 6 months to check if it is still required. Parents should be encouraged to choose a suitable time during school holidays. Refer to deprescribing of melatonin and treatment breaks for details.

- In primary care, medication should be reviewed as part of annual medication review - for those children on ADHD medication, melatonin should be reviewed alongside their ADHD medication as part of their annual specialist (ASR) review where clinically appropriate.
- Maximum duration of treatment is 2 years as per local agreement in line with trial data.

Patients with swallowing difficulties:

- First line: Melatonin (Adaflex®) tablets, crushed and mixed with water directly before administration (licensed).
- Second line: Melatonin (Ceyesto®) 1 milligram per millilitre oral solution.

Melatonin (Slenyto®) for treatment of insomnia in patients with ASD/SMS

Slenyto® is licensed for the treatment of insomnia in children and adolescents aged 2 to18 with Autism Spectrum Disorder (ASD) and / or neurogenetic disorders with aberrant diurnal melatonin secretion and /or nocturnal awakenings, where sleep hygiene measures have been insufficient.
Prescribing status: Amber 2 (initiation by specialist and stabilisation for 12 weeks then continuation in primary care).

- The sleep patterns in children with autism are often different from those children with ADHD. Children with ASD often experience multiple awakenings through the night.
- Melatonin (Slenyto®) prolonged-release tablets (available as 1 milligram and 5 milligrams) and should be prescribed by brand.
- Starting dose 2 milligrams once daily administered 30 to 60 minutes before bedtime and with or after food.
- If an inadequate response has been observed, the dose should be increased to 5 milligrams, with a maximal dose of 10 milligrams once daily.
- Should be swallowed whole, and not broken, crushed, or chewed. May be mixed into food such as yoghurt, orange juice or ice cream to aid swallowing.
- Specialist to review after first 3 months before requesting that prescribing is transferred to primary care.
- In primary care the child/young person should have a 2-week break from medication every 6 months to check if it is still required. Parents should be encouraged to choose a suitable time during school holidays. Refer to deprescribing of melatonin and treatment breaks for details.
- In primary care medication should be reviewed as part of annual medication review - for those children on ADHD medication, melatonin should be reviewed alongside their ADHD medication as part of their annual specialist (ASR) review where clinically appropriate.
- Maximum duration of treatment is 2 years as per local agreement in line with trial data.

Information on Slenyto® & Adaflex®

- For the most up to date information on cautions, contraindications, side effects and interactions please refer to the Summary of Product Characteristics (SPC) of these products Slenyto® and Adaflex®.
- Cautions
    - Avoid in patients with autoimmune diseases.
    - Should be used with caution in patients with epilepsy.
    - Information for patient's and carers is available as a leaflet.

Information on Ceyesto® (melatonin 1 milligram per millilitre oral solution)

- For the most up to date information on cautions, contraindications, side effects and interactions please refer to the Summary of Product Characteristics (SPC) of this product Ceyesto®.
- Cautions
    - Avoid in patients with autoimmune diseases.
    - Should be used with caution in patients with epilepsy.
    - Information for patient's and carers is available as a leaflet.
    - Licensed for administration via silicone gastric, duodenal, or nasal feeding tubes.
    - Care should be taken as to the propylene glycol content of liquid preparations. [NB. Melatonin liquid manufactured by Colonis Pharma Ltd should not be prescribed].

Ongoing management of insomnia

On-going management of insomnia in children and adolescents with ADHD, ASD or SMS by specialist or health care professional in primary care.

- Continue to use sleep hygiene measures and sleep diary.
- Monitor continued positive impact on sleep.
- Stop treatment if ineffective i.e. no response after 3 months.
- Child should have a 2 week break from medications every 6 months to check if it is still required. Refer to deprescribing of melatonin and treatment breaks for details.
- Monitor weight, growth velocity and sexual development and refer to specialist if outside normal parameters.

Deprescribing of melatonin and treatment breaks

- All patients who have been optimised on melatonin should have a 2 week break every 6 months to assess for on-going need. This is because some patients 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 medication.
- Ensure good sleep hygiene and routine has been implemented. Where available a sleep diary to inform this.
- Where a trial discontinuation is deemed appropriate, the melatonin should be stopped for at least one week. If there is no change in sleep onset,

morning wake time or quality of sleep during this break, then melatonin should be stopped.

- Where a dose reduction is deemed appropriate, discuss the speed of reduction with the patient/family/carer and taper the dose down at an increment and interval which the patient feels comfortable with. The dose can be reduced by up to 2 milligrams every 4 to 6 weeks.
- If the sleep difficulties recur the melatonin should be re -titrated up to the previous dose where sleep was maintained, but a further trial reduction should be attempted 6 months later.
- Reinforce the importance of good sleep hygiene to reduce insomnia.
- Review patients, ideally with reference to data from a sleep chart to assess the impact of the change.
- Melatonin is not known to cause dependency and there are no known harmful effects if treatment is interrupted or abruptly stopped.

Melatonin treatment should not be considered as indefinite. The long term safety of melatonin therapy in children has not been established. The annual review should determine if treatment remains efficacious for the individual and if the patient still requires melatonin therapy or if sleep hygiene measures are now sufficient.

Treatment break tips

- Pick a time that is least stressful for carers e.g., school holidays, no big events planned.
- The treatment break can happen at any dose. No titration is absolutely necessary.
- If there is no clear benefit, the melatonin can be stopped.
- Use a sleep chart before and during the treatment break where appropriate.
- If it decided to restart the melatonin, consider starting at a lower dose as this may be more effective after a treatment break.

Transition to adult services

A pragmatic approach should be used for young people who are transitioning into adult services. Whilst any intervention which risks causing a deterioration in the patient's clinical picture would be counterproductive, a revisiting of sleep hygiene measures along with consideration of new services available to support the young adult would be encouraged. A sleep diary may also be beneficial at this stage to ascertain if any ongoing melatonin prescriptions are still conferring a clinically significant benefit.

Contact details for specialist advice.

Merton CAMHS, Mitcham

- Tel: 0203 513 6062
- Email: Merton SPA via eRS, subject: psychiatry advice or consult with GP

Kingston & Richmond CAMHS

- Email: Kingston and Richmond SPA via eRS, subject: psychiatry advice/consult with GP

Sutton CAMHS, Wallington

- Email: Sutton SPA via eRS, subject: psychiatry advice/consult with GP

Wandsworth CAMHS, Springfield Hospital

- Email: Wandsworth SPA via eRS, subject: psychiatry advice/consult with GP

Medicine information services

- Specialist pharmacy advice is available through local medicines information (MI) services.
- Patients across the London boroughs of Kingston, Merton, Richmond, Sutton, and Wandsworth can contact the SWLSTG MI service on 0203 513 5829.
- Healthcare professionals should use the contact form.
- Patients/healthcare professionals from the London borough of Croydon can contact the SLaM MI service on 020 3228 2317.

Disclaimer

The recommendations in these guidelines do not override the responsibility of healthcare professionals to make decisions according to the circumstances of the individual patient, in consultation with the patient and/or their carers or guardian.

Document History

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Appendix 1: Treatment break information for parents/carers

Melatonin is a medication used to help children and young people establish a regular sleep pattern. However, the long-term safety of melatonin use in children has not been fully studied, so it should not be used indefinitely. Once a regular sleep pattern is achieved, some children may be able to maintain sleep without melatonin or may need a lower dose.

To check if melatonin is still needed, it is recommended that all patients have a treatment break every 6 months. Your specialist would have discussed this with you when melatonin was first prescribed.

Important points:

- Melatonin is not known to cause dependency and there are no known harmful effects if treatment is stopped suddenly.
- Taking breaks from melatonin helps assess if your child still needs it.

When is a good time to consider a treatment break?

It is important that you choose a time that is suitable for your family and circumstances where sleep disruption will have the least impact.

School holidays are often a good time to consider a break.

How to carry out a treatment break

There are two possible options:

1. Stop melatonin completely for 1 to 2 weeks. This can be done at any dose.
2. Reduce the dose gradually. The dose can be reduced by up to 2 milligrams every 4 to 6 weeks, at a pace that feels comfortable for you and your child.

What happens during a treatment break?

- If there is no change in sleep (e.g. no issues getting to sleep, waking up, or sleep quality), then melatonin should be stopped. Inform your GP.
- If the sleep problems return, the melatonin should be increased back up to the dose that worked before. inform your GP of the new dose and plan another treatment break in 6 months.

Good sleep hygiene

Good sleep habits are important for healthy sleep, whether or not melatonin is used. Maintaining good sleep hygiene will support your child's sleep even if your child's sleep, even if melatonin is stopped.

- Sleep hygiene advice is available from the following websites:
- Sleep problems - Every Mind Matters - NHS Sleep Hygiene Tips - Headspace
- Sleep tips for children: Relaxation Tips - The Sleep Charity