SHARED CARE PRESCRIBING GUIDELINE
Melatonin for treatment of sleep disorders in children and adolescents (age 1-17 years)

NOTES to the GP

The information in the shared care guideline has been developed in consultation with South East London CCG and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing **melatonin for the treatment of sleep disorders.**

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local Borough Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email back to a secure nhs.net account to the requesting clinician if you are in agreement to participate in shared care.

If you are not in agreement, please include reasons for this.

GP DECISION FORM

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of melatonin for the treatment of sleep disorders in children and adolescents can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE
Melatonin for treatment of sleep disorders in children and adolescents

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient/carer Agreement:**
Hospital requesting shared care:	Patient / carer agrees to shared care ☐ Patient /carer does not agree to shared care ☐
GP Name:	
This is to confirm that I agree to participate in shared care for Melatonin for the treatment of Sleep disorders for this patient as outlined in this shared care document	
GP Signature:	
Date signed:	

ACTION

1. HOSPITAL / COMMUNITY CONSULTANT

	Tick to confirm
▪ Explain shared care to patient/ carer and obtain agreement	☐
▪ Date agreement obtained: _____	
▪ Indicate requesting hospital /clinic	☐
▪ Complete and sign agreement	☐
▪ Email (to secure email) full shared care guideline (including signed agreement to GP)	☐
▪ Place original in patient's notes	☐

2. GP PRACTICE

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** to either:

Email address (via secure nhs.net): …… [TRUST to ADD email address]

- If **you do not agree** to participate in shared care, contact consultant and borough Medicines Optimisation Team **within 2 weeks** of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the borough Medicines Optimisation Team should be informed.
- Once decision reached file a copy in the patient's medical notes.

Melatonin for sleep disorders in children and adolescents

1. CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with a minimum of **2** months' supply of therapy.

2. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Make the necessary diagnosis as part of a thorough assessment. This should include a thorough history and a sleep diary if there is any doubt about the extent of the problem.
- Establish and document any allergies and previous hypersensitivity.
- Discuss the treatment options with the patient/carer(s) to include explanation of the nature of the melatonin, the need for Shared Care (once dose stabilised), ensuring and documenting that they have a clear understanding of benefits, side effects, frequency of administration and monitoring requirements and obtaining appropriate consent to treatment.
- Provide written information on melatonin to families. https://www.medicinesforchildren.org.uk/melatonin-sleep-disorders
- Initiate treatment with melatonin if agreed.
- Prescribe melatonin as a second-line treatment option where non-pharmacological strategies such as sleep hygiene advice have failed, and underlying causes are managed and continue to prescribe during the dose titration phase until the patient's condition is stable or predictable.
- The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
  - A copy of the shared care guidelines with the relevant amendments made under agreement to participate in shared care (page 2).
  - That a prescription for a minimum of the first 2 months supply has been given
  - A request that the GP continue prescribing after a minimum of 2 months post initiation
  - Information on when the patient will next be reviewed and by whom.
  - Clear information on the exact formulation that the patient has been initiated on.
- Review patients every 12 months to assess continuing benefit of melatonin. A trial withdrawal should be considered at each medication review. This can take the form of a treatment holiday where the melatonin is withdrawn over the period of one week. The Consultant/Specialist should feedback to the GP the outcome of the withdrawal.
- To ensure appropriate monitoring is undertaken.
- Establish and document any patient allergies and previous hypersensitivity.
- Report any suspected adverse drug reaction (ADRs) to the Medicines and Healthcare Products Regulatory Agency (MHRA) via the Yellow Card scheme. https://yellowcard.mhra.gov.uk/
- Promptly communicate any changes, recommendations, outcomes or other important information to the GP.
- Provide advice to the GP, or patient if they have clinical queries relating to the condition or use of melatonin.
- Take back the care of the patient should the GP feel unable to continue to manage the prescribing of melatonin.

General Practitioner responsibilities

- Ensure that they are aware of the details of the shared care agreement
- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is required within 2 weeks of receipt of this guideline by completing and returning the agreement on page 2.
- If you do not agree to shared care you must discuss with requesting consultant or local clinical commissioning group medicines management team within 2 weeks of receipt of shared care request.
- To prescribe ongoing prescriptions of melatonin (as per the brand that the patient had been initiated on in the specialist clinic) once patient is stabilised on an established dose by the consultant (should be after initial minimum 2 months' supply from specialist).
- Discontinue the medication if necessary, or requested.
- Refer the prescribing back to the specialist should unmanageable problems arise and allow an adequate notice period for mechanisms to be put in place to provide the next prescription e.g. for an appointment to be made if necessary (4 weeks is the suggested minimum).
- Ensure compatibility of concomitant medication with melatonin.
- To agree monitoring requirements with specialist – see page 6 for ongoing review.

General Practitioner responsibilities (continued)

- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team.
- To advise the specialist if non-compliance is suspected.
- To refer back to specialist if the patient's condition deteriorates.
- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme: https://yellowcard.mhra.gov.uk/

Patient's / Carer's responsibilities

- To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies, or recreational drugs.
- To inform community pharmacists that they are using melatonin before purchasing medication over the counter.
- To attend all hospital and GP appointments.
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others.
- To complete a sleep diary over 10-14 nights or as directed by the specialist before initiation and during treatment to help evaluate efficacy.
- To read the patient information leaflet included with the medication.
- To report any adverse effects or warning symptoms to GP or hospital specialist.
- To report to GP and Specialist team if pregnant or breastfeeding.
- To request for repeat prescriptions to be requested in a timely manner.
- To inform GP and hospital of any changes in addresses or telephone contact numbers.

3. CLINICAL INFORMATION

Melatonin is a naturally occurring hormone produced by the pineal gland in the brain. It appears more effective in helping children to fall asleep sooner, (reducing sleep latency rather than reducing waking in the middle of the night). It can slightly increase the total time asleep, but this is variable and over some time children taking melatonin may start to wake earlier.

Indication(s)

Melatonin is indicated for treating a range of sleep disorders in children. Primarily these will be sleep onset insomnia (problems falling asleep at an age appropriate time despite appropriate bedtime routines and sleep hygiene) or sleep rhythm problems like delayed sleep phase syndrome. Both these sleep disorders are seen more commonly in children who have neurodevelopmental disorders including visual impairment, cerebral palsy, attention deficit hyperactivity disorder, autism and learning difficulties.

More detail on the preferred preparations and indications can be found in the Guidance for prescribing melatonin for sleep disorders in paediatrics (children and adolescents) in South East London .

Place in Therapy

Evidence shows that melatonin should be prescribed after an appropriate behavioural sleep intervention has been trialled. There is additional evidence that there are advantages continuing a behavioural sleep intervention even when melatonin is prescribed as the two work well in combination

- Symptoms of sleep disturbance should have been present for at least 6 months, or sleep disturbance is so severe that it is causing significant family disturbance.
- Sleep hygiene/behavioural measures have been trialled without success.

Dose & route of administration

Preparations and their place in in therapy (refer to the pathways for dosing information)

Preparation	Licensing status in paediatrics	Place in therapy	Other points to note
Melatonin 2mg modified release tablets (Circadin®) (Summary of Product Characteristics [SPC] available here.	Off-label use in paediatrics of a licensed product. Circadin® is licensed for use as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over.	First line choice unless patient meets criteria for the other preparations noted below.	**For patients with swallowing difficulties:** • Circadin® tablets can be crushed to a fine powder and mixed with water or given with cold soft food such as a teaspoon of yoghurt or jam. Use a small amount of food to ensure the full dose is taken. The prescription should state that the medication is to be crushed prior to administration. • Circadin® tablets can also be halved (using a tablet cutter) **For administration via an enteral feeding tube:** • Circadin® tablet can be crushed to a fine powder and added to 5 - 10ml of water and mixed well.
Melatonin 1mg and 5mg prolonged release mini-tablets (Slenyto®) SPC 1mg prolonged release tablet SPC 5mg prolonged release tablet	Licensed for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient.	Reserved for use in patients who meet the Slenyto® licensed cohort.	• Circadin™ remains the first line preparation in patients who have insomnia due to attention deficit hyperactivity disorder (ADHD) but do not have ASD. • Slenyto™ is not licensed for use in adults. • Data are available for up to 2 years' treatment. • SPC notes monitoring of patient at regular intervals (at least every 6 months).
Melatonin 1mg per 1mL oral solution	Unlicensed preparation (special)	Reserved for use in patients with fine-bore enteral feeding tubes (gauge less than 9) where there is risk of tube occlusion or if there are compliance issues with the crushed tablets.	• The preferred oral solution is Kidmel® due to a more acceptable excipient profile. • In cases where the enteral feeding tube is no longer required, the need for liquid preparation should be reviewed.

Long term data and safety of melatonin

In the more recent largest placebo-controlled studies to date involving children with learning difficulty, autism and epilepsy (Coppola et al. 2004; Garstang and Wallis 2006; P. Gringras, Gamble, and Jones 2012; Buckley et al. 2020), there were no excess adverse effects in the treatment group over that recorded for placebo, and in particular seizures were not worsened. A Cochrane review found no worsening of seizure frequency in patients with epilepsy given melatonin. (Brigo, Igwe, and Del Felice 2016). There was no detectable impact on puberty in a paper by Malow et al. (Malow et al. 2006)

Switching melatonin preparations

Switching of stable patients prescribed Circadin® to alternative melatonin preparations is not supported by this guidance. However switching from unlicensed oral solution to tablets (in a whole or crushing) following review could be more cost-effective.

Prescribing by brand

To avoid confusion in the selection of products, it is recommended that melatonin preparations are prescribed by brand.

Daily dose of melatonin

Based on local expert opinion, in most patients a total daily dose of melatonin up to 6mg daily is usually sufficient to manage the patient's sleep disorder. In line with the BNF for Children, the maximum daily dose of melatonin should not exceed 10mg daily.

Transition to adult services

As part of the process of transitioning to adult services, the continued need for melatonin and choice of preparation should be reviewed by the adult team that the patient transfers to. Where continued melatonin treatment is considered clinically appropriate in adulthood, the preparation should be reviewed to ensure it is appropriate (for example, Slenyto® is currently only licensed in ages 2 – 18 years or consider if patients receiving the oral solution can change over to the tablet formulation).

Duration of treatment

- The duration of treatment should be determined on an individual basis. The aim is to establish healthy sleeping habits with the lowest effective dose of melatonin.
- It is suggested that at least 6 months of an improved sleep pattern should elapse before withdrawal takes place. These can take the form of 5 day complete break and a change in sleeping pattern observed. For some children withdrawal is not successful and treatment may be necessary for the longer term.

Criteria for stopping treatment

- Significant adverse reaction.
- Lack of efficacy.
- At request of patient/family.
- Specialists should review the need for continued treatment at each appointment (at least every 6 -12 months) and advise the GP of continuation, changes or discontinuation of treatment.

Ongoing review of patients on melatonin for sleep disorders

Please also see 'Guidance for prescribing melatonin for sleep disorders in paediatrics (children and adolescents) in South East London' **for further information.**

Consultant:

- Patients will remain under the specialist paediatric team and the specialist paediatric team will retain responsibility for regular review of treatment (6 monthly recommended). Patients will be reviewed by the specialist team against the outcomes noted in the pathways. The process for implementing any treatment breaks (e.g. 5 days in every month or annual treatment breaks) will be communicated to the GP by the paediatric specialist.

GP

- Report any suspected adverse effects to the MHRA: https://yellowcard.mhra.gov.uk/
- If melatonin still improves sleep but no evidence of increased effectiveness immediately following break - maintain on optimal dose and evaluate with care completed 1 week sleep diary every 6 months
- If melatonin still improves sleep but evidence of increased effectiveness immediately following break - maintain current optimum dose but with regular 5 day breaks e.g. every month

Practical issues including other relevant advice/information

Reminder: The information here is **not** exhaustive – Please consult the current Summary of Product Characteristics prior to prescribing for full details of adverse effects and all potential drug interactions cautions and contraindications(available via www.medicines.org.uk)

Melatonin is generally well tolerated. However the full adverse effect profile is unclear due to the small size of trials and unlicensed status.

- The most frequently reported adverse reactions reported were fatigue, mood swings, aggression, irritability, somnolence, headache, sudden onset of sleep, sinusitis, and hangover. There have also been some reports of confusion, pruritus, hypothermia, tachycardia, nightmares, mild depression, morning grogginess and skin rashes.
- Melatonin may cause drowsiness, so should be used with caution if the effects of drowsiness are likely to be associated with a risk to safety.
- No clinical data exist concerning the use of melatonin in individuals with autoimmune diseases. Therefore melatonin is not recommended for use in patients with autoimmune diseases.
- Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Concomitant use with fluvoxamine, alcohol, benzodiazepines/non-benzodiazepines hypnotics, thioridazine and imipramine is not recommended. Please refer to Summary of Product Characteristics for full list of interactions (see reference below)
- Elevated endogenous melatonin levels have been associated with an increased incidence of nocturnal asthma, although there is at least one study in adults that demonstrated an improvement in sleep in adults with asthma following administration of 3mg melatonin, with no apparent worsening of asthma symptoms.
- Paradoxical wakefulness has been reported. Melatonin may also affect serotonin levels. In overdose, blurred vision and dizziness have been observed and possible nystagmus. Based on the known physiological effects of

melatonin there could be potential for inhibition of reproductive functions and delayed puberty. Effects on foetuses or breast-fed children are unknown, but their circadian rhythm could be disturbed.

- There is a known potential for melatonin to affect seizure control in patients with epilepsy. Some reports suggest an improvement, whilst others indicate a worsening of control. The effects of introduction and titration of melatonin in epileptic patients should be closely monitored. There may also be theoretical implications when melatonin is used in conjunction with drugs that lower the seizure threshold. Tolerance does not appear to be a problem, but clinicians should remain alert to the possibility.
- Any suspected adverse effects should be reported using the Yellow Card system. https://yellowcard.mhra.gov.uk/ Clinicians should make their colleagues aware of any problems they identify.
- Melatonin metabolism is mainly mediated by CYP1A enzymes. Therefore, interactions between melatonin and other active substances as a consequence of their effect on CYP1A enzymes are possible.

NB. For full details of adverse effects and drug interactions refer to latest Summary of Product Characteristics.

Information provided to the patient

- Helping Your Child Sleep – information for parents of disabled children – published by Contact a Family (2018). This is available either in Clinic or at https://contact.org.uk/media/1183103/helping_your_child_sleep.pdf
- Sleep Problems in Children and Young People; Yemula C.R. Dwarakanathanb, Yemula R (2014) Published by Health Insights 4 U Ltd. http://healthinsights4u.com/3d-flip-book/sleep-problems-in-children-and-young-people-a-simple-guide-for-parents/
- Medicines for Children have also produced a PIL and is available via https://www.medicinesforchildren.org.uk/melatonin-sleep-disorders
- A sleep diary is available from https://patient.info/health/insomnia-poor-sleep/features/sleep-diary
- Sleeping Well. http://www.rcpsych.ac.uk/mentalhealthinfo/problems/sleepproblems/sleepingwell.aspx

Evidence Base for treatment and key references

- Guidance for prescribing melatonin for sleep disorders in paediatrics (children and adolescents) in South East London October 2020
- Summary of Product Characteristics Circadin® https://www.medicines.org.uk/emc/product/2809 last accessed 08/04/2021
- Summary of Product Characteristics Slenyto® https://www.medicines.org.uk/emc/product/10023/smpc last accessed 08/04/2021
- Melatonin for sleep disorders. Medicines for Children https://www.medicinesforchildren.org.uk/melatonin-sleep-disorders last accessed 08/04/2021
- BNF for children (current) https://bnfc.nice.org.uk/drug/melatonin.html#indicationsAndDoses last accessed 26/11/2020
- The Maudsley Prescribing Guidelines 13th edition ISBN-978-1-119-44260-8
- NICE (2013). ESUOM2 Sleep disorders in children and young people with attention deficit hyperactivity disorder: melatonin. Available via https://www.nice.org.uk/advice/esuom2/resources/sleep-disorders-in-children-and-young-people-with-attention-deficit-hyperactivity-disorder-melatonin-1503234972035269 last accessed 26/11/2020
- Guy's and St Thomas', Kings College and University Lewisham Hospitals. Paediatric Formulary 1st electronic Edition http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80/content/88cf803c-b5bb-4a18-b156-dedce900d6d0 last accessed 26/11/2020
- http://www.lpp.nhs.uk/media/42776/pharmacy_bulletin_melatonin2013v1.pdf (login required)
- Personal Communication: Prof. Paul Gringas, Professor of children's sleep medicine and neuro-disability Guy's and St Thomas' NHS Foundation Trust

4. COMMUNICATION AND SUPPORT

For patient specific clinical issues GPs to contact the named lead specialist on the clinical letter

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
Medication – Prescribing advice, interactions, availability of medicines Evelina London Children's Hospital Medicines Helpline	Tel: 020 7188 3003 (For urgent enquiries) Email: gst-tr.Evelinapharmacy@nhs.net (Accessed weekly)

Guy's and St. Thomas' NHS Foundation Trust - Hospital switchboard: 0207 188 7188	
Medication – Prescribing advice, interactions, availability of medicines Evelina London Children's Hospital Medicines Helpline	Tel: 020 7188 3003 (For urgent enquiries) Email: gst-tr.Evelinapharmacy@nhs.net (Accessed weekly)
GSTT Community Child and Adolescent Mental Health Service (CAMHS) Prof Paul Gringras Consultant Paediatrician - ELCH	Tel: 020 7188 4649 Email: paul.gringras@gstt.nhs.uk
Lewisham and Greenwich Hospitals Queen Elizabeth Hospital Switchboard: 020 8836 6000 Lewisham Hospital Switchboard: 020 8333 3000	
Consultant/specialist team **For Queen Elizabeth Hospital, Woolwich** Dr Sanjay Sahu Consultant Paediatrician Paediatrics Department Stadium Rd, London SE18 4QH **For University Hospital Lewisham** Dr. Sarah Panjwani Dr. Brindha Dhandapani Consultant Community Paediatricians CAMHS, Kaleidoscope Lewisham Centre for Children and Young People 32 Rushey Green London SE6 4JF	Tel: 020 8836 4521 Email: sanjay.sahu@nhs.net Tel: 020 7138 1100 (Switchboard) Email: sarahpanjwani@nhs.net Email: brindha.dhandapani@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Lewisham and Greenwich NHS Trust Medicines Information Services	Tel: 020 8836 4900 Email: LG.QE-Medinfo@nhs.net
South London and Maudsley (SLAM): switchboard 020 3228 6000	
Consultant/specialist team For patient specific queries contact the named specialist on the clinic letter For drug enquiries contact the Medicines Information service (see details below)	
Medication – Prescribing advice, interactions, availability of medicines Maudsley Medicines Information Services	Tel: 020 3228 2317
Oxleas NHS Trust switchboard 01322 625 700	
Consultant/specialist team **Bexley Community Paediatrics** Acorns CDC, Queen Mary's Hospital Sidcup **Greenwich Community Paediatrics** Oxleas NHS Foundation Trust 1 Wensley Close, Eltham SE9 5AB	Tel: 020 3004 0092 Email: oxl-tr.BexleySCS-SPA@nhs.net Tel: 020 8836 8621 Email: oxl-tr.childrenstherapies@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Medicines Information at Oxleas	Tel: 01322 625 002 Email: oxl-tr.medicinesinfo@nhs.net
Bromley Healthcare Community Services	
Consultant/specialist team Dr Mark O'Leary, Consultant Community Paediatrician Consultant Community Paediatrician Bromley Healthcare CIC Ltd Denise Cox, ADHD Nurse Phoenix Centre	Tel: 0208 315 4680 Email: markoleary@nhs.net Tel: 0208 315 4757 Email: denise.cox4@nhs.net