Melatonin Guidelines for the Treatment of Sleep Disorders in Children

Purpose
Melatonin has been classified as Simple Amber\textsuperscript{1} in the LMSG traffic light classification for certain conditions. This document aims to provide guidance on the use of melatonin within its specified paediatric indications and clarifies roles and responsibilities of secondary care and primary care.

Scope
The Simple Amber classification for melatonin covers the following:

1. Sleep disorders in children with Attention Deficit Hyperactive Disorder (ADHD), autism, visual impairment, learning difficulties and developmental delay;
2. Continued use in adulthood when the medication was initiated in childhood as per point one and proved effective;
3. Prescribing of melatonin m/r tablets 2mg (Circadin\textsuperscript{®}) and melatonin liquid 1mg/ml only (prescribing of other preparations will remain with secondary care).

Secondary Care Clinician Responsibilities

- Initiation of prescription and titration of dose to the optimum level using the minimum effective dose (see Appendix for preferred products);
- Monitoring for response and adverse drug reactions (ADRs) during the titration period;
- Liaison with the general practitioner (GP) to share the child’s care when a stable dose has been achieved and proven benefit has been established;
- Regular reviews (at least annually) and GP to be notified of any changes (but see also section below titled ‘Prescribing for Patients Discharged from Secondary Care’);
- Where necessary, arranging transfer to adult services.

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**GP Responsibilities**

- Monitoring the child’s overall health and well being;
- Informing the secondary care clinician of any ADRs observed or any abnormalities from physical checks;
- Prescribe ongoing supplies of melatonin (see Appendix for preferred products);
- Refer back in to the initiating service by the age of 17 to determine if the drug is still appropriate moving into adulthood.

**Patient/parent Responsibilities**

- Ensure that behavioural interventions/sleep hygiene measures continue to be implemented even whilst on medication;
- Ensure compliance with the medication.

**Community Pharmacist Responsibilities**

- Pharmacist has a professional responsibility to ensure that any unlicensed medication ordered is of good quality;
- Provide appropriate measuring device (e.g. spoon or oral syringe) with the medication.

**Prescribing of melatonin**

Melatonin is not usually considered first line in sleep disorders. The following steps are typically taken before melatonin is prescribed.

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**Flowchart**

1. Sleep chart/ diary for 2 weeks or clear account of sleep difficulties
2. Trial behavioural interventions or sleep hygiene measures for up to 4 weeks
   - Success: Continue with measures
   - Fail: Consider melatonin with behavioural interventions/ sleep hygiene measures

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Engagement from the family is vital and there may be instances where it is difficult or impossible to establish behavioural interventions or sleep hygiene measures because the patient and/or family are struggling to cope with the current situation. In these instances, melatonin may be initiated at the same time as behavioural interventions or
sleep hygiene measures and then withdrawn once the other interventions are established. Simple measures include ensuring that there is an established bedtime routine, removing television and computer games from the child’s room and ensuring that the room conditions (temperature, light and noise) are at an optimum level to promote sleep. In children with ADHD who are finding it difficult to settle in the evening, their ADHD medication may be optimised before considering melatonin.

Melatonin is usually initiated at 2-3mg at night using the most appropriate formulation and increased depending on response to up to 10mg at night (occasionally higher doses are used but this will be prescribed by the specialist). The medication should be given or taken around 30-60 minutes before expected bedtime. Circadin® is a controlled release formulation so should be swallowed whole. The controlled release profile should help with sleep maintenance and thus reduce or stop night time waking. Circadin® tablets can be halved using a tablet cutter and this should not affect the controlled release profile of the formulation. At the discretion of the clinician Circadin® can be crushed and dispersed in water if there are swallowing difficulties or if an immediate release profile is desired (see licensing).

Circadin® is considered first line on the basis of licensing, cost and quality of the product. Melatonin liquid 1mg/ml can be used in patients who are unable to take Circadin® or where Circadin® does not have the desired effect. The use of liquid should be regularly reviewed and switched to Circadin® when the patient can swallow tablets. In certain circumstances, other melatonin preparations will be initiated to meet the specific needs of the patient. Prescribing of these other preparations, such as capsules, will remain in secondary care.

Melatonin can be stopped abruptly should the need arise. There should be no side effects associated with this.

Patients on melatonin will be reviewed by secondary care at least annually (but see also section below titled ‘Prescribing for Patients Discharged from Secondary Care). There are no monitoring requirements for melatonin apart from checking for side effects and continued efficacy.

Where appropriate, treatment should be withdrawn periodically to access continued need. This is part of an individualised plan which should be specified by the consultant if the patient is discharged.

**Side effects**

Melatonin is generally well tolerated. Full adverse effect profile is unclear due to small size of trials in children. The most commonly reported side effects are: headache, dizziness, nausea and drowsiness. Other side effects include fatigue, confusion, pruritus, hypothermia, tachycardia, nightmares, mild depression, morning grogginess, and skin rashes. Melatonin can affect seizure control in patients with epilepsy, however,
information is conflicting. Children with epilepsy should be closely monitored for any increased incidence of seizures\(^5\).

**Licensing**

Circadin\(^\circ\) is licensed in the UK for patients over 55 years of age\(^3\). Its use in children and adults under 55 years is therefore off label. The MHRA and various prescribing guidelines\(^2,6\) advise that a licensed preparation should be considered first, even if it is for an off label use. As Circadin\(^\circ\) is licensed in the UK, its quality is assured and therefore it is safer than using an unlicensed product.

Currently, melatonin liquid 1mg/ml is unlicensed. In a paediatric setting, it is common to prescribe unlicensed preparations as long as there is a clinical need and there is not a licensed product to fully meet this need\(^6\). A letter of special clinical need may be required.

**Prescribing for Patients Discharged from Secondary Care**

After diagnosis and stabilisation, some patients may not necessarily need to remain under secondary care. In these cases, the patient can be discharged from secondary care with a clear plan for the GP on how to manage the on-going prescribing of melatonin. In any case, the GP should re-refer the patient back to secondary care at around 17 years of age so that the specialist can assess continued need for melatonin into adulthood.

**Background and Further Information**

Sleep disturbance in children with neurological or behavioural disorders is common and can be a major source of distress for the patient and family. Furthermore, sleep disturbance can have an impact on the child’s behaviour and ability to concentrate during the day. In ADHD for example, up to 50% of children could have sleep related problems.

Melatonin is an endogenous hormone produced by the pineal gland in the brain. It is important in the regulation of circadian rhythms in humans and animals and a number of studies have shown that exogenous melatonin has beneficial effects on the sleep patterns of these groups of children\(^5\). Many paediatricians and child psychiatrists are using melatonin for difficult sleep problems in the UK.

**Patient Information**

[Leicestershire Partnership Trust Leaflet Getting Enough Sleep](https://www.healthforkids.co.uk/)

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Further Advice and Support

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<th>Supervising Consultant or Dr Krutika Patel</th>
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<tr>
<td>Child and Adolescent Mental Health Service</td>
<td>Consultant Paediatrician/Lead Consultant FYPC</td>
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<tr>
<td>Leicestershire Partnership NHS Trust</td>
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<tr>
<td>Tel: 0116 225 2900</td>
<td>Tel: 0116 225 6743</td>
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<tr>
<td>Fax 0116 225 2899</td>
<td>Fax: 0116 225 3850</td>
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<tr>
<td>email: <a href="mailto:alvina.ali@leicspart.nhs.uk">alvina.ali@leicspart.nhs.uk</a></td>
<td>email: <a href="mailto:krutika.patel@leicspart.nhs.uk">krutika.patel@leicspart.nhs.uk</a></td>
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References


2. Dealing with specials (June 2010). Pharmacy Professional, p.27-32


Written by Tejas Khatau – Lead Pharmacist Families Young People and Children’s Services (Leicestershire Partnership NHS Trust).

In consultation with Dr Prasanna, Dr Brooke, Anthony Oxley, Dr Bretherton, Dr Karim, Teresa Norris, Sarah Baines, Chris Tinegate, Zeibun Patel, David Harris (UHL),

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Appendix

Preferred Melatonin Preparations

Background

- Prescribing data shows that a variety of melatonin preparations are being prescribed;
- This document is designed to ensure that the needs of the patients are met through consistent, safe and cost-effective prescribing of melatonin preparations;
- For existing patients who are not on the preferred melatonin preparations below, consider switching to Circadin® or another preferred melatonin preparation below if appropriate;
- If Bio-melatonin or a melatonin preparation not listed below needs to be initiated, please explain clearly in the notes why this has been selected over the preferred products in the document. These products are not simple amber.

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| Melatonin m/r tablets 2mg (Circadin ®) | - Tablets can be halved using tablet cutter (this should not affect the controlled release profile);
                                        - Tablets can be crushed, dispersed in water and taken by mouth. This will then need to be taken in the same way as an immediate release product.
                                        - UK licensed but use in children and crushing would make it an off-label use. Explain off-label status to patient/parent and document this in the notes. |
| **Second Line**                  |          |
| Melatonin oral solution 5mg/5ml  | - Unlicensed. Explain unlicensed status to patient/parent and document this in the notes;
                                        - Now in part VIIIB of Drug Tariff, therefore price is predictable and capped for community prescriptions. Minimum price applies therefore consider prescribing at least 200ml if clinically appropriate. |
| **Restricted Choice**            |          |
| Bio-Melatonin tablets 3mg        | - EU licensed.
                                        - Can be considered if the clinical needs of the patient are met by neither Circadin® (whole or crushed) nor the 5mg/5ml oral solution. |

1. MIMS. Accessed from [http://www.mims.co.uk](http://www.mims.co.uk) on 26/04/2012;
3. Personal communication with Pharma Nord (UK) on 19.03.2012 (excluding VAT).