

Melatonin prescribing for sleep disorders in children and adolescents

Melatonin is approved locally for use in sleep disorders in children and adolescents with neurological or neurodevelopmental disorders. Circadin is the recommended melatonin preparation for prescribing. Thurrock CCG, and Basildon and Brentwood CCG do not support the prescribing of other melatonin brands and preparations, or unlicensed specials preparations.

Melatonin preparations available and licensing:

- **Circadin (melatonin) 2mg prolonged-release (PR) tablets: recommended melatonin preparation for prescribing.**
 - Licensed for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 years or over.
 - Not licensed for use in children, off-label use in children.
- **Slenyto (melatonin) 1mg and 5mg prolonged-release tablets: not supported for prescribing.**
 - Licensed for the treatment of insomnia in children and adolescents aged 2 to 18 years with Autism Spectrum Disorder (ASD) and/or Smith-Magenis syndrome (SMS), where sleep hygiene measures have been insufficient.
 - Use outside of the licensed use would be off-label.
 - The *Scottish Medicines Consortium* (SMC) has advised (September 2019) that melatonin prolonged-release (Slenyto) is not recommended for use within NHS Scotland for the treatment of insomnia in children aged 2 years and over with Autism Spectrum Disorder and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient, as the clinical and economic case was not demonstrated.
 - The *All Wales Medicines Strategy Group* (AWMSG) has advised (November 2019) that melatonin prolonged-release (Slenyto) is not recommended for use within NHS Wales for the treatment of insomnia in children aged 2 years and older with Autism Spectrum Disorder and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient. The case for cost-effectiveness has not been proven.
- **Melatonin 3mg tablets and melatonin 1mg/ml oral solution (Colonis Pharma Ltd): not supported for prescribing.**
 - Licensed for the short-term treatment of jet lag in adults (18 years and over).
 - Do not prescribe melatonin for jet lag on NHS prescription as GPs are not responsible for providing NHS prescriptions for conditions which may arise while abroad or travelling.
 - Not licensed for use in children.
 - The Summary of Product Characteristics for both formulations states '*The safety and efficacy in children and adolescents aged 0 – 18 years have not been established. Melatonin 3mg film-coated tablets and melatonin 1mg/ml oral solution should not be used in children and adolescents due to safety and efficacy concerns.*'
 - Melatonin 1mg/ml oral solution contains the excipients sorbitol (140mg/ml) and propylene glycol (150.50mg/ml), making it less suitable for use in children, particularly under the age of 5 years.
- **Unlicensed melatonin tablets, capsules and liquid formulations (brands include Bio-melatonin 3mg tablets, KidNaps 1mg/1ml oral solution): not supported for prescribing.**

MHRA guidance recommends that licensed products should be used wherever possible, in preference to an unlicensed product, even if it means using a licensed product off-label and outside its licensed indications. Therefore, from a quality and safety perspective, licensed Circadin is the locally recommended melatonin preparation used off-label in children. It is a safer choice under the MHRA risk hierarchy, a regulated product, and better value for money.

Community paediatricians will initiate and prescribe Circadin. In exceptional circumstances, such as a feeding tube (gastrostomy/jejunostomy) or following a failed trial and response to Circadin, an alternative melatonin product may be recommended by the specialist. This will be a small minority of children with individual exceptional circumstances and the recommendation will be detailed in the clinic letter.

Circadin dosing information:

- Circadin is available as 2mg PR tablets. Dependent on the dose required, the tablet can be halved or quartered (off-label use) using a tablet cutter.
- If halved most of the prolonged-release properties will be maintained.
- If quartered or crushed this will provide an immediate-release preparation.

Recommendations for swallowing difficulties or for an immediate-release preparation:

Patients with swallowing difficulties or for an immediate-release preparation:

- Crush the appropriate number of Circadin 2mg PR tablets, and mix with water or with a small amount of yogurt (off-label use).
- Crushing will not affect the active ingredient (melatonin).
- Crushing will affect the prolonged-release properties of the product, and provide an immediate-release melatonin preparation.
- Crushed tablets may need to be given closer to bedtime (30 minutes before bedtime).
- The prescription should state that the medication is to be crushed prior to administration, for inclusion on the directions label of the medication.
- Do not prescribe unlicensed specially formulated melatonin liquids.

General management:

- Ensure that children have undergone a trial of behavioural sleep interventions before considering prescribing melatonin.
- There is limited information available regarding the long-term effects of melatonin (data is available for up to six months in adults and two years in children).
- Ensure that the child is reviewed for continued need for and effectiveness of melatonin after the first three months, then at six monthly intervals for up to two years treatment.
- Specialist to consider a trial withdrawal of treatment after two years melatonin treatment in children, as efficacy and safety data are not available beyond two years treatment.

Review recommendations:

- **New patients:** Prescribe melatonin as **Circadin 2mg PR tablets**, either taken whole, halved or crushed (crushed for an immediate-release preparation or for swallowing difficulties).
- **Do not prescribe** Slenyto 1mg and 5mg prolonged-release tablets, melatonin 3mg tablets (Colonis Pharma Ltd) or melatonin 1mg/ml oral solution (Colonis Pharma Ltd).
- **Do not prescribe** unlicensed melatonin tablets, capsules and liquid formulations.
- **Existing patients: Review** children prescribed unlicensed melatonin preparations (tablets, capsules and liquid formulations) for the continued need for melatonin, any adverse effects and for suitability for a switch to Circadin, for quality, safety and cost effectiveness reasons.
- Switch melatonin tablets, capsules, and liquid formulations to Circadin 2mg PR tablets as follow:
 - Melatonin 1mg tablets or capsules - half a Circadin tablet, crush for immediate-release
 - Melatonin 2mg tablets or capsules - one Circadin tablet, crush for immediate-release
 - Melatonin 3mg tablets or capsules - one and a half Circadin tablets, crush for immediate-release
 - Melatonin 5mg tablets or capsules - two and a half Circadin tablets, crush for immediate-release
 - Melatonin 10mg tablets or capsules - five Circadin tablets, crush for immediate-release
 - Melatonin liquid formulation (various strengths) - half/whole Circadin tablet(s) crushed, dose dependent

Providers commissioned to provide services on behalf of Thurrock CCG and Basildon and Brentwood CCG are reminded that they are required to follow the local joint formulary and prescribing guidance, or relevant Medicines Management agreement.

Position Statement No.	59
Title	Melatonin prescribing for sleep disorders in children and adolescents
References	<p>emc Summary of Product Characteristics. Circadin 2mg PR tablets. Flynn Pharma Limited. https://www.medicines.org.uk/emc/product/2809. Accessed 20/05/20.</p> <p>emc Summary of Product Characteristics. Slenyto 1mg PR tablets. Flynn Pharma Limited. https://www.medicines.org.uk/emc/product/10023/smpc. Accessed 20/05/2020.</p> <p>emc Summary of Product Characteristics. Slenyto 5mg PR tablets. Flynn Pharma Limited. https://www.medicines.org.uk/emc/product/10024/smpc. Accessed 20/05/2020.</p> <p>emc Summary of Product Characteristics. Melatonin 3mg film-coated tablets. Colonis Pharma Limited. https://www.medicines.org.uk/emc/product/10405/smpc. Accessed 20/05/2020.</p> <p>emc Summary of Product Characteristics. Melatonin 1mg/ml oral solution. Colonis Pharma Limited. https://www.medicines.org.uk/emc/product/10419/smpc. Accessed 20/05/2020.</p> <p>Data and information provided by Flynn Pharma Ltd. 20/06/2020.</p> <p>Scottish Medicines Consortium (SMC), SMC No. SMC2168, (August 2019). https://www.scottishmedicines.org.uk/medicines-advice/melatonin-slenyto-full-smc2168/</p> <p>All Wales Medicines Strategy Group (AWMSG), AWMSG No. 3947, (November 2019). http://www.awmsg.org/awmsgonline/app/appraisalinfo/3947</p> <p>Circadin: http://www.circadin.com/about-circadin/ga/</p> <p>Hui Ming Chua, Nathalie Hauet Richer, Magda Swedrowska, Stephen Ingham, Stephen Tomlin and Ben Forbes. Pharmaceutics. 2016; 8 (2). Dissolution of Intact, Divided and Crushed Circadin Tablets: Prolonged vs. Immediate Release of Melatonin.</p> <p>Essex Partnership University NHS Foundation Trust, Section 12 Treatment of Children and Adolescents. https://eput.nhs.uk/wp-content/uploads/2019/05/Section-12-Treatment-of-Children-and-Adolescents-Jun-2019.pdf</p> <p>PrescQIPP Bulletin 245: Melatonin (February 2020). https://www.prescqipp.info/media/4586/245-melatonin-21.pdf</p>
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Author	Medicines Management Team
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