

Prescribing information for melatonin (unlicensed use) for the treatment of sleeping disorders in children and adolescents

This prescribing information document outlines the prescribing responsibilities between the specialist and GP. GPs are invited to participate. If the GP feels that such prescribing is outside their area of expertise or have clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, clinical responsibility for the patient's health remains with the specialist.

If a specialist asks the GP to prescribe but the GP is not happy to continue prescribing, they must inform the specialist within 2 weeks of receiving the request.

Consultant details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	NHS Number:
Email:	Email:	Date of birth:
Contact number:	Contact number:	Contact:

Introduction

Sleep disturbance in children and adolescents is common, especially in those with neurological and/or behavioural disorders^{1,2}. Sleep disturbance may include delayed onset of sleep, frequent waking, early morning waking or day-night reversal of sleep pattern³

Melatonin is a hormone secreted by the pineal gland which has an important role in the regulation of circadian rhythm. Administration of synthetic melatonin promotes the onset of sleep and has been used for the management of sleep difficulties in adults and children.

Unlicensed indication (the focus of this document):

Melatonin is used to improve the onset and duration of sleep in infants, children and adolescents with neurological and/or behavioural problems who have refractory severe sleep disturbance. It can also be used to improve onset and duration of sleep in children and adolescents with congenital or acquired neurological/neuro-developmental problems including conditions such as learning difficulties, Autistic Spectrum Disorders, Cerebral Palsy, visual impairment, epilepsy and neurodegenerative disorders.

The treatment of choice for sleep disturbance is behavioural modification (sleep hygiene etc.); melatonin should only be prescribed after a full trial of behavioural management has been tried and failed. Melatonin should be used in conjunction with behavioural management techniques. Treatment with melatonin should be initiated and supervised by a specialist, but may be continued by general practitioners. The need to continue melatonin therapy should be reviewed every 6 months.

Dosage and administration

Problems with sleep initiation /sleep maintenance/fragmental sleep and/or early morning awakening

Initially melatonin MR 2mg tablets (Circadin ®) once at night (the dose should be taken 1-2 hours before bedtime after food. If crushed, take half an hour before bedtime).

If there has been insufficient response after 7-14 days, the dose can be increased in 2mg steps up to a maximum of 10mg

If there is no improvement in the child's sleep pattern after 7-14 days on the maximum dose, melatonin should be discontinued. This can be done immediately and without the need for gradual withdrawal.

Reviewing treatment

If treatment is successful, a trial reduction in dose should be attempted after 6 months as 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.

If sleep patterns are maintained, dosage can be reduced by 2mg every 4-6 weeks. If difficulties recur, the original dose should be reinstated immediately but a further trial reduction should be attempted 6-12 months later. The specialist will initiate this at a clinic review if considered appropriate.

Some children/adolescents with a development or neurological problem may require long term treatment.

Where clinically appropriate, existing patients prescribed alternative unlicensed products should be switched to the nearest whole tablet of Circadin®. For example:

- Patients currently prescribed a dose of unlicensed melatonin which can administered in multiples of 2mg should be switched to an equivalent dose of Circadin® e.g. 2mg of unlicensed melatonin to 1 x 2mg Circadin®; 6mg of unlicensed melatonin to 3 x 2mg Circadin®.
- Patients not currently prescribed an equivalent dose, may be switched to the nearest dose e.g. 3mg unlicensed melatonin to Circadin® 1 x 2mg tablet (2mg daily dose).

Products and strengths available

- Melatonin 2mg prolonged release tablet (Circadin®)
- Melatonin 5mg/5ml oral solution SF

Circadin® tablets can be crushed for patients with swallowing difficulties (when crushed, the modified characteristics of Circadin® are lost and it acts as an immediate release preparation). Unlicensed liquid formulations should only be used for exceptional cases where tablet formulations are unsuitable.

Specialist responsibilities

- To assess the suitability of the patient for treatment with melatonin, and confirm that a full trial of behavioural management has been attempted and failed. A sleep diary is useful in determining the nature and severity of the sleep disorder, prior to commencing treatment.
- Explain the unlicensed use of melatonin and obtain consent for treatment.
- Provide the patient/patient's carer/s with suitable written and verbal information about the drug's benefits and side effects before starting medication.
- Prescribe the medication until the dose is stabilised and the patient has demonstrated an effective response
- Request whether the GP is willing to participate in continued prescribing.
- Regular follow-up of patient (at least 6 monthly) to assess continued need for treatment
- Advise GP on dosage adjustment and when a trial withdrawal of melatonin should be undertaken.
- Have a mechanism in place to receive rapid referral of a patient from the GP, in the event of deteriorating clinical condition and ensure that clear backup arrangements exist for GPs to obtain advice and support.
- Report adverse events to the MHRA (via Yellow Card)
www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Primary Care responsibilities

- Respond to the specialist's request for primary care prescribing.
- Prescribe melatonin according to the dose specified by the specialist
- Issue further prescriptions at appropriate intervals (usually monthly)
- Ensure no drug interactions with other medicines
- Contact the specialist for management advice as required.
- Stop treatment on advice of specialist
- Report adverse events to the MHRA (via Yellow Card)
www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Adverse effects, Precautions and Contra-indications⁴

Contraindications

- Hypersensitivity to melatonin or to any of the excipients of the formulation.

Adverse Effects

The most commonly reported side-effects with melatonin are headaches, dizziness, nausea, and drowsiness (although several studies report similar incidence of side effects in placebo groups). Very occasionally, children can show a paradoxical reaction of overactivity and irritability, a state recognised for all sedative-hypnotics when used with children. There are also concerns that melatonin may adversely affect seizure control, gonadal development and asthma control and at present there are no robust data available to support or refute any of these concerns⁴.

See product SPC for full list of possible adverse drug reactions (www.medicines.org.uk)

Drug Interactions

- Alcohol should not be taken with Circadin® because it reduces the effectiveness of Circadin® on sleep.
- Circadin® may enhance the sedative properties of benzodiazepines and non-benzodiazepine hypnotics, such as zaleplon, zolpidem and zopiclone.

See product SPC for full list of drug interactions (www.medicines.org.uk)

Communication

For any queries relating to this patient's treatment with melatonin, please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions. Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org).

¹ Lin-Dyken DC, Dyken ME, Use of melatonin in young children for sleep disorders. *Infants and young children* 2002; 15(2): 20-38

² Ross C et al. Melatonin treatment for sleep disorders in children with neurodevelopmental disorders: an observational study. *Developmental medicine and Child Neurology* 2002; 44(5): 339-343

³ Jan JE et al. The treatment of sleep disorders with melatonin. *Developmental medicine and Child Neurology* 1994; 36: 97-107.

⁴ Circadin® MR 2mg Tablets – Summary of Product Characteristics. Available at www.medicines.org.uk