

## Melatonin for children

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).

This guideline reinforces the basic premise that:

When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the “sharing of information with the individual GP and their mutual agreement to the transfer of care.”

These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

### Indications:

Melatonin is indicated for the treatment of sleep disorders in children and young people with developmental and psychiatric disorders. This is an ‘off-label’ indication.

### Dosage and administration:

- Child 1 month–18 years: initially 2–4 mg Circadin® increased if necessary after 1 week to 4–6 mg; maximum dose 10 mg (4)
- The dose should be given 30 to 90 minutes before bedtime.
- Not all patients will respond to melatonin and it should be stopped in patients who do not show significant improvement in symptoms. Treatment can be stopped abruptly. The patient’s paediatrician should normally take the decision to stop treatment where appropriate and communicate this decision to the patient’s GP. The GP can stop treatment immediately after a serious adverse drug reaction if deemed appropriate.
- Circadin® will be used as the first line drug. Generally these tablets should be swallowed whole with a drink. However if the child cannot swallow Circadin® tablets they can be crushed and dispersed in liquid or soft food before administration. Circadin® can also be crushed and dispersed in water for administration via large bore feeding tubes however the prolonged release properties of the tablets will be lost and its effects may not last through the night. The powder will not dissolve completely and the tube will need to be flushed (this will be off-license).
- Unlicensed melatonin preparations will only be used within shared care in those children with feeding tubes which have previously become blocked by Circadin®

### Additional Information:

Melatonin is a pineal hormone which is involved with co-ordinating the body’s sleep/wake cycle. Children with neurodevelopmental disorders are at risk of sleep problems, typically getting to sleep, sleep/wake rhythm disturbances and reduced duration of sleep (insomnia). This may be associated with abnormally timed or inadequate secretion of melatonin<sup>1</sup>.

Poor night time routines, psychiatric and medical comorbidities and unwanted effects of stimulant medication may contribute to sleep problems in children with ADHD. Sleep hygiene and behavioural interventions are sometimes helpful and should be tried before drug treatment is introduced. Children with autism spectrum disorder are often less responsive to behavioural therapy<sup>1</sup>.

Classical hypnotic or sedative drugs are typically ineffective in children with neurological disorders and melatonin has become the mainstay of pharmacological treatment for sleep disturbance in children, particularly sleep onset difficulties<sup>2</sup>.

Evidence to support the use of melatonin is weak with two small randomised controlled trials and one follow up study providing limited evidence on the safety and efficacy of melatonin in children with ADHD experiencing sleep problems. No high quality evidence is available for the licensed prolonged release melatonin in children with sleep disorders and ADHD. The evidence indicates that melatonin may reduce sleep onset latency by approximately 20 minutes and may improve average sleep duration by 15 to 20 minutes when taken for between 10 days and 4 weeks. Discontinuation of melatonin led to relapse of sleep onset insomnia in most of the cases where it was used for more than 30 days<sup>3</sup>.

Off-label use of licensed Circadin® provides reassurance about manufacturing quality and follows MHRA recommendations. Therefore this guideline uses Circadin® as first line treatment in children.

### Monitoring requirements:

Standard monitoring of growth and sexual development is recommended, i.e. to check height, weight and pubertal development. This is primarily the responsibility of the specialist paediatrician but any concerns from the primary care clinician should be reported to the paediatrician.

### Action to be taken if abnormal results/adverse effects:

Such cases should be discussed with the child's specialist paediatrician.

### Contraindications:

Hypersensitivity to the active substance or to any excipient.

### Cautions:

- Some reports suggest melatonin improves seizure control when used in patients with epilepsy; others indicate that it may worsen seizure control. When used in patients with epilepsy, it is important to closely monitor the effect of melatonin on seizure frequency.
- Caution is advised in patients with renal disorders and melatonin should not be used in patients with liver disorders.
- Circadin® should not be used in patients with auto-immune, liver disease and some rare hereditary glucose tolerance disorders (due to it containing lactose).

### Adverse effects:

- Melatonin is generally well tolerated. Sedation and fatigue, abnormal dreams, insomnia, headaches, restlessness, irritability, nervousness, anxiety, increased pulse, skin disorders, itching, nasopharyngitis, back pain, arthralgia and nausea have all been reported as side effects associated with melatonin use.
- The above details are not a complete list and the BNF and the SPC remain authoritative. Full list of side-effects is given in the Circadin® summary of product characteristics (SPC), available from [www.emc.medicines.org.uk](http://www.emc.medicines.org.uk) (4).
- There is a known potential for melatonin to affect seizure control in patients with epilepsy. See cautions box above. 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. Clinicians should make their colleagues aware of any problems they identify.

### Specialist Paediatrician responsibilities:

- Make diagnoses and communicate these to the GP and other professionals involved in the patient's care.
- Discuss treatment options with patient, their parent(s) and carer(s), including sleep hygiene and behavioural management and include explanation of off label nature of Circadin® in children. Obtain appropriate consent to treatment and to share care with the GP.
- Provide a patient/carer information leaflet: available at [www.medicinesforchildren.org.uk/search-for-a-leaflet/melatonin-for-sleep-disorders](http://www.medicinesforchildren.org.uk/search-for-a-leaflet/melatonin-for-sleep-disorders)
- Initiate treatment with melatonin if agreed and prescribe the first month's supply.
- Use Circadin® as first line drug choice. Titrate dose to satisfactory effect.
- To contact patient's GP to request prescribing under shared care. This letter to GP should include full clinical details, a link to the shared care guideline and, in the cases where the patient's feeding tube was blocked by Circadin®, must explain why an unlicensed brand of melatonin has been recommended.
- Ensure the patient has at least 2 weeks supply remaining from the date the GP accepts the request to continue prescribing (to allow the surgery time to set up the prescription and provide it to the patient).
- Follow up at least every 6 months to ensure continuing benefit of melatonin.
- When appropriate, undertake periodic treatment withdrawals, or advise the GP in writing how and when to undertake them.
- To ensure the patient is reviewed by a member of the specialist team to monitor response to treatment (including adverse effects) regularly (at least every 6 months).
- To advise the GP regarding continuation of treatment, including the length of treatment.
- To discuss any concerns with the GP regarding the patient's therapy.
- Communicate any changes, recommendations, outcomes or other important information to GP.
- Provide advice to the GP if they have clinical queries relating to the condition or use of melatonin.

**GP's responsibilities:**

- To refer appropriate patients to secondary care for assessment.
- Ensure that the patient, their parent(s) and carer(s) has understood and consented to the off label use of melatonin. Patient information leaflet is available at [www.medicinesforchildren.org.uk/search-for-a-leaflet/unlicensed-medicines](http://www.medicinesforchildren.org.uk/search-for-a-leaflet/unlicensed-medicines)
- To agree to prescribe for patients in line with the shared care agreement.
- Carry out further dose titration according to the schedule suggested, or discontinue the medication, when necessary or requested.
- To report any adverse reaction to the CSM and the referring consultant.
- To continue to prescribe for the patient as advised by the consultant.
- To inform the consultant if the patient discontinues treatment for any reason.
- To seek the advice of the consultant if any concerns with the patient's therapy.
- To conduct an annual medication review.

**Patient and parent/carer responsibilities:**

- Agree to request prescriptions from the GP in good time; obtain the first GP prescription within 2 weeks of being informed that shared care will be in operation.
- Report any concerns or adverse effects to the GP, Paediatrician or Pharmacist.

**Secondary care review:**

- Where patients benefit from treatment the specialist paediatrician will follow up every 6 months to ensure continued need. Sleep hygiene measures and support should be given.
- It is suggested that at least six months of an improved sleep pattern should elapse before withdrawal is attempted. Withdrawal can take the form of treatment holidays, where the melatonin is gradually withdrawn over a period of 3-4 weeks and change in sleeping pattern observed. This may include reducing the dose gradually or having drug free days (perhaps at weekends initially to avoid adverse effects on school days). The specialist will organise this withdrawal and inform the GP to hold prescriptions for that time period, and where necessary to re-start.
- For some children however withdrawal is not successful and treatment may be necessary long-term.

Availability: 2mg modified release tablets Circadin ® Cost £15.39 for 30 tablets.

Costs for unlicensed melatonin capsules vary considerably in price

WUTH source their melatonin 3mg capsules from Mawdsley Brooks (Specials), Unit 4, Crompton Rd Business Park, Doncaster DN2 4PW, Tel 0130 255 3000

**Back up advice and support:** Community Paediatrics

**Telephone:** 0151 334 4000 and ask for appropriate consultant's secretary

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**References:**

1. Melatonin for sleep problems in children with neurodevelopmental disorders. Drug and Therapeutics Bulletin October 2015; Vol 53 No 10
2. Waldron DL, Bramble D, Gringas P. Melatonin: Prescribing practices and adverse events [11]. Archives of Disease in Childhood 2005; 90:1206-1207.
3. NICE Evidence Summary 4 January 2013. Sleep disorders in children and young people with attention deficit hyperactivity disorder: melatonin <https://www.nice.org.uk/guidance/esuom2/ifp/chapter/prescribing-melatonin>
4. Summary of Product Characteristics – Circadin. Accessed 8.1.2106 <http://www.medicines.org.uk/emc/medicine/25643>