NHS North West Surrey Clinical Commissioning Group

Ashford and St. Peter's Hospitals NHS
NHS Foundation Trust

SHARED CARE PRESCRIBING GUIDELINE

MELATONIN - Circadin® (off label use)for the Treatment of Persistent Sleep Disorders in Children over 3years old with ADHD

North West Surrey CCG Medicines Optimisation Group: Amber

NOTES to the GP

Amber drugs: *Prescribing to be initiated by a hospital specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs.*

The questions below will help you confirm this:

- *Is the patient's condition 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. Sign and return a copy of page 6 to the requesting consultant at the Secondary Care Trust. Until the requesting consultant at the Secondary Care Trust has received a signed copy of page 6 indicating that shared care has been agreed all care (including prescribing) remains with the consultant at the Secondary Care Trust.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your practice pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF-C.

Introduction

Insomnia is a widespread problem in children with neurodevelopmental or psychiatric disorders such as autistic spectrum disorder and attention deficit hyperactivity disorder (ADHD).

Behavioural therapy can be very effective in some forms of paediatric insomnia however children with neuropsychiatric disorders tend to have a lower response rate to behavioural therapy and may require drug treatment.

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced by the pineal gland during the dark hours of the day and night which appears to support the normal circadian rhythm and aid sleep onset. It is used as a treatment of sleep disorders in children. It is most helpful where sleep onset is a significant problem, but is rarely useful to maintain sleep if a child is waking during the night. Melatonin should not be used in isolation but should be combined with a behavioural programme, involving Clinical Psychology where necessary. The use of a weekly sleep diary before and during treatment will assist the monitoring of response.

The use of melatonin is supported by NICE in their Clinical Guidelines on the diagnosis and management of chronic fatigue syndrome / myalgic encephalomyelitis (CFS/ME) in adults and children (CG53, 2007). The guideline states that melatonin may be considered for children and adolescents with CFS/ME who have sleep difficulties, but only under specialist supervision.

Short term use of melatonin may also occasionally be useful in a range of isolated circumstances where other methods have failed. It should not be considered in the management of sleep problems in otherwise normal children.

Once a regular sleep pattern has successfully been achieved and maintained, there should be a trial withdrawal of treatment. In some children with neurodevelopmental / psychiatric problems, longer term treatment may be needed, but intermittent trials off treatment should be considered.

Currently there are no licensed treatments for sleep disorders in children in the UK. Circadin® is the only UK licensed product which contains melatonin. It is a 2mg prolonged release tablet. It is licensed for the short-term treatment of primary insomnia characterised by poor quality sleep patterns in patients who are aged 55 or over. The Medicines and Healthcare products Regulatory Agency (MHRA) would prefer an 'off-label' licensed product to be used if it can meet the clinical need, rather than an unassessed, unlicensed product. Circadin® should therefore be used wherever possible.

(See Melatonin [Circadin®] Summary of Product Characteristics (SPC) for full list)

If the child is finding it hard to fall asleep (rather than stay asleep) then more immediate release is needed, Circadin may be crushed to provide an immediate release profile. Where a patient has problems staying asleep but can't swallow a tablet whole, part tablets or very coarsely crushed tablets will retain some of the modified release profile.

If the clinical circumstances require a different unlicensed melatonin formulation the specialist will retain prescribing as the hospital can purchase at a lower cost and patient is likely to require frequent specialist contact.

Dose
Initiate at 2mg 1-2 hours before bedtime.
Increase dosage according to response. Dose can be increased to 4-6mg daily after 1-2 weeks.
Maximum BNF-C dose 10mg
Circadin® may be crushed or chewed to give an immediate-release profile (when crushed use of Circadin® is outside of its marketing authorisation). A useful Circadin® patient information leaflet is available on the Prescribing Advisory Database http://pad.res360.net/PAD/Search/DrugCondition/340
If the child wakes during the night, an extra dose of melatonin should not be given.

Cautions
Patients with epilepsy (increased seizure activity has been reported, but there is also anecdotal evidence that seizure activity improves as a result of improved sleep)
Lactose intolerance

Contraindications
Hypersensitivity to Melatonin or to any of the excipients. Pregnancy or breastfeeding.

Side effects
Melatonin is generally well tolerated in children, but long term side effects have not been evaluated. Adverse effects that have been reported rarely include: daytime drowsiness, headache, dizziness, a reduction in body temperature, transient depressive symptoms, mild tremor, mild anxiety, abdominal cramps, irritability, confusion, nausea and hypotension.
For a full list of adverse effects refer to the Summary of Product Characteristics.
Some have advised use with caution in children with epilepsy and monitoring of seizure frequency; in practice this has not been a problem.
Melatonin can safely be withdrawn suddenly without risk of adverse effects

Adverse effect	Frequency	Management
Headaches	Uncommon (more than 1 in 1,000 to less than 1 in 100 people might get these)	Simple analgesia (e.g. paracetamol). Refer back to psychiatric team if persistent or troublesome.
Abnormal dreams	Uncommon	No management concerns. Offer reassurance that memory of dreams has improved.
Nausea	Uncommon	Usually transient. Try taking melatonin with or after food.
Dizziness	Uncommon	Try not to change posture too quickly. Refer back to psychiatric team if persistent or troublesome.
Leukopenia	Rare *(more than about 1 in 10,000 to less than 1 in 1000 people might get these)*	Stop medicine refer back to specialist. No routine full blood count is recommended.

Interactions
There is limited data on drug interactions with melatonin.
In theory, the effects of melatonin may be additive with other medicines that cause CNS depression e.g. antidepressants, antipsychotics, other hypnotics and sedating antihistamines
Fluvoxamine: can significantly increase melatonin levels.
Warfarin: INR may be increased. Melatonin might also increase the anticoagulant effect of other drugs with anticoagulant or antiplatelet properties.
Herbal remedies with anticoagulant or antiplatelet (e.g. Ginkgo biloba, Ginseng) or sedative properties (e.g. St John's Wort, Valerian) may also enhance the therapeutic and adverse effects of melatonin.

Immunosuppressive therapy: melatonin can stimulate immune function and might interfere with immunosuppressive therapy.
Nifedipine: melatonin can increase BP and heart rate in patients treated with nifedipine
Cimetidine: can increase melatonin levels
Ciprofloxacin and other quinolones: can increase melatonin levels

Criteria for Use
Second-line where non-pharmacological strategies have failed and underlying physical causes are managed.
Treatment should be initiated by or under the supervision of a specialist and transferred to GP for prescribing after 3 months or when the patient's dose is stable

Duration of treatment:
Duration of treatment should be determined on an individual basis.
Treatment should be discontinued every 12 months to assess if it is still beneficial.
GPs should prescribe only 28 days at a time with a review date of every 12 months.

RESPONSIBILITIES and ROLES

Specialist responsibilities

1. To assess the patient and establish the need for sleep onset treatment in neurodevelopmental disabilities.
2. Consider and discuss treatment options. This should include consideration of contra-indications, interactions and cautions, a discussion of the reasons for treatment, the possible adverse effects and the lack of information in relation to longer-term outcomes including effectiveness and adverse effects
3. To consider melatonin where non-pharmacological strategies have failed, and underlying physical causes are managed where they exist.
4. To consider only where parents, carers or, where appropriate the patient, has completed a sleep questionnaire and sleep diary highlighting problems with sleep latency.
5. Provide verbal and written information to the parents, carers, and where appropriate the patient, and answer their questions about the off licence use of melatonin.
6. Explain to the patient / carer their roles as below, ensuring the patient/carer is aware of the need to review the melatonin every 12 months.
7. Obtain written consent for the off label prescribing of Circadin® melatonin.
8. Perform baseline checks of physical health (including height, weight)
9. Initiate off label melatonin (Circadin®) 2mg prolonged release tablets
10. Request agreement of shared care with primary care prescriber: a detailed clinic letter highlighting relevant patient information should be sent to the GP requesting shared care including:
    - Information that all conditions in above points have been discussed and appropriately actioned
    - The date of the next follow up review

    Shared care should only be requested if the patient is stable.
11. Undertake any necessary monitoring at face to face clinic appointments (12 monthly when stable): including height, weight, sexual development (this has been seen in animals but not in human use of melatonin) and assess the continuing need for melatonin considering stopping melatonin e.g. 14 day break using an appropriate sleep monitoring tool. Although leukopenia is a known (rare) side effect, regular FBCs are not specifically required.
12. Assess and monitor the patient's response to treatment and make dose adjustments where necessary.
13. If treatment is ineffective and discontinued check for possible complications following discontinuation.
14. Assess the continuing need for melatonin at 12 monthly review and consider stopping melatonin e.g. 14 days break every 12 months using an appropriate sleep monitoring tool
15. Maintain good communication with the GP and provide urgent advice on the following telephone number 01932 722126 or email paediatric.2@asph.nhs.uk A written letter should be sent to the

GP after each clinic visit. Keeping the GP fully informed about the patient's condition and medication. The specialist will be available to answer queries from the GP and carers
16. Notify the GP of the patient's failure to attend 12 monthly review and give advice on stopping the medication
17. To take responsibility for stopping the melatonin or to agree aftercare when the patient reaches 18 years of age

General Practitioner responsibilities

1. Subsequent prescribing of melatonin as Circadin® at the dose recommended once the treatment has been established, the patient stabilised and the care of the patient has been transferred and accepted.
2. To inform the consultant if unwilling to enter into shared-care arrangements
3. To record any changes in therapy in the prescribing record on receipt of such communication from secondary care and to act upon these.
4. Refer patients back to the specialist if there is delayed sexual development, failure to gain weight and height for the expected age and familial characteristics or if there are on-going sleep problems, side-effects or other difficulties
5. Advise patients to attend their 12 monthly hospital appointments
6. To report any adverse drug reactions to the specialist and to the Medicines and Healthcare Products Regulatory Authority (MRHA) as part of the Yellow Card Scheme. https://yellowcard.mhra.gov.uk/

Patient's / Carer's role

1. Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with off label use of Circadin® melatonin.
3. Tell the specialist or GP of any other medication being taken, including over-the-counter products.
4. Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP
5. To attend 12 monthly appointments

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address:
Specialist:	Dr Bozhena Zoritch	01932722126	bozhena.zoritch@asph.nhs.uk Paediatric.2@asph.nhs.uk
Hospital Pharmacy:	Deborah Hopper	01932723359	Deborah.Hopper@asph.nhs.uk

Melatonin – information for families

This page has information for families about melatonin, a medicine that is used to help children who have trouble sleeping.

What is melatonin?

Melatonin is a natural hormone we all have. It is made in the brain. It is produced at night and helps regulate our sleep pattern. It helps our body know when it's time to go to sleep and when it's time to wake up.

Melatonin medicines contain a man-made version of this hormone.

No company currently holds a UK license to supply melatonin to be given to children. Your specialist will have given careful consideration to prescribing it, and will discuss this fully with you.

Why has it been prescribed?

Melatonin is prescribed by specialist doctors to help children and young people who have problems sleeping, when other ways of trying to help them sleep have not worked. These other methods should not stop now, but should continue along with the melatonin treatment.

How should it be taken?

Melatonin should be taken at the dosage prescribed by the specialist / GP. It must not be changed without their advice. It should be taken as a single dose, 30 to 60 minutes before sleep time. If the child wakes during the night, do not give an extra dose of melatonin.

Does melatonin have any side effects?

Everyone reacts differently to medicines and will not necessarily suffer from any of the side effects mentioned here. The most common problem with melatonin is that it simply does not make the sleep any better. Other than this, side effects are fairly uncommon, but may include headache, dizziness and abnormal dreams. Other side effects may include restlessness, increased sweating, stomach pains, dry mouth. There are differing reports on the effect of melatonin in children who have epilepsy or asthma. Any child with epilepsy or asthma will be monitored very closely. If your child develops any worrying symptoms, please discuss them with your doctor.

Is it safe to take other medicines with melatonin?

It is safe for a child to take paracetamol in the dosage recommended for their age alongside melatonin. For most other medicines, there has been no study of using them with melatonin. If you are discussing other medicines for your child with any doctor or pharmacist, tell them that your child is taking melatonin.

How long should my child take melatonin for?

It is usually recommended to continue with melatonin for several months if it is found to be useful. Then you can discuss with your specialist or GP how best to reduce the dosage to see how your child sleeps without it.

Where can we get more information or ask questions about melatonin?

This brief leaflet covers only some aspects of treatment with melatonin.

The specialist, who prescribed the melatonin, or other members of his /her team, will be pleased to discuss it further with you. They will answer any questions that you have, now or in the future.