Shared Care Guideline: Melatonin

Tees, Esk and Wear Valleys NHS
NHS Foundation Trust

NHS
County Durham and Darlington Area Prescribing Committee

Before starting treatment
Ensure a detailed sleep history has been taken. Advise non-pharmacological sleep hygiene measures, e.g. a fixed bedtime routine, avoid caffeine-containing foods and drinks at least 6 hours before bedtime, avoid TV / use of electronic devices at least one hour before bedtime [these measures should continue alongside melatonin treatment, even if they have failed to improve sleep on their own]

Switching to circadin
There is no definitive guidance on switching.
Common sense would suggest there is no need to adjust the daily dose when doing this, unless the patient is taking an "odd" mg dose, i.e. 3mg, 5mg, 7mg, etc, which cannot be delivered with Circadin. In these circumstances it is advised that the dose is initially adjusted down to the nearest multiple of 2 mg, and increased by a 2 mg increment if there is a reduction in response.

Patient & carer information
The off-label use of Circadin® or use of an unlicensed melatonin product should be discussed with the patient and/or carer, using the appropriate handy fact sheet about "Unlicensed use of licensed medicines" or "Unlicensed medicines" on the Choice and Medication website.
The patient and/or carer's consent should be documented in the clinical records (Paris).
The patient and/or carer should be provided with a patient information leaflet about melatonin from the Choice and Medication or the Medicines for Children website.

Transfer of prescribing
The transfer of prescribing can only take place in line with the shared care agreement outlined on the following pages.

Which product should you use?
Circadin (2mg modified release tablets) is currently the only licensed melatonin preparation in the UK. Other preparations are unlicensed and significantly more expensive. These tablets can be crushed if immediate-release action is required.

Circadin
- The intact/whole Circadin® tablet releases melatonin in a controlled and prolonged manner over at least 8 hours, although approximately 40% of the total dose is released within the first hour and may be regarded as effectively 'immediate-release'.
- The tablet broken into quarter fragments provides for melatonin release over approximately 4 hours and an 'immediate release' component of approximately 60%.
- Crushing Circadin® tablets would render them immediate-release, rather than modified-release: careful halving may preserve some of the modified-release characteristics.

Dose, administration and duration
The aim of treatment is to establish a healthy sleep pattern with the lowest effective dose of melatonin.
- Starting dose (children aged 2 years and over, and adults): 2 mg
- If no benefit after 2 weeks, increase by 2 mg increments up to a maximum dose of 10 mg (most patients should respond at doses of 6 mg or less)
- If no benefit seen after 2 weeks at the maximum dose, stop treatment.
- If treatment is beneficial*, then at least 6 months of an improved sleep pattern should elapse before withdrawal takes place. Withdrawal should occur over a period of 3-4 weeks with observation of changes in sleep pattern. For some patients, withdrawal is not successful and long-term treatment may be necessary – review such patients every 6 months to ensure continuing benefit.
- Some clinical experience suggests that the efficacy of melatonin may be lost if it is taken for longer than two years; withdrawal prior to this may re-establish sensitivity to allow melatonin to be successfully re-introduced.

Melatonin should be taken 30-60 minutes before bedtime / target onset of sleep, and on an empty stomach since the absorption may be delayed when taken with large meals.
In patients with swallowing difficulties, the tablets can be crushed and dispersed in water, milk or orange juice immediately prior to administration, or the oral solution can be prescribed for administration via a PEG or gastrostomy tube. If a liquid preparation is required (noting the ability to crush circadin) then melatonin oral solution 5mg/5ml x 200mls is the most cost-effective.
*benefits of treatment include – reduction in sleep onset latency, reduced awakening, and improved behaviour

Drug	**Melatonin** **First line (licensed product):** Melatonin MR 2mg tablets (Circadin®) Circadin® can be crushed if unable to swallow tablets, swallowing difficulties or immediate-release action is required **(off-label).** **Second line only if crushing tablets inappropriate:** Melatonin 5mg/5ml alcohol free oral solution (200ml) (unlicensed product)
Speciality	Children & occasional use in Adults
Indication	Melatonin is used "off-label" for chronic sleep disturbance resulting in severe stress for the patient and/or family, in children, young people and adults with the following conditions: • Neurological or behavioural disorders including: o Attention Deficit Hyperactivity Disorder o Autistic Spectrum Disorders o Emotional dysregulation o Chronic sleep-onset insomnia • Neurodevelopment disabilities (e.g. delayed brain maturation, sensory dysfunction - especially visual, and dysfunction of sleep centres) • Chronic fatigue syndrome / myalgic encephalomyelitis with associated sleep difficulties (as recommended in NICE clinical guideline 53). It is also used in "off label" in Parkinson's patients where a trial of clonazepam has failed and also REM behavioural disorders, if recommended by a sleep neurologist. Circadin is not approved on the formulary or included as part of this shared care guideline for its licensed indication as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over.
Overview	Before starting treatment, traditional non pharmacological methods must have been tried and failed. **The aim is to establish healthy sleep habits with the lowest effective dose of melatonin**.
Specialist's Responsibilities	**Initial investigations:** Assess suitability of patient for treatment. Discuss benefits and side effects of treatment with the patient / parent / carer to include the unlicensed nature of melatonin. **Initial regimen:** An initial dose of 2 mg (given 30-60 minutes before bedtime). In the absence of improvement after 2 weeks, dose may be increased by 2mg increments **up to a maximum dose of 10mg**. Most patients respond at doses of 6mg or less. If no response after 2 weeks at maximum dose – stop treatment If response achieved, continue for at least 6 months, then attempt withdrawal over a period of 3-4 weeks, with observation of changes in sleep pattern. If long-term treatment necessary, review every 6 months to assess continuing benefit. **Clinical monitoring:** Specialist review to ensure continuing benefit and observation of growth parameters & pubertal development. **Frequency:** Every 6 months to 12 months. **Safety monitoring:** Monitoring for response and adverse drug reactions (ADRs) during the initiation period. Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP. **Prescribing duration:** At least six months of an improved sleep pattern should elapse before withdrawal takes place. Advise GP when a trial withdrawal of melatonin should be undertaken. For some children however withdrawal is not successful and treatment may be necessary long term.

	Prescribing arrangements: Titrate the dose of melatonin to a satisfactory effect over a minimum of 8 weeks before transferring to the GP. Write to GP to share the patient's care only when a stable dose has been achieved and proven benefit has been established. **Documentation:** • Obtaining agreement of GP to participate in shared-care arrangement for melatonin therapy (by sending a copy of this document). • Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment. Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required.
GP's Responsibilities	**Maintenance prescription:** Prescribe melatonin in accordance with the specialist's recommendations. Usual maintenance between 2-6mg (max. 10mg). **Clinical monitoring:** To report to and seek advice from the specialist on any aspect of patient care which is of concern to the GP and may affect treatment. **Safety monitoring:** Height & Weight (children). **Frequency:** Annual. **Duration of treatment:** Stop or adjust treatment on advice of, or in consultation with, a specialist. **Re-referral criteria:** • Failure to attend for review • Intolerance of drugs • Communications failure **Documentation:** Reply to request for shared-care as soon as practical (within 28 days).
Adverse Events	Adverse events: See below — Action: Report / discuss with specialist. Melatonin is generally well tolerated. Common side effects include headaches, abnormal dreams, nausea and dizziness. All suspected reactions (including those considered not to be serious and even where the causal link is uncertain) should be reported to the specialist and the MHRA.
Contra-indications **Cautions** **Drug Interactions**	Please refer to the BNF and/or SPC for full information. http://www.medicines.org.uk/emc/medicine/25643 Contra-indications: hypersensitivity to the active substance or to any of the excipients Cautions: autoimmune disease Clinically relevant drug interactions: Fluvoxamine may increase melatonin exposure
Other Information	• Circadin® can be crushed if unable to swallow tablets, swallowing difficulties or immediate-release action is required (off-label). • For patients with swallowing difficulties, crush tablets and dispersed in water, milk or orange juice immediately prior to administration. • Melatonin 5mg/5ml alcohol free oral solution (200ml) (unlicensed) is the most cost effective oral liquid preparation, but is significantly higher cost than Circadin® tablets. The liquid can be administered via PEG or gastrostomy tube. • Kidnaps® oral solution should not be prescribed as this contains alcohol.
Contact Details	**Name:** **GMC No:** **Address:** **Telephone:**