

Shared Care Guideline: Melatonin

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 to Circadin from unlicensed products. Common sense would suggest there is no need to adjust the daily dose when doing this, unless the patient is taking an “odd” dose, i.e. 3, 5, 7 mg, 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 efficacy.

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 electronic patient record.

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

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® (2 mg modified release tablets) is a licensed melatonin preparation, recommended for first line use whenever possible; these tablets can be crushed if an immediate-release action is required.

Slenyto® (1 mg & 5 mg prolonged release tablets) is licensed for the treatment of insomnia in children & adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome; it is approved only for the treatment of new patients with this indication

Circadin®

- The intact/whole Circadin® tablet releases melatonin in a controlled and prolonged manner over at least 8 hours; 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 renders 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.

- Circadin® - starting dose (children aged 2 years & 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)
- Slenyto® - starting dose (children aged 2 years & over)= 2mg; if an inadequate response has been observed, the dose should be increased to 5 mg, with a maximum dose of 10 mg.
- 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. Consider a treatment holiday at each review
- 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, Circadin® should be taken on an empty stomach, the absorption may be delayed when taken with large meals; Slenyto® may be taken with or after food. In patients with swallowing difficulties, Circadin® tablets can be crushed and dispersed in water, milk or orange juice; Slenyto® tablets can be put in food such as yoghurt, orange juice or ice cream immediately prior to administration to facilitate swallowing & improve compliance. Oral solution can be prescribed for administration via a PEG or gastrostomy tube when crushed tablets may be problematic – the licensed/drug tariff product (1 mg/ml oral solution - Colonis) contains sorbitol & propylene glycol so an unlicensed product without these excipients is recommended instead – see [prescribing decision algorithm](#).

**reduction in sleep onset latency, reduced awakening, and improved behaviour*

Title	Melatonin Shared Care Guideline		
Approved by	Drug & Therapeutics Committee	Date of Approval	28 th March 2019 (amended 25/3/21)
Protocol Number	PHARM-0025-v4.1	Date of Review	1 st October 2022

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Drug/Product	<p>First line (licensed product/off-label use): Melatonin MR 2 mg tablets (Circadin®) Circadin® can be crushed if patient is unable to swallow tablets, has swallowing difficulties or an immediate-release action is required</p> <p>Alternative (licensed product/use): Melatonin PR 1 mg & 5 mg tablets (Slenyto®) only for the treatment of insomnia in children & adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome (N.B. Circadin not licensed for this indication)-</p> <p>Only if crushing tablets inappropriate, e.g. PEG administration (unlicensed product): Melatonin 1 mg/ml oral solution x 200 ml (Rosemont Pharmaceuticals) – unlicensed product</p>
Specialty	Children & Young People Services (CYPS); occasional use in Adult Mental Health services
Indication	<p>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:</p> <ul style="list-style-type: none"> • Neurological or behavioural disorders for example: <ul style="list-style-type: none"> ○ Attention Deficit Hyperactivity Disorder ○ Autistic Spectrum Disorders • Neurodevelopment disabilities (e.g. Smith-Magenis syndrome, 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). <p>It is also used “off label” in REM behavioural disorders, if recommended by a sleep neurologist.</p> <p><i>N.B. Circadin® is <u>not approved</u> 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.</i></p>
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	<p>Initial investigations: Assess suitability of patient for treatment. Discuss benefits and side effects of treatment with the patient / parent / carer to include the off-label use and/or unlicensed status of the melatonin product being prescribed.</p> <p>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 in appropriate increments up to a maximum dose of 10 mg. Most patients respond at doses of 6 mg 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.</p> <p>Clinical monitoring: Specialist review to ensure continuing benefit and observation of growth parameters & pubertal development.</p> <p>Frequency: Every 6 months to 12 months.</p> <p>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.</p> <p>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.</p> <p>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. Ensure</p>

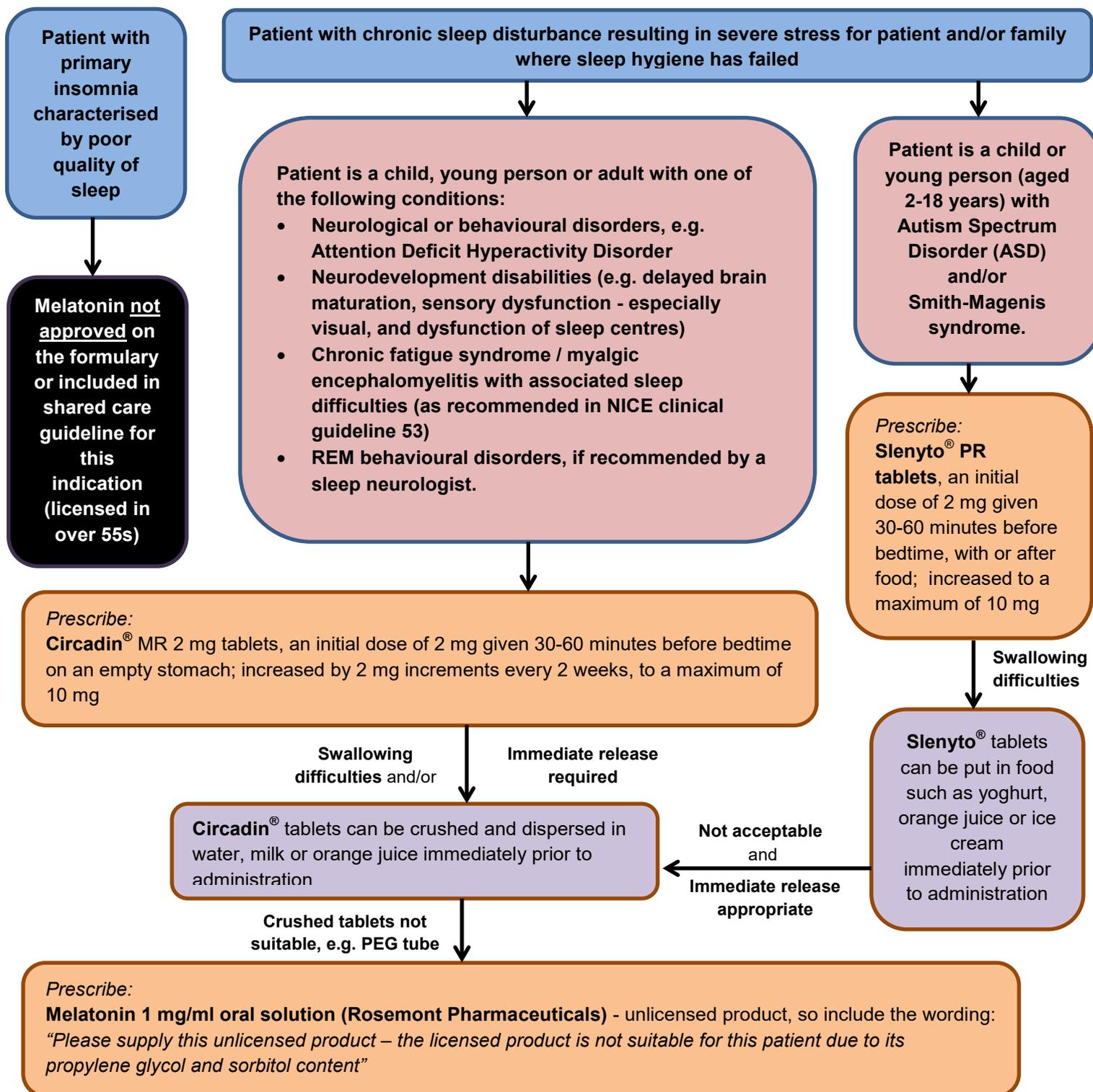
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Specialist's Responsibilities <i>(continued)</i>	<p>the formulation and dose of melatonin is clearly specified.</p> <p>Documentation:</p> <ul style="list-style-type: none"> Obtaining agreement of GP to participate in shared-care arrangement for melatonin 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	<p>Maintenance prescription: Prescribe melatonin in accordance with the specialist's recommendations. Usual maintenance between 2-6 mg (max. 10 mg).</p> <p>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.</p> <p>Safety monitoring: Height & weight (children).</p> <p>Frequency: Annual.</p> <p>Duration of treatment: Stop or adjust treatment on advice of, or in consultation with, a specialist.</p> <p>Re-referral criteria:</p> <ul style="list-style-type: none"> Failure to attend for review Intolerance of drugs Communications failure <p>Documentation: Reply to request for shared-care as soon as practical (within 28 days).</p>				
Adverse Events	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="background-color: #cccccc;">Adverse events</th> <th style="background-color: #cccccc;">Action</th> </tr> </thead> <tbody> <tr> <td>See below</td> <td>Report / discuss with specialist.</td> </tr> </tbody> </table> <p>Melatonin is generally well tolerated. Common side effects include headaches, abnormal dreams, nausea and dizziness.</p> <p>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.</p>	Adverse events	Action	See below	Report / discuss with specialist.
Adverse events	Action				
See below	Report / discuss with specialist.				
Contra-indications Cautions Drug Interactions	<p>Please refer to the BNF and/or SPC for Circadin® or Slenyto® for full information.</p> <p>Contra-indications: hypersensitivity to the active substance or to any of the excipients</p> <p>Cautions: autoimmune disease</p> <p>Clinically relevant drug interactions: Fluvoxamine may increase melatonin exposure</p>				
Other Information	<ul style="list-style-type: none"> Circadin® can be crushed if patient is unable to swallow tablets, has swallowing difficulties or an immediate-release action is required (off-label). For patients with swallowing difficulties, Circadin® tablets can be crushed and dispersed in water, milk or orange juice immediately prior to administration. Slenyto® tablets can be put into food such as yoghurt, orange juice or ice cream to facilitate swallowing and improve compliance Melatonin oral solution (unlicensed) is significantly higher cost than Circadin® tablets, and should be reserved for when crushed tablets are not appropriate for administration via PEG or gastrostomy tube. Kidnaps® oral solution should not be prescribed as this contains alcohol. 				
Contact Details	<p>Name: TEWV Base: Email: Telephone:</p>				

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Melatonin – Prescribing Decision Support Algorithm



Product	Cost per day (Drug Tariff, Sept 2020)		
	2 mg dose	6 mg dose	10 mg dose
Circadin 2 mg MR Tablets	£0.51	£1.54	£2.57
Slenyto 1 mg PR Tablets	£1.37	£4.12	£6.87
Slenyto 5 mg PR tablets			
Melatonin 1 mg/ml oral Solution (Rosemont)	£0.60	£1.80	£3.00

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AMBER ▲

**REQUEST FOR SHARED CARE (TRANSFER OF PRESCRIBING) OF
MELATONIN**

GP details:

Patient details (name/address/DOB/NHS number):

Diagnosis:

Medication details (list dose, frequency and brand if appropriate. Specify clinical indications if first line option not prescribed or non-standard formulation prescribed)

The patient is stabilised on:

Discontinued medication (list details of any drugs discontinued when this AMBER treatment initiated):

Last prescription issued (details of date and length of supply):

Monitoring results to date:

Planned specialist review:

Actions requested of GP:

Please continue to issue monthly (28 days) prescriptions until advised otherwise

The treatment has been explained to the patient and they understand they should contact you for future prescriptions.

You will be informed of any changes to treatment, if you are not required to issue prescriptions or if treatment is to be discontinued.

Please contact the prescriber on the number below if there is any change in the patient's condition or social circumstances, if the patient fails to regularly collect prescriptions, if non-compliance with treatment is suspected or you require any other advice.

Specialist team contacts:

Contact details (e-mail/telephone no):

Care coordinator (name):

Consultant (name):

Prescriber (name):

Signature:

Date:

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Acceptance of shared care for Melatonin

Patient's name:	NHS Number:
Address:	
Medication:	
I confirm receipt of prescribing transfer information for the above patient and accept my responsibilities within agreed shared care arrangements	
GP name: <i>(Please print name in BLOCK CAPITALS)</i>	
Signature/ Practice Stamp:	
Date:	
Please scan & e-mail back to:	
E-mail:	
or return by post as soon as possible to:	

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