NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Melatonin Prescribing Support in Children and Adolescents

Prescribing of melatonin should only be considered where other sleep hygiene methods alone have been unsuccessful

1. **Melatonin is generally prescribed locally for children with sleep disturbances associated with learning difficulties, Attention Deficit Hyperactivity Disorder (ADHD) or autism.**

2. **Melatonin should only be prescribed in Primary Care on the advice of a specialist clinician. See Quick Reference Guide**

3. **Circadin 2mg MR tablets (off-label) is the 1st line formulary choice of melatonin across Cambridgeshire and Peterborough.**

4. **Circadin 2mg MR tablets can be crushed and dispersed in water or milk or added to soft food like yoghurt, without losing its efficacy (off-label). However, this will result in a loss of the MR property of the tablets.**

5. **Crushed Circadin 2mg MR tablets can be considered where an immediate release formulation is required.**

6. **There is no routine ongoing monitoring required specifically for melatonin in primary care other than monitoring for possible adverse effects and continued need.**

7. **If treatment is successful, a trial reduction in the dose should be attempted after 6 months as some patients would 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.**

8. **Efficacy of melatonin may be lost if prescribed for longer than two years continuously. It suggests that if melatonin is withdrawn prior to this, sensitivity may be re-established, and melatonin successfully re-introduced at a lower dose if still required.**

9. **If further advice or support is required, the Community Paediatrics Team or CAMHS can be contacted (contact details below).**

Indications and prescribing good practice

Whenever possible the patient (and their parents / guardian) should be involved in the decision making about initiating treatment and should be given information about melatonin in order to make an informed choice. Printable leaflets including information about good sleep hygiene can be found at https://www.nhs.uk/live-well/sleep-and-tiredness/healthy-sleep-tips-for-children/ and on the Cambridgeshire Community Services NHS Trust website https://www.cambscommunityservices.nhs.uk/what-we-do/children-young-people-health-services-cambridgeshire/cambridgeshire-0-19-healthy-child-programme/sleep

Melatonin is a pineal hormone which may affect sleep pattern. Melatonin is generally prescribed locally for children with sleep disturbances associated with learning difficulties, Attention Deficit Hyperactivity Disorder (ADHD) or autism. Occasional reports of its use for children with chronic fatigue syndrome or Asperger's syndrome have also been noted.

There is currently only one formulation of melatonin available in the UK licensed for use in children, Slenyto® prolonged release tablets.[1] However, this is only licensed for a defined cohort of patients. The East of England Priorities Committee does not currently recommend prescribing of Slenyto®.

The formulations of melatonin which can be prescribed across Cambridgeshire and Peterborough are:

- **1st line: Circadin® 2mg MR tablets (off-label)**

  - If required to support with swallowing, when divided into halves Circadin MR tablets have been shown to preserve most of the prolonged-release characteristic.

  - Circadin® MR tablets may be crushed and dispersed in water or milk or added to soft food like yoghurt, without losing its efficacy (off-label). However, this will result in a loss of the MR property of the tablets.

  - This is still considered the first option in patients who might not benefit from the MR formulation or who are unable to swallow tablets whole.

- **2nd line: Melatonin 10mg/5ml oral suspension AF (AF – alcohol free).** ***The prescription should also be annotated as propylene glycol free*** **(unlicensed)**

  - Where an immediate release formulation is required, and off-label use of Circadin is not clinically acceptable to the patient, and the rationale is documented in the patient's clinical notes (justification for an unlicensed preparation vs. off-label) then an unlicensed melatonin oral suspension could be considered. However, this is significantly more expensive and may have a short-shelf expiry.

- **All other formulations of melatonin are not recommended and are considered non-formulary.**

For more information on melatonin formulations and the rationale for choices across Cambridgeshire and Peterborough see 'Melatonin prescribing for Paediatric Patients (Formulation Choice)'

On the advice of a Specialist Clinician

Treatment with melatonin should only be started on the advice of a specialist clinician, which may include Paediatric Consultant, Child Psychiatrist or Non-Medical Prescriber with a specialist interest in paediatric sleep disorders, in-line with this prescribing guidance.

Prescribing and monitoring of melatonin will usually be the responsibility of the GP.

Dosage

Consult the latest edition of the British National Formulary for Children https://bnfc.nice.org.uk/

Initially 2 mg once daily, increased to 4mg once daily after 5 days if required. The dose should be taken before bedtime. [2]

If treatment at 4mg daily remains ineffective at controlling sleep, advice of a specialist clinician should be sought as daily doses of 6mg and above are rarely required.

Patients and carers should be advised on initiation that treatment with melatonin and the need for continued use, will be reassessed every 6 months via a treatment holiday (see below).

Renal impairment[1]: The effect of any stage of renal impairment on melatonin pharmacokinetics has not been studied. Caution should be used when melatonin is administered to such patients.

Hepatic impairment[1]: There is no experience of the use of melatonin in patients with liver impairment. Published data demonstrates markedly elevated endogenous melatonin levels during daytime hours due to decreased clearance in patients with hepatic impairment. Therefore, melatonin is not recommended for use in patients with hepatic impairment.

Monitoring and Treatment Holidays in Primary Care

There is no pathology monitoring generally required for melatonin.

A melatonin treatment holiday should be attempted every 6 months as some children / adolescents 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 melatonin.

This could be considered during school holidays or over an extended weekend. However, timing of a treatment holiday should be in discussion with the patient / guardian and consider individual circumstances where the impact of potential sleep disruption can be minimised.

If sleep patterns are maintained during the treatment holiday, stopping melatonin permanently should be considered. Or alternatively, if treatment with melatonin is still required, dosing can be reduced by 2mg. If the difficulties recur the original dose should be reinstated, but a further trial reduction / treatment holiday should be attempted 6 months later, and every 6 months thereafter.

Some clinical experience from the National Child and Adolescent Learning Disability Psychiatry Network[3] suggests that the efficacy of melatonin may be lost if prescribed for longer than two years continuously. It suggests that if melatonin is withdrawn prior to this, sensitivity may be re-established, and melatonin successfully re-introduced at a lower dose if still required.

Reinforcement of good sleep hygiene should be discussed at each 6-monthly review and should be continued by the child / adolescent in conjunction with melatonin prescribing.

Individual patients may require additional monitoring based on co-morbidities or interacting medicines. It is likely these patients would remain within secondary care / community services and any primary care monitoring will be agreed on a case by case basis.

Melatonin is not currently recommended across Cambridgeshire and Peterborough for adult patients (any indication). Young people who are transitioning towards adult services or reach 18 years should be reviewed in conjunction with advice from the specialist services where applicable.
If sleep concerns remain, treatment should follow standard guidance for adults with sleep problems. See:

- Clinician information: https://patient.info/doctor/insomnia
- Patient leaflet, comprehensive: https://www.cpft.nhs.uk/download.cfm?ver=1730
- Patient leaflets, brief:
- https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=11887&type=0&servicetype=1
- https://www.nhs.uk/conditions/insomnia
- Patient video (TED talk): https://www.ted.com/talks/dan_kwartler_what_causes_insomnia?language=en

Contraindications and Cautions[1]

Melatonin may cause **drowsiness**. Therefore the product should be used with caution if the effects of drowsiness are likely to be associated with a risk to safety.

No clinical data exist concerning the use of melatonin in individuals with **autoimmune diseases**. Therefore, melatonin is not recommended for use in patients with autoimmune diseases.

In view of the lack of clinical data, use in **pregnancy** and by women intending to become pregnant is not recommended. **Breast-feeding** is not recommended in women under treatment with melatonin.

For further information please consult the latest edition of the British National Formulary for Children (BNFC) or Summary of Product Characteristics (SPC) for full details: http://www.medicines.org.uk/emc/

Adverse effects[1]

For further information please consult the latest edition of the British National Formulary for Children (BNFC) https://bnfc.nice.org.uk/ or Summary of Product Characteristics (SPC) for full details: http://www.medicines.org.uk/emc/

Short-term use of melatonin appears to be safe for most people. Documented long term studies, greater than 2 years are lacking, however adverse effects associated with melatonin are generally uncommon.

Possible side-effects include:

- **Uncommon (≥1/1,000 to <1/100) :** Irritability, nervousness, restlessness, insomnia, abnormal dreams, nightmares, anxiety, migraine, headache, lethargy, psychomotor hyperactivity, dizziness, somnolence, hypertension, abdominal pain, abdominal pain upper, dyspepsia, mouth ulceration, dry mouth, nausea, hyperbilirubinaemia, dermatitis, night sweats, pruritus, rash, pruritus generalised, dry skin, pain in extremity, glycosuria, proteinuria, asthenia, chest pain, liver function test abnormal, weight increased.

Drug Interactions[1]

For further information please consult the latest edition of the British National Formulary for Children (BNFC) https://bnfc.nice.org.uk/ or Summary of Product Characteristics (SPC) for full details: http://www.medicines.org.uk/emc/

Melatonin interacts specifically with the following drugs:

- Caution should be exercised in patients on **fluvoxamine**, which increases melatonin levels. The combination should be avoided.
- Caution should be exercised in patients on **5- or 8-methoxypsoralen** (5 and 8-MOP), which increases melatonin levels.
- Caution should be exercised in patients on **cimetidine** a CYP2D inhibitor, which increases plasma melatonin levels.
- Caution should be exercised in patients on **oestrogens** (e.g. contraceptive or hormone replacement therapy), which increase melatonin levels.
- CYP1A2 inhibitors such as **quinolones** may give rise to increased melatonin exposure.
- CYP1A2 inducers such as **carbamazepine and rifampicin** may give rise to reduced plasma concentrations of melatonin.

Melatonin also belongs to the class of anxiolytics/hypnotics, which may interact with:

- ACE inhibitors, adrenergic neurone blockers, alcohol, alpha-blockers, anaesthetics, angiotensin-II receptor antagonists, tricyclics or tricyclic-related antidepressants, opiates, antihistamines, antipsychotics, baclofen, beta-blockers, calcium-channel blockers, clonidine, diazoxide, diuretics, hydralazine, lofexidine, methyldopa, minoxidil, mirtazapine, moxonidine, nitrates, opioid analgesics, ritonavir, tizanidine.

Cigarette smoking may decrease melatonin levels.

Patient information

- Healthy Sleep Tips for Children: https://www.nhs.uk/live-well/sleep-and-tiredness/healthy-sleep-tips-for-children/
- CPFT Paediatric Psychology Team Toolkit - Sleep Difficulties: https://www.cpft.nhs.uk/psychology-toolkit/
- *CCS Patient Information Leaflet: https://www.cambscommunityservices.nhs.uk/docs/default-source/leaflets---community-paediatrics/0042---management-of-sleep-problems.pdf?sfvrsn=6*

Advice and Support

Community Paediatrics (Cambridgeshire Community Services NHS Trust) are available, Monday-Friday 9am-5pm, to provide general advice and support on the prescribing of melatonin (Telephone: 0300 029 50 50)

North Cambridge, South Cambridge, Cambridge City and Ely
Community Paediatrics, The Peacock Centre, Brookfields Hospital, 351 Mill Road, Cambridge. CB1 3DF Tel: 01223 218072
Email: ccs-tr.communitypaediatricssouth@nhs.net

Huntingdon and Fenland
Community Paediatrics, The Oak Tree Centre, 1 Oak Drive, Huntingdon. PE29 7HN Tel: 01480 425300
Email: ccs-tr.clinicalsupport@nhs.net

For patients who are receiving treatment under The Community Child and Adolescent Mental Health Services (CAMHS) in Cambridgeshire and Peterborough, contact Single Point of Access Clinicians on 01480 428115 Monday to Friday 09:00-17:00 or via e-mail accesscamhs@nhs.net

References

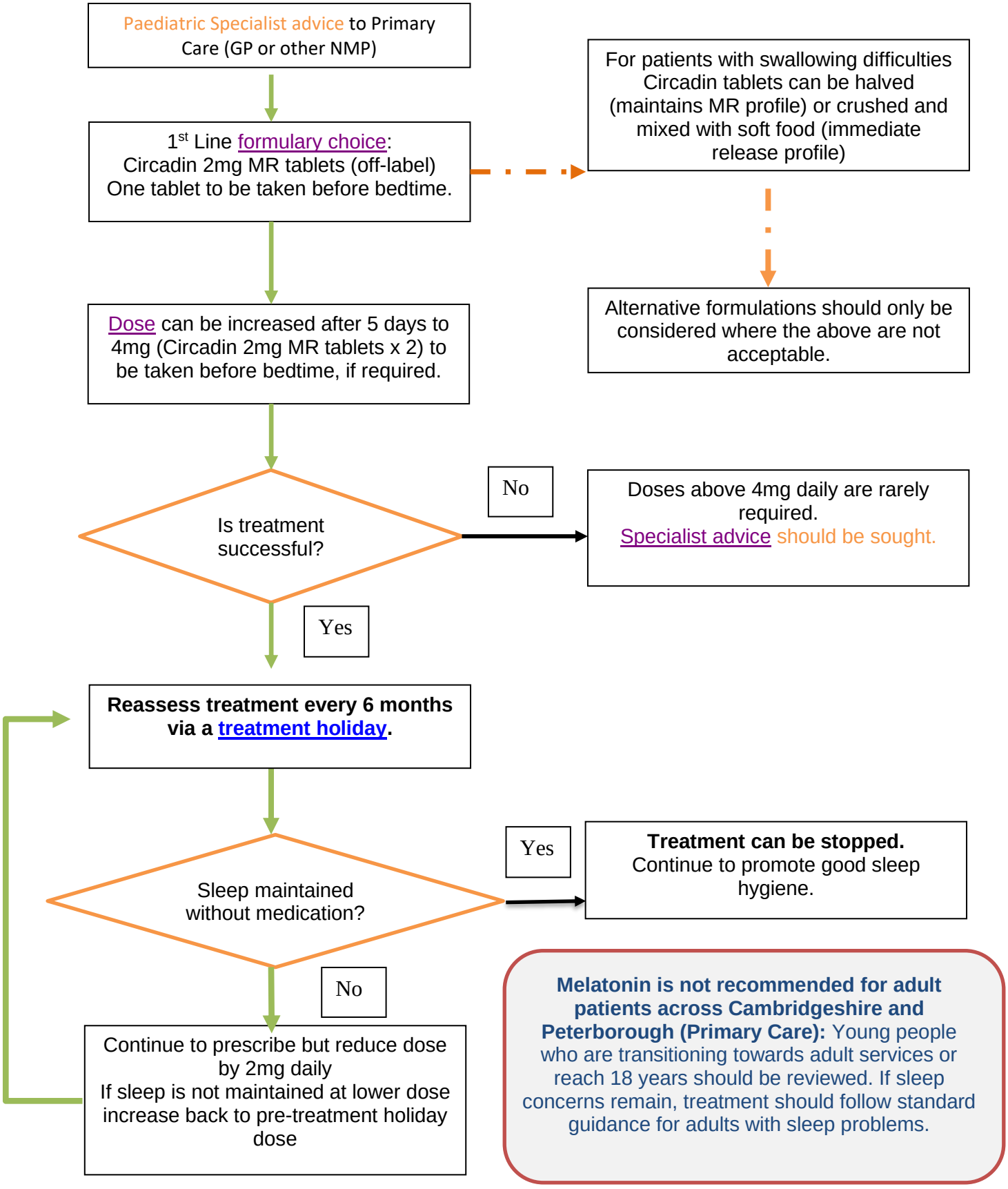
1. Summary of Product Characteristics (SPC). Accessed 14/09/2020 via http://www.medicines.org.uk/emc/
2. British National Formulary for Children Accessed 14/09/2020 via https://bnfc.nice.org.uk/
3. National Children and Adolescent Learning Disability Psychiatry Network. 2008

Authors

Dr Rachel Bower (Cambridgeshire Community Services NHS Trust)
Ann Darvill (Cambridgeshire Community Services NHS Trust)
Dr Karina Hart (Cambridgeshire Community Services NHS Trust)
Dr Nicola Herberholz (Cambridgeshire Community Services NHS Trust)
Dr Gillian Mitchell (Cambridgeshire Community Services NHS Trust)
Dr Becky Jones (Cambridgeshire and Peterborough Clinical Commissioning Group)
Kelly Broad (Cambridgeshire and Peterborough Clinical Commissioning Group)
Approved by CPJPG November 2020 Update required October 2022

NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Quick Reference Guide to the Prescribing of Melatonin for Children and Adolescents where other sleep hygiene methods alone have been unsuccessful



Melatonin is not recommended for adult patients across Cambridgeshire and Peterborough (Primary Care): Young people who are transitioning towards adult services or reach 18 years should be reviewed. If sleep concerns remain, treatment should follow standard guidance for adults with sleep problems.