

Portsmouth and South East Hampshire Area Prescribing Committee
Basingstoke, Southampton and Winchester District Prescribing Committee

Shared Care Agreement

Melatonin for sleep disorders in children

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This shared care protocol has been developed to support the combination of the best of both primary and secondary care for the benefit of the patient. It facilitates seamless transfer of patient treatment from secondary to primary care and provides an information resource to support clinicians providing primary care to the patient.

It supports but does not replace discussion and agreement on an individual patient basis about transfer of care.

Introduction

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced by the pineal gland during the dark hours of the day-night cycle. The pineal gland produces it in a circadian manner, in response to darkness. The link with circadian rhythms has led to its use in the treatment of sleep disorders underpinned by learning disability, autistic spectrum disorders, and ADHD. It is also effective as a chronobiotic in delayed sleep phase syndrome used as an adjunct to bright light therapy at low doses around 4-6 hours before dim light melatonin onset.

The use of melatonin is supported by NICE Clinical Guideline 53: *Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management*. CG 53 states that melatonin may be considered for children and adolescents with CFS/ME who have sleep difficulties, but only under specialist supervision.

Melatonin is classified as a medicine in the UK: Circadin® is a sustained release formulation of melatonin that is licensed in the UK for the treatment of primary insomnia in adults aged 55 years and over.

There are no licensed products of melatonin in the UK for the treatment of childhood insomnia. Circadin® mini-tablets are currently being evaluated in a phase III multi-centre trial in children with neurodevelopmental disorders but at present its use in this age group will be off-label.

In practice the use of melatonin for the treatment of paediatric sleep disorders is common clinical practice.

Unlicensed preparations of melatonin are available – the standards of manufacture and quality control of these unlicensed specials may be unpredictable.

Referral Criteria

The specialist will request shared care when the patient has responded well to melatonin and the patient is stable on a particular dose.

Indication

- **Melatonin is only indicated where non-pharmacological strategies have been tried, but sleep latency remains a significant problem.**
- Melatonin may be considered for children and adolescents with CFS/ME who have sleep difficulties.
- For use in children of at least 1 year of age with neurodevelopment disability, autism, visual impairment or neuropsychiatric disorders and chronic sleep disturbance, including chronic fatigue syndrome, where both:
 - Symptoms of sleep disturbance have been present for at least six months or sleep disturbance is so severe that it is causing significant family disturbance.
 - The sleep problem has been thoroughly evaluated and a disorder of sleep that is likely to respond to melatonin has been diagnosed (e.g. sleep onset insomnia/delayed sleep phase syndrome, likely endogenous melatonin deficiency or phase reversal), importantly disorders of sleep not responsive to melatonin have been excluded (e.g. limb movement disorder in ADHD and sleep disordered breathing)

Dosage, administration and other prescribing information

- **Initial dose 2mg (given 30-60 minutes before bedtime). In absence of improvement after 1-2 weeks, the dose is increased by 2mg incrementally according to response. Maximum dose is 10mg /day although there is evidence that there is little additional benefit at doses over 6mg (MENDS RCT).**
- **Melatonin MR tablets 2mg (Circadin®) is the first - line melatonin product as it has a UK licence. Although it is only licensed in adults over 55 years old it is preferable to use a licensed medicine for an unlicensed indication rather than an unlicensed medicine where a licensed preparation is available. There are no preparations of melatonin licensed for children in the UK.**
- For children waking during the night, the same dose or a smaller dose can be repeated during the night. The 2mg SR Circadin® tablet can be halved using a tablet cutter and it will retain its slow release characteristics.
- For children with difficulties swallowing, the tablet can be crushed to a fine powder and mixed with water or given with cold soft food such as a teaspoon of yoghurt or jam. Use a small amount of food to ensure the full dose is taken.
- For administration via an enteral feeding tube, the tablet can be crushed to a fine powder and added to 15 - 30ml of water and mixed well. This should be drawn into an oral syringe and administered taking care to rinse the mortar/tablet crusher with water and administering the rinsings also. The feeding tube should be flushed with 30ml water before and after drug administration.
- **NOTE:** crushing the MR tablet will mean that it is no longer modified release. Circadin® is formulated as a modified release tablet to ensure continuous melatonin action throughout the night. Immediate release or crushed modified release tablets only act for 2 to 3 hours.
- **Special order liquid medicines or capsules are unlicensed and expensive and should ONLY be used where absolutely necessary. The melatonin liquid of choice is Melatonin 5mg/5ml Oral Solution.**
- If required the prescription should state that the medication is to be crushed prior to administration.

- A drug holiday should be introduced at least annually to assess the continued need for treatment. This could take place a month before the annual review with the patient and / or the carer keeping a sleep diary. The outcome of any drug holiday must be recorded in the patient's notes.

Contraindications

- Known hypersensitivity to melatonin or any excipients.

Cautions

- 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.
- Circadin contains lactose. Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Hospital Specialist Responsibilities

Treatment with melatonin should be initiated by an experienced specialist in sleep medicine, CAMHS practitioner, paediatrician or learning disabilities specialist.

- Establish a diagnosis. A thorough history should always be taken and a sleep diary used if there is any doubt about the extent of the problem.
- Initiate treatment after discussion of the treatment options available with the patient and carer(s).
- Inform the patient/carer of the unlicensed nature of melatonin, the need for shared care (once dose stabilised), and obtain appropriate consent to treatment.
- Advise the patient/carer to follow sleep hygiene measures (bedtime and wake up routine, avoidance of daytime sleep for children of an appropriate age) and to repeat the sleep diary at intervals throughout treatment with melatonin, if practicable.
- Prescribe the initial supply (for at least 4 weeks treatment) and continue prescribing until the patient is stable on a particular dose.
- Write to the GP when the melatonin is initiated, to ask the GP whether he/she is willing to participate in the ongoing prescribing and general care as outlined in this shared care agreement. A copy of this shared care agreement should be sent with the letter.
- Offer the patient outpatient appointments at least annually and regular appointments with the community teams or paediatric support team. At these appointments the efficacy of melatonin should be reassessed, and discontinued if appropriate.
- Ensure compatibility of melatonin with concomitant medication.
- Report any suspected adverse drug reactions (ADRs) to the Medicines and Healthcare products Regulatory Agency (MHRA) via the yellow card scheme.
- When appropriate, undertake periodic treatment withdrawals, or advise the GP in writing how and when to undertake them.
- Promptly communicate any changes, recommendations, outcomes or other important information to the GP.

Provide advice to the GP or patient if they have clinical queries relating to the condition or use of melatonin.

Disease and drug monitoring

No routine tests required.

GP Responsibilities

- The GP is responsible for the general health and well-being of the patient. He/she will only prescribe melatonin if there is some evidence of ongoing efficacy.
- If the GP considers that the patient should be reviewed they should contact the initiating prescriber; CAMHS or paediatric team, but will continue to prescribe until the reassessment has taken place (unless an adverse effect has occurred).
- The GP must review the need for continuing the melatonin at least every 6 months, referring back to the hospital specialist as appropriate. Indefinite continuation of melatonin without specialist review is not recommended.
- Prescribe melatonin once the patient is stable on a particular dose.
- Communicate any problems to the specialist looking after the patient.
- Ask the specialist to take back the prescribing should unmanageable problems arise and allow an adequate notice period (4 weeks is a suggested minimum).
- Report any suspected adverse drug reactions (ADRs) to the Medicines and Healthcare products Regulatory Agency (MHRA) via the yellow card scheme.
- Inform secondary care specialist immediately if unable to take on shared care.

Adverse Effects

- Melatonin is generally well tolerated. Side effects are uncommon.
- For a complete list of side effects refer to Circadin SPC
<http://www.medicines.org.uk/emc/medicine/25643>

Drug Interactions

- Caution should be exercised in patients on 5- or 8-methoxypsoralen, cimetidine, oestrogens, quinolones, which may increase melatonin levels by inhibiting its metabolism.
- Refer to Circadin SPC for full details <http://www.medicines.org.uk/emc/medicine/25643>.

Patient/carer responsibilities

- Ensure they have a clear understanding of the treatment.
- Take/give the melatonin as advised.
- Share any concerns in relation to treatment with the specialist, GP or pharmacist
- Report any adverse effects or warning symptoms to the specialist, GP or pharmacist whilst taking/giving the medication
- Attend booked appointments for review and monitoring of therapy.

Products to prescribe / costs per month (in primary care)

	First line	Second line	Third line (Prescribe only if there is a justified clinical reason why the patient cannot tolerate tablets swallowed whole or crushed.)
Name of product	Melatonin 2mg Modified Release tablets (Circadin®)	Melatonin 3mg tablets (Bio-Melatonin®)	Melatonin 5mg/5ml oral solution (Please note other melatonin solutions and suspensions have a higher cost and should not be prescribed).
Route of administration	Oral - may be crushed - acts as an immediate release preparation.	Oral - can be crushed. Can be administered via PEG tube.	Oral solution
Recommended starting dose	2mg once daily, 1-2 hours before bedtime and after food. If crushed, take half an hour before bedtime.	Initially 3mg once daily taken half an hour before bedtime.	Initially 2-3mg once daily.
Titration of dose	Increase by 2mg depending on response every 7-14 days.	Increase to 6mg depending on response after 7 – 14 days.	Increase by 2-3mg depending on response after 7-14 days.
Maximum dose	8mg	10mg daily but additional benefits from doses above 6 mg are uncertain.	
Adjunctive treatment regimen	Sleep hygiene (advice)	Sleep hygiene (advice)	Sleep hygiene (advice)
License status	Licensed medicine in UK (off-label use)	Unlicensed in UK. (Licensed in EU)	Unlicensed.
Approximate cost per month in primary care	2mg x 30 = £15.39	3mg x 60 = £16.84	200ml = £77.84

This guidance should be read in conjunction with the BNF and the summary of product characteristics (SPC/data sheet) available via [Home - electronic Medicines Compendium \(eMC\)](#)

Sources of Information

Sussex Partnership Trust	Name / position	Telephone	Email
Specialist / Consultant	Havant: Dr Asha Gowda (Consultant, Havant)	02392 224560	N/A
	Dr Fiona Holden (Consultant, Fareham & Gosport)	01329 822220	N/A
Hospital Pharmacy	Worthing Hospital	01903 205111 (ext 85698)	pharmacy@wsht.nhs.uk
	CAMHS Pharmacist	07825 118323	graham.brown@wsht.nhs.uk
Out of hours	On call physicians	N/A	N/A

Solent NHS Trust	Name / position	Telephone	Email
Consultant	Dr Julia Waine	023 9268 4700	
CAMHS Portsmouth	Falcon House, St James Hospital, Locksway Road, Portsmouth, Hampshire, PO4 9EH	023 9268 4700	SNHS.CAMHS-general@nhs.net
Pharmacy	St Mary's Hospital Portsmouth	023 92680280	

References

- BNF for Children 2014-15
- Shared Care Guideline, Melatonin for sleep disorders/difficulties in children, Basingstoke, Winchester & Southampton District Prescribing Committee, 2015
- <http://www.circadin.com/about-circadin/qa/> date accessed 7/9/2015
- Online drug tariff date accessed 10/9/2015
- Personal communication with NHS Business Services 10/9/2015
- Personal communication with Oxford Pharmacy Stores 11/9/2015
- Cicadin Summary of Product Characteristics <http://www.medicines.org.uk/emc/medicine/25643> date accessed 11/9/2015
- Evidence Review: Melatonin for sleep disorders in children with neurodevelopmental disorders, Basingstoke, Southampton and Winchester District Prescribing Committee, November 2015.