

HEREFORDSHIRE SHARED CARE GUIDELINE MELATONIN for Children with Severe Sleep Disorders

Introduction

Melatonin is not licensed for use in children but Circadin® (UK licensed for 55 years and over) and Bio-Melatonin (EU licensed) are preferred for off-license use in line with MHRA guidance. Although the evidence base for Melatonin is limited, it is more substantial than that available to support the use of any alternative hypnotic in this population.

Melatonin is indicated for the treatment of sleep disorders in children and young people with developmental and psychiatric disorders. This is an 'off-label' indication.

Melatonin is a pineal hormone which may affect sleep pattern. Production is affected by light exposure detected by the retina; it is thought that this rhythm is disturbed in children with brain damage or visual disturbance. Randomised-controlled trials and clinical experience suggests that it may be of value for treating sleep onset insomnia and delayed sleep phase syndrome in children with conditions such as visual impairment, cerebral palsy, ADHD, epilepsy, autism, and learning difficulties. Little is known about its long-term effects in children, and there is uncertainty as to the effect on other circadian rhythms including endocrine or reproductive hormone secretion. Treatment with melatonin should be initiated and supervised by a specialist, but may be continued by general practitioners under a shared-care arrangement. **The need to continue melatonin therapy should be reviewed every 6 months.**

Treatment Aim

To establish a regular nocturnal sleep pattern, particularly when behavioural modification has been unsuccessful or is very difficult to achieve, for children with severe sleep disturbances

Dose (by mouth)

Child 1 month–18 years:

Initially 2 mg before bedtime increased if necessary after 1–2 weeks to 4–6 mg; **max. 10 mg**

The dose should be given 30-60 minutes prior to bedtime

Problems with sleep maintenance or early morning waking

Modified release melatonin is indicated in the first instance. The licensed preparation melatonin modified release tablet 2mg (Circadin®) should be used first line where appropriate.

Problems with sleep initiation

Standard release melatonin is indicated for children and adolescents who have problems with sleep initiation. The starting dose is usually 2-3mg given 30-60 minutes before bedtime. If there is no response or insufficient response after a minimum of 14 days therapy the dose is increased to 6mg. In certain circumstances the dose can be increased up to a maximum dose of 10mg.

Problems with both sleep initiation and sleep maintenance/fragmental sleep/early morning awakening

In children and adolescents who have problems with both sleep initiation and sleep maintenance/early morning awakening, a **Modified** release preparation (Circadin®) is indicated. In some children a combination of standard melatonin and modified release melatonin may be required, up to a maximum total dose of 10mg.

A time period of 7-14 days is usually sufficient to determine if a specific dose is effective, and if ineffective, melatonin can be stopped without the need for gradual withdrawal

Preparation and Availability

Melatonin should be prescribed as one of the locally preferred preparations namely:

- Modified release (MR) Circadin 2mg tablets (a licensed UK brand)
- Standard release tablets: Bio-Melatonin 3mg tablets (unlicensed in UK)

Prescribing melatonin by its generic name is NOT locally recommended as this may lead to expensive unlicensed 'specials' products being supplied in primary care.

Administration tips:

Circadin® tablets have to be swallowed whole or cut in half and swallowed without chewing to retain the modified release characteristics.

However Circadin® may be crushed for an immediate release effect: crush to a fine powder and mix with water or give with a small amount of cold soft food such as a teaspoon of yoghurt or jam. *(This is an exception to the standard rule where modified release preparations should be swallowed whole).*

Bio-Melatonin may be crushed just before administration and mixed with food. In crushed form it may be used via a gastrostomy.

If neither of the above two locally preferred products is suitable other preparations are available including capsules, which can be opened and the contents sprinkled on food. Liquid preparations are likely to be significantly more expensive; 5mg/5ml solution is the most cost effective where clinically required.

Contraindications and Cautions

Contraindicated in children under one month of age, autoimmune disease, hepatic impairment (manufacturer advises avoid), pregnancy - no information available (manufacturer advises avoid), breast-feeding present in milk (manufacturer advises avoid). Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactose malabsorption should not take this medicine

Cautions: possible drug interactions (see BNF/SPC for up to date list. Interaction with fluvoxamine is potentially hazardous - plasma concentration of melatonin increased—concomitant use should be avoided). Renal impairment: no information available—manufacturer advises caution. If hypersensitivity to the active substance or to any of the excipients. As melatonin may have a pro-convulsant effect (unproven) seizure frequency should be monitored when prescribing in patients with epilepsy. Avoid alcohol.

Side Effects

Melatonin is generally well tolerated. Sedation and fatigue, headaches, skin disorders, restlessness, increased pulse, itching and nausea have all been reported as side effects associated with melatonin use. In epilepsy melatonin has been reported both to improve and to worsen seizure control.

The above details are not a complete list – refer to the [BNF-C](#) and the [summary of product characteristics](#) (SPC) for a full list of side effects and interactions www.medicines.org.uk/emc

Pregnancy/Lactation

Due to lack of clinical data, use in pregnant women and by women intending to become pregnant is not recommended.

Breast-feeding is not recommended in women under treatment with melatonin.

Monitoring

Pre-treatment (see Consultant request letter to GP for these results)

During initiation of treatment, sleep patterns should be documented to monitor efficacy. In people with epilepsy, close monitoring of seizure frequency is advised. Review patients every six months to ensure that continued treatment with Melatonin is appropriate and effective.

Toxicity

Parameter	Frequency of Monitoring	Action
Monitor seizure frequency in patients with epilepsy	Individual care plans with information to carers and GP on when to contact specialist for advice	

It has been suggested that melatonin may affect the reproductive system by inhibiting the hypothalamic-pituitary-gonadal axis. Growth and sexual development monitoring is advisable, especially with long term melatonin use. This is primarily the responsibility of the Consultant clinician but any concerns from the primary care clinician should be reported to the Consultant clinician.

[Melatonin is monitored intensively by the CHM and MHRA - Please report any adverse reaction to the CHM, using the yellow card system <http://yellowcard.mhra.gov.uk>]

Efficacy

Parameter	Frequency of Monitoring	Action
Sleep pattern	Review every six months by specialist	Adjust dose as necessary and inform GP

Cost and Purchasing Information

Circadin tablets 2mg MR 30 tablets £15.39

Bio-Melatonin tablets 3mg 30 tablets £38 approx.

Alternative unlicensed melatonin preparations available from Oxford Pharmacy Store (NHS supplier of specials www.oxfordpharmacystore.co.uk) Tel: 01865 321085 ops.orders@oxfordhealth.nhs.uk

The most cost effective liquid preparation (unlicensed special) is 5mg/5ml solution 200ml £53.20
NB costs may vary, correct at March 2017, delivery charges apply in addition for special order medicines

Contacts – back up advice and support

Contact Details	Phone	E-mail
Consultant Paediatricians	01432 364123 Bleep 065	Shambhu.Shah@wvt.nhs.uk
Medicines Info	01432 364017	Joanne.Howe@wvt.nhs.uk
Learning Disabilities	01432 260481	
CAMHS	01432 378940	p.ronzoni@nhs.net

NICE Evidence Summary [ESUOM2 Jan 2013] Sleep disorders in children and young people with attention deficit hyperactivity disorder: melatonin: <https://www.nice.org.uk/advice/esuom2/chapter/Key-points-from-the-evidence>

Shared Care Responsibilities

	Consultant/Specialist Responsibilities
1	Discuss benefits and side effects of treatment with patient and obtain informed consent for off-label unlicensed use
2	Ask GP if they are willing to participate in Shared Care and inform the GP in writing of the required dose and any dose changes
3	Carry out any pre-treatment assessment or tests
4	Initiate treatment, prescribing melatonin as a locally preferred product, providing the patient /carer with the first month's supply and a written patient information leaflet
5	Monitor response to treatment regularly and review the patient's condition, making dose adjustments as necessary until the dose is stable - usually at a point where there is improved sleep pattern on a certain dose with no reported side effect
6	To advise the GP regarding continuation of treatment, including the length of treatment. Ensure clear arrangements for GP back-up, advice and support. Discuss any concerns with the GP
7	Review patient every 6 months to ensure that continued treatment with melatonin is appropriate and effective

	GP Responsibilities
1	Reply to the request for Shared Care within 14 days of request
2	Once dose is stable prescribe Melatonin as a locally preferred product. Check for continued efficacy and side-effects
3	To report any adverse reaction to the MHRA and the referring consultant
4	To inform the consultant if the patient discontinues treatment for any reason & liaise with the consultant regarding any complications of treatment
5	Stop treatment on advice of the Consultant

	Patient / Carer Responsibilities
1	Read information provided and give consent for the chosen treatment
2	Inform consultant and GP of any other medication they may be taking or start taking during treatment, including over the counter medicines or herbal remedies
3	Request prescriptions in a timely fashion, remembering that the community pharmacist may need a few days to order this medicine
4	Store and handle the medication safely
5	Take prescribed medication as instructed
6	Reports any side effects to GP or Consultant