

SHARED CARE

DRUG: MELATONIN

PROTOCOL NUMBER: CV 54

Circadin ® 2mg m/r is the melatonin preparation of choice in Cardiff and Vale UHB and Cwm Taf LHB and should generally be prescribed first line. This is licensed preparation which will be prescribed for an unlicensed population – paediatrics. There may be a small number of patients for whom this preparation is not suitable, and in these circumstances Melatonin Oral solution 5mg/5ml should be prescribed.

Indication For children and adolescents (up to and including 18 years) with significant sleep onset difficulties who have at least one of the following:

- Ocular Visual Impairment
- Learning Disabilities
- Neuro-developmental Disorder including Autistic Spectrum Disorders; ADHD where

i) 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

ii) Sleep hygiene/ behavioural measures have been trialled and failed

General guidance

This protocol sets out details for the shared care of patients taking melatonin and should be read in conjunction with the General Guidelines for Shared Care. Sharing of care requires communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **The doctor who prescribed the medication legally assumes responsibility for the drug and the consequences of its use.** The prescriber has a duty to keep themselves informed about the medicines they prescribe, their appropriateness, effectiveness and cost. They should also keep up to date with the relevant guidance on the use of the medicines and on the management of the patient's condition.

Background

Melatonin is a hormone secreted by the pineal gland in a circadian manner, in response to darkness. Its main function is the regulation of circadian rhythm and sleep, playing an important role in setting the correct timing of sleep-wake cycles.

Sleep disorders in children with neurological and neuro-developmental disorders are very common. Causes include delayed brain maturation, altered function of sensory organs, especially vision, and abnormalities of the sleep centres. The particular types of sleep difficulties seen include delayed sleep onset, frequent waking, early morning waking and day-night reversal patterns. It is well known that improving sleep patterns leads to a general improvement in health, behaviour and well-being.

Detailed sleep histories are key to the diagnosis of sleep disorders, which can be a major source of stress for the whole family and limited solutions are available. Drug therapy should only be commenced after behavioural interventions and sleep hygiene measures have been carried out.

Hypnotics and sedatives are often used to improve sleep patterns but have adverse side effects and there can be resistance and tolerance.

There is increasing evidence from small randomised controlled trials to suggest that melatonin is effective in reducing sleep onset latency in children with neuro-developmental disorders. Trial evidence is inconsistent regarding effect on night waking and total sleep time.

There are no licensed preparations of melatonin in the UK for treatment of childhood insomnia. Circadin ® is a sustained released formulation of melatonin that is licensed in the UK for the treatment of primary insomnia in adults aged 55 years and over. MHRA advice is if there is a licensed product available it should be used, even if it is for an unlicensed indication.

If melatonin is being considered, behavioural interventions and sleep hygiene measures should be used first and maintained during the trial. The benefits of behaviour change continue longer over time than drugs.

A trial of melatonin is recommended once: (see Appendix 1)

1. The clinical criteria are met
2. A baseline sleep diary has been obtained (Appendix 2)
3. Behavioural measures have been initiated (Appendix 3)
4. An Information Leaflet has been given to the family and their GP (Appendix 4)

Advice about sleep hygiene should be discussed with the family, backed up with written information (Appendices 3 and 4), and in consultation with the Health Visitor, School Nurse, Community Children's Nurse or Community Nurse for Learning Disabilities, as appropriate.

Sleep Diaries

Sleep diaries and parent information are important. Prior to a trial of melatonin, a baseline sleep diary should be completed to aid diagnosis of the type of sleep disorder (Appendix 2). Further diaries are used to monitor effectiveness and influence decision making. Some children may have noticeable improvement in their sleep pattern after the first dose of melatonin. Others may not show improvement for several days or even weeks.

Responsibilities

A. Consultant responsibilities

1. When treatment is **initiated** send Shared Care request form with Shared Care protocol to GP
2. Baseline and continued monitoring of clinical parameters
3. Initiate therapy following full discussion with the patient (and/or carer) of benefits and risks advising that this product is not licensed for use in paediatrics
4. When a GP positive response to SC has been received and patient has been stabilised send a letter to GP "handing over" the Shared Care of the patient to the GP.
5. Respond to any request from GP to review the patient due to adverse effects of therapy.
6. Advise the GP on continuing (including dose changes) or stopping melatonin following medical review of the patient and associated drug therapy (including drug holidays). Advise the GP when therapy should be discontinued for patients receiving medication long-term and provide necessary supervision and support during drug discontinuation phase. If therapy continues into teenage years, care should be transferred to young persons or adult services as appropriate.

7. Ensure behavioural measures are ongoing.
8. Notify GP if patient is failing to attend for appropriate monitoring and advise GP on appropriate action

B. GP responsibilities.

1. Within one week of receipt return the completed Shared Care request form to indicate whether or not willing to undertake Shared Care
2. Prescribe melatonin as part of the shared care agreement once the patient has been stabilised.
3. Monitor the general health of the patient
4. Ensure behavioural measures are ongoing.
5. Stop treatment on advice of specialist
6. Report adverse effects of therapy to the consultant and the Medicines and Health Care products Regulatory Agency (MHRA). Any concerns should be fully discussed with the named Paediatrician or Child Psychiatrist.
7. Act on advice provided by the Consultant if patient does not attend for appropriate monitoring.

C. Patient (and/or carer) responsibilities

1. Consent to treatment with melatonin.
2. Attend regular appointments with specialist centre and GP
3. Report any side effects to the specialist or GP whilst taking melatonin.
4. Ensure behavioural measures are ongoing.

Dosage Regimen

The aim is to establish healthy sleep habits with the lowest effective dose. At least six months of an improved sleep pattern should elapse before withdrawal takes place. Withdrawal may occur over a period of 3-4 weeks. For some children however withdrawal is not successful and treatment may be necessary long term.

By mouth: Child 1 month to 18 years, initially 2mg (given 30-60 minutes before bedtime). In the absence of an improvement the dose can be increased by 2mg increments after 1 to 2 weeks to 4mg, 6mg or 8mg; to a maximum dose of 10mg daily as indicated.

Administration

The medication should be taken 30-60 minutes prior to bedtime on an empty stomach.

Circadin ® 2mg m/r tablets can be halved using a tablet cutter and still retain their 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. The prescription should state that the medication is to be crushed prior to administration. NB – crushing the m/r tablet will mean that it is no longer modified release.

For administration via an enteral feeding tube, the tablet can be crushed to a fine powder and added to 15-30ml of water, mix well. This should be drawn into a 50ml 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 prior to and post drug administration.

Monitoring

Patient monitoring – initially in the Paediatric setting within 8 weeks of initiation and then 6 monthly in the longer term. This includes both height and weight annually.

Monitoring, particularly with regard to growth and the onset of puberty/sexual development, is advised in children during long term administration, especially in those receiving melatonin for periods of a year or more. Monitoring of growth and the onset of puberty/sexual development will continue after melatonin is stopped whilst the child remains under the care of the paediatric teams.

Treatment should be stopped in patients who do not continue to benefit from its use. Withdrawal of melatonin can be immediate or gradual over a period of weeks to monitor for recurrence of sleep disorders, depending on the frequency of use.

Adverse effects

Further studies are required to know more about the short and long term effects of melatonin. Children appear to metabolise melatonin faster than adults and therefore need higher doses. In general it is a well tolerated drug, and no consistently significant side effects have been reported. Adverse reactions reported are at similar levels to those reported with placebo. There have however been anecdotal reports of: abdominal pain, constipation, dry mouth, weight gain, drowsiness, dizziness, migraine, asthenia, sleep disorders, restlessness, nervousness, irritability, sweating, pharyngitis, back pain, headache, bed wetting, nightmares, and visual disturbance. Rarely reports of: Flatulence, halitosis, hypersalivation, vomiting, hypertriglyceridaemia, aggression, agitation, fatigue, impaired memory, mood changes, hot flushes, priapism, increased libido, leucopenia, thrombocytopenia, muscle cramp, lacrimation, visual disturbances, skin reactions.

Concern has been expressed that exogenously administered melatonin could theoretically affect gonadal development in children. Young people up to the age of 20 years produce melatonin endogenously in high levels and levels are inversely related to gonadal development

Contraindications

Autoimmune disease – avoid as no clinical data exist concerning the use of melatonin in autoimmune diseases;

Hepatic impairment – clearance of melatonin reduced - avoid;

Pregnancy – no information – avoid;

Renal impairment – no information available – caution.

Hypersensitivity to the active substance or to any of the excipients

Patients with rare heredity problems of galactose intolerance, LAPP lactase deficiency, or glucose-galactose malabsorption.

Interactions

Case reports, clinical experience and theoretical principles suggest the following –
Caution with concomitant use of oestrogens, quinolones; may increase melatonin levels
Caution with carbamazepine and rifampicin; may reduce melatonin levels

- May enhance sedative properties of benzodiazepines and non-benzodiazepine hypnotics.
- Cigarette smoking may decrease melatonin levels
- Interactions may also occur with anticoagulant / antiplatelet drugs, anti-diabetic agents, cimetidine, contraceptives, flumazenil, fluvoxamine, immunosuppressants, nifedipine and verapamil.

Special recommendations

As there are currently many unlicensed melatonin preparations available with varying costs prescribers are advised to prescribe melatonin m/r by its brand name Circadin ®. Special order liquid medicines are unlicensed and expensive and should ONLY be used where absolutely necessary, where a patient is unable to tolerate the tablets being crushed or carers are not able to do so; in these cases Melatonin Oral Solution 5mg/5ml should be prescribed.

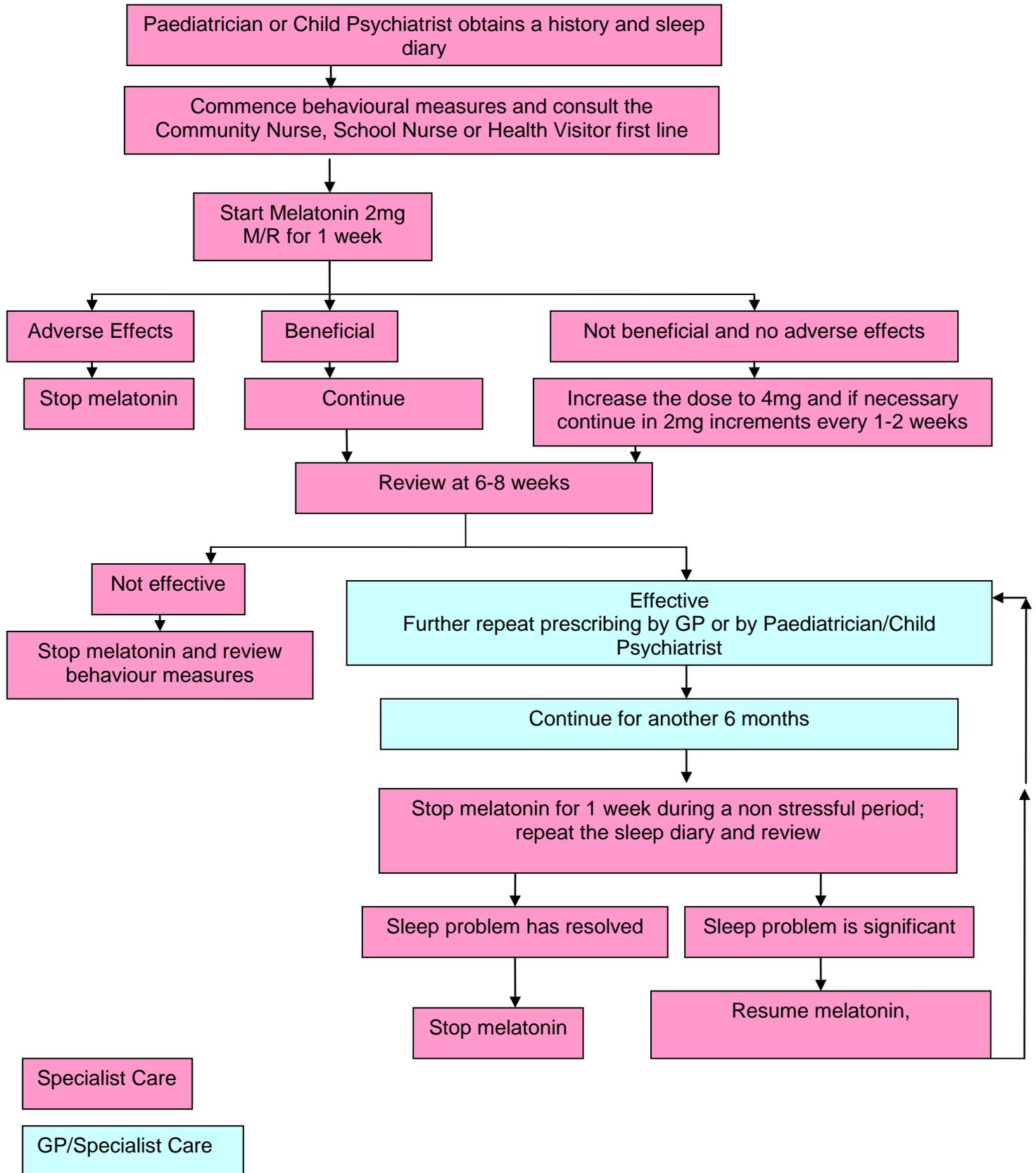
For children who wake during the night Circadin tablets should be crushed in order to bypass the modified release characteristics of Circadin and to provide an immediate effect.

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 parent keeping a sleep diary. The outcome of any drug holiday must be recorded in the patient's notes.

Date of review March 2017

Appendix 1

Shared Care Protocol for Prescribing Melatonin in Children and Adolescents with Significant Sleep Onset Difficulties



APPENDIX 2

SLEEP DIARY

CHILD'S NAME _____ **DATE OF BIRTH** _____

| | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday |
|---|---------------|----------------|------------------|-----------------|---------------|-----------------|---------------|
| Week Beginning/...../..... | | | | | | | |
| Time taken to bed | | | | | | | |
| Number of times gets out of bed and why | | | | | | | |
| Time & place fell asleep | | | | | | | |
| What helped him/her settle | | | | | | | |
| Number of times up overnight and for how long | | | | | | | |
| If up, what did he/she do | | | | | | | |
| Time he/she got up in the morning or if needed wakened | | | | | | | |
| How many daytime naps and length of time | | | | | | | |

Total sleep (hrs)

APPENDIX 3

GOOD ADVICE ON SLEEPING FOR BABIES AND INFANTS



1. Keep a regular bedtime for your baby.
2. Make sure that the baby's room is quiet and dark.
3. It is important that you wake your baby at a regular hour each morning.
4. Place your baby on his back to sleep.
Do not let baby sleep beside a radiator or fire.
No electric blanket or water bottle is required.
Do not smoke in the same room as your baby/child.
5. Keep room temperature to a comfortable level. High temperatures disturb sleep. Temperature 18°C or 65°F.
6. Make sure not to over heat. Lightweight blankets for him/her are ideal.
7. Environmental noise should be kept to a minimum (no loud TVs).
8. Relaxing music or bedtime story is ideal.
9. Make sure that your baby does not go to bed hungry, but do not give a child over 6 months old feeds/drinks during the night.
10. Avoid stimulating activity in the hour before bedtime; bath-time should be relaxing.
11. Do not let the child have prolonged naps in the late afternoon. If the child still needs to sleep, schedule the nap for early afternoon before 2pm.
12. Help your baby to learn to fall asleep alone in his / her own bed, without your presence.



APPENDIX 4



GOOD ADVICE ON SLEEPING FOR OLDER CHILDREN



Name:

Sleep environment

Make sure the child's room is comfortable.

The room should be darkened and quiet.

The temperature should be cool – not hot as this disrupts sleep.

A non-stimulating bedroom is ideal, pack up the toys in large boxes at night time.

It would be ideal not to have a telly or video machine in the bedroom.

Things to avoid

Do not let the child have excessive late afternoon naps (e.g. after 2pm).

No over excitement near bedtime (bath should be relaxing and functional).

No caffeine drinks e.g. tea, coffee, and cola before bedtime.

No large late meals.



Encouragement

Set a constant bedtime routine e.g. waking at the same time everyday, also at weekends and holidays.

Keep a regular relaxing bedtime routine e.g. snack, warm bath, story and bed.

Try to have a good playtime and run about outside each day.

Get as much sunlight as possible each day.

Help your child to learn to fall asleep alone in his/her bed without your presence.

Encourage your child to have a healthy snack before bed but no overnight bottles once the child is over 6-9 months.

It is most important to have a regular relaxing restful routine for bedtime.