

## Melatonin treatment protocol – chronic sleep disturbances in children

1.	<b>Medicine name:</b> Melatonin
2.	<b>Background:</b> Melatonin is a hormone produced by the pineal gland in a circadian manner, in response to darkness. The rise of melatonin precedes the onset of sleep by about 90 minutes. There is significant clinical experience with the use of melatonin for the treatment of paediatric sleep wake cycle disorders. Results in terms of improved sleep patterns have been generally favourable and adverse effects minimal.
3.	<b>Indication(s):</b> For use in children with chronic sleep disturbance where: <ul style="list-style-type: none"> <li>• Symptoms of sleep disturbance have been present for at least six months or sleep disturbance is so severe that the family are heading for crisis.</li> <li>• After failure of sleep hygiene improving measures e.g. a fixed bedtime routine.</li> </ul>
4.	<b>Prescriber details:</b> GP under the direction of specialist (paediatrics, child and adolescent psychiatry or other appropriate specialist in sleep disturbances).
5.	<b>Dosage:</b> <u>Using the Circadin® formulation</u> Initially 2mg daily 30 – 60 minutes before desired sleep time for one week. If this is sufficient to address insomnia continue at this dose.  If insomnia continues, the dose may be increased to 4mg daily for one week. If this is sufficient to address insomnia continue at this dose.  If insomnia continues, the dose may be increased to 6mg daily for one week. If this is sufficient to address insomnia continue at this dose.  If insomnia continues, the dose may be increased to 8mg daily for one week. If this is sufficient to address insomnia continue at this dose.  If there has been no response to a dose of 8mg daily, treatment should be discontinued and the patient referred back to the initiating specialist.  Doses up to 12mg daily may occasionally be used on advice of the specialist.  <u>Using the bio-melatonin formulation</u> A similar dosing schedule to that stated above is used. Doses are instead increased in increments of 3mg up to a usual maximum of 9mg at night.
6.	<b>Formulations / administration:</b> Circadin® (melatonin) 2mg modified release tablets is the formulation that is recommended for first line use. Circadin is licensed in the UK for the short-term treatment of primary insomnia in patients who are aged 55 or over. <b>Circadin® is a modified release tablet. However, they can be crushed and mixed with water / juice / food to provide an immediate release formulation.</b> Note that the tablets

will usually take a few minutes to form a good dispersion. The crushed tablets can also be administered via NG / gastrostomy tubes.

Melatonin 3mg tablets (Bio-melatonin®) are also available for children who have struggled with administration of the above product. Bio-melatonin® tablets can be crushed and mixed with water / food / juice. They can also be administered via NG / gastrostomy tubes. Bio-melatonin® is not licensed in the UK and is more expensive than Circadin®. However, it is licensed in Hungary for the management of sleep disturbance in children. Bio-melatonin® should be prescribed on VISION as “melatonin 3mg tabs”. Bio-melatonin brand (Pharma Nord UK) should be noted under directions. Prescribe in multiples of 60 as it is in the tariff as an original pack size of 60.

Unlicensed liquid formulations of melatonin are available from specials manufacturers. Such formulations are not recommended for routine use in NHS Tayside as the quality of these products can vary and they are more expensive. They may occasionally be used in children who have refused to take either brand of melatonin tablets either swallowed whole or mixed with water / juice / food. The liquids come in various strengths eg 3mg/5ml and 6mg/5ml. Do not prescribe the 1mg/ml as this is in the tariff at a highly inflated price in comparison to the other strengths.

**6. Contra-indications:**

Use in pregnant women or in breastfeeding women is not recommended due to a lack of clinical data.

**7. Side-effects/cautions:**

Melatonin is generally well tolerated and no significant adverse effects have been reported with pharmacologically regulated melatonin. Both increased and reduced seizure frequency have been reported in children with epilepsy (use with caution). Use with caution in children with lactose intolerance (for Circadin®) and in people with autoimmune disease.

Fluvoxamine should be avoided in people taking melatonin.

There may be increased sedation and drowsiness when melatonin is taken concurrently with antidepressants, benzodiazepines and non – benzodiazepine hypnotics.

**8. Monitoring - response to treatment:** When the decision is made to start treatment the initiating specialist should advise parents to stop melatonin for a period of 2 weeks every 6 months. If sleep pattern has been re-established parents should stop treatment. If sleep pattern has not been re-established treatment should be restarted at the dose they were on previously. This advice should be included in the letter that is sent to the GP asking them to start treatment.

**9. Monitoring – treatment safety:** Monitor seizure frequency in children with epilepsy.

**10. Additional information:** Parents should be given a copy of the melatonin information leaflet (attached) by the initiating specialist.

**11.\* Written by: Iain Hewitt**

**Date: July 2016**

**Approved by: Dr Elise Merry and Dr Janet Dance**

**Date: August 2016**

**(Input also provided by GP Sub Committee when the initial protocol was written)**

**12.\* Review date: August 2018**

**References:**

- (1) BNF for children 2012 / 2013 edition
- (2) Health Technology Assessment: RCT of melatonin in children with neurodevelopmental disorders and impaired sleep. Health Technology Assessment 2012; 16 (40): 1 – 239.
- (3) Marcia L Buck. The use of melatonin in children with sleep disturbances. Paediatric Pharmacotherapy Vol 9 No. 11 November 2003.



## **Melatonin Information Sheet**

### **Introduction**

Melatonin is a sleep regulatory hormone produced by the pineal gland.

### **Uses**

Melatonin is used to treat sleep disorders in children with cerebral palsy, learning difficulties, autism, epilepsy, hyperactivity, chronic insomnia etc.

### **Presentation**

Currently the recommended product in Tayside is a 2mg tablet. The tablets can be crushed and mixed with water, sprinkled on or mixed into food. They can also be administered via feeding tubes.

### **Dose**

Children from one month to 18 years may be prescribed 2mg melatonin, 30 to 60 minutes before bedtime. The dose may be increased to 4mg, 6mg or 8mg. Higher doses may occasionally be used. Melatonin should be stopped every 6 months to monitor if still required. Some patients may benefit from an additional dose to be given on waking during the night.

### **Legal Aspects**

The brand of melatonin that is used in Tayside is not licensed for use in children. A GP may prescribe this medicine on the recommendation of a specialist within the rules of "The Medicines Act 1968 (exemptions)" but has the option not to prescribe and in this case your specialist may prescribe this for your child.

### **Side Effects**

Very few side effects have been reported locally. However, an increase in seizure activity in children with epilepsy has been reported. Also there are reports of fatigue, headache and irritability.