Name: Attach Banda Label here Address: Date of Birth: NHS number:

Coventry & Warwickshire
Area Prescribing Committee

Melatonin

SCA: For the treatment of insomnia in children and adults with neurological and/or behavioural problems, including ADHD and autism. Also in older adults with dementia where alternative hypnotics have failed.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of melatonin can be shared between the specialist and general practitioner (GP). The recent introduction of a licensed product, advice from the MHRA regarding imported products and Area Prescribing Committee support has facilitated the participation of GPs in shared care.

GPs are **invited** to participate. GPs should not be asked to initially prescribe but may be asked to continue prescribing for those patients in whom melatonin has proved successful. Prescribers should familiarise themselves with the guidelines and the monitoring requirements before agreeing to undertake prescribing. If the GP is not confident to undertake these roles, then he/she is under no obligation to do so. In such an event, the total clinical responsibility for the patient, including issuing prescriptions, remains with the specialist. **If a specialist asks the GP to prescribe this drug, the GP should reply to the request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment & are in agreement with it

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Diagnose the condition and assess if the patient is suitable for treatment with melatonin.
2	Provide patient/carer with relevant information on use, side-effects and need for monitoring of medication. Explain any unlicensed uses.
3	Provide treatment until stabilised including advice to patient/carer on sleep hygiene.
4	Arrange shared care with patient's GP by faxing the template letter advising GP about the unlicensed status. Communicate follow up arrangements & when to refer back. Continue to prescribe until GP has agreed to take over prescribing.
5	Monitor response to treatment, side-effects etc.
6	Agree to review patient's condition when requested by the patient's GP.
7	Notify GP of review date (at least six monthly). Send a written summary to the GP whenever the patient is reviewed.
8	Advise discontinuation of medication if no improvement is seen after a reasonable trial.
9	Discontinue treatment at appropriate intervals under careful supervision – when condition stable, to assess the need to continue medication.
10	Provide any other advice or information for the GP if required including rapid referral arrangements and contacts.
11	Report adverse events to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard (If in Coventry & Warwickshire Partnership Trust via the Clinical Governance Pharmacist – see Medicines Policy section 20) and GP.

	General Practitioner responsibilities
1	Ensure patient has information & knowledge to understand the therapeutic issues relating to the patient's clinical condition.
2	Reply to the request for shared care as soon as practicable by faxing back signed form. If declining the request, please indicate the reason for declining.
3	Prescribe the melatonin adjusting in line with specialist recommendations (continued prescribing is appropriate for patients attending specialist review).
4	Practice to discuss with the dispensing pharmacy likely typical costs (standard release melatonin is an unlicensed special)
5	Report significant deviations from the prescribing pattern to the specialist.
6	Monitor and record the therapy between specialist reviews as necessary based on the individual and monitoring guidance stated overleaf.
7	Report to/seek advice from the specialist on any aspect of patient care of concern to the GP which may affect treatment.
8	Refer to specialist if patient's condition deteriorates, or if there are concerns over patient compliance.
9	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
10	Report adverse events to the MHRA on a yellow Card (www.mhra.gov.uk/yellowcard), the specialist and the appropriate Medicines Management team.

	Patient/carer's role
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with melatonin.
3	Inform specialist or GP of any other medication being taken, including over-the-counter products.
4	Report any adverse effects or warning symptoms to the specialist or GP whilst taking melatonin.
5	The patient may <u>also</u> choose to report any adverse drug reaction direct to the MHRA on a Yellow Card , available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours). The form can also be downloaded from www.mhra.gov.uk/yellowcard

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Pharmacy Dept:				
Other:				

SUPPORTING INFORMATION (see SPC for complete details/specific guidance http://emc.medicines.org.uk)

Licensed indications:

The APC recognises that the use of melatonin in the treatment of insomnia in children and adults with neurological and/or behavioural problems (including ADHD and autism) is unlicensed. However the APC supports the use of such unlicensed melatonin prescribing by specialists and GPs when done so in accordance with this SCA.

Coventry and Warwickshire Partnership Trust have an approved Position Statement on the use of Circadin® and Unlicensed Melatonin Products. This states the following:

"Following the MHRA advice, the modified release Circadin® formulation is the preferred choice for children and adolescents or learning disability and other service users. If there are swallowing difficulties, the tablet can be crushed to a fine powder and mixed with water or given with a small amount of cold soft food such as a teaspoon of yoghurt or jam. If crushing is not an option, there are sources of melatonin manufactured in the UK according to GMP guidance and these are the preferred option to Circadin®. CWPT preferred alternative choices in this situation are Melatonin capsules (Special Products Ltd) 2mg or 3mg, or Melatonin liquid 1mg in 1ml (Special Products Ltd)."

Patients with Autistic Spectrum Disorder (ASD) may respond more effectively to standard release melatonin rather than modified release Circadin®. Consequently whilst clinical experience is refined, clinicians may elect to prescribe standard release melatonin as first line for people with ASD.

Dosage and administration:

Within the CWPT preferred prescribing list, **Circadin® 2mg tablets are the first line, preferred option.** If these are not suitable, then the recommended alternative option is Melatonin capsules (2mg, 3mg) (Special Products Ltd brand). The qualified choice is KidMel® melatonin liquid (available from Special Products Ltd). Other melatonin products are available which are manufactured to the standards of Good Manufacturing Practice, but are more costly.

Child 1 month–18 years (unlicensed)

Sleep onset insomnia and delayed sleep phase syndrome

Initially 2–3mg increased if necessary after 1–2 weeks to 4–6mg; max. 10mg

Adult

Insomnia (short-term use)

Circadin® is licensed for prescribing in over 55 years, 2mg once daily 1–2 hours before bedtime, after food for up to 13 weeks.

Administration tips:

- If there are swallowing difficulties, the Circadin® tablet can be crushed to a fine powder and mixed with water or given 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).*
- 2mg capsules and 3mg modified-release capsules The standard capsules can be opened and the contents mixed with yogurt or fruit juice for administration to allow administration via feeding tubes.
- Melatonin has no discernible withdrawal symptoms.

Monitoring: (*in children and adolescents)

Baseline Tests

(Specialist)· Height* and weight*, Sleep diary and Puberty*

Routine Tests

(GP)· Height* and weight* annually

Disease monitoring

(Specialist)· Have a consultation with the patient and family every month until optimum dose established. Following this they will be seen 1-2 times per year for review.

Consider the need for a trial reduction of medication as considered appropriate.

Cautions - *possible drug interactions* (see BNF Appendix 1/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*.

Contra-indications: *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.

Drug interactions (see also above under cautions):

- Fluvoxamine – Potentially hazardous interaction. See under "Cautions" above.
- 5- or 8-methoxypsoralen (5 and 8-MOP increases melatonin levels by inhibiting its metabolism.
- Cimetidine (CYP2D inhibitor) increases plasma melatonin levels, by inhibiting its metabolism.
- Cigarette smoking may decrease melatonin levels due to induction of CYP1A2.
- Oestrogens (e.g. contraceptive or hormone replacement therapy), increase melatonin levels by inhibiting its metabolism by CYP1A1 and CYP1A2.
- 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.
- Alcohol should not be taken with melatonin, because it reduces the effectiveness of melatonin on sleep.
- Melatonin may enhance the sedative properties of benzodiazepines and non-benzodiazepine hypnotics.

Cost: The annual cost to the NHS varies dependant on the manufacturer, dose and possible supplier on-cost additions.

At a 2mg daily dose, annual cost is:

- **Preferred choice** as per Coventry and Warwickshire Area Prescribing Committee: **Circadin®MR tablets 2mg: £187** (April 2015 Drug Tariff)
- **Alternative choice:** Melatonin standard release caps 2mg (**Special Products Ltd**): there is no standard NHS/Drug Tariff price of melatonin capsules: local prescription data shows cost varies from £332 to £569.

References: *Circadin® SPC accessed 19/10/11, Circadin® PIL 2/2008, BNF for Children 2010-11, BNF 62 (Sept 2011). London New Drugs Group APC/DTC Briefing Melatonin in paediatric sleep disorders Sept 2008. UKMI NG drugs guide B.Murphy Jan 2004. Psychotropic Drug Directory 2009, Shared care Guidelines – Worcestershire (July 2009), Lothian (Oct 2009) and Leeds (12/2008). CWPT Position Statement Circadin 2011.*