SHARED CARE AGREEMENT: MELATONIN (CHILDREN)

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NB: This document should be read in conjunction with the current Summary of Product Characteristics where appropriate

This shared care agreement applies to children and young people with a neurodevelopmental diagnosis and associated insomnia who have been initiated on melatonin by Specialist Children's Services

DRUG AND INDICATION:	
Generic drug name:	MELATONIN
Formulations:	3mg immediate release tablets 2mg modified-release tablets 1mg/ml oral solution – if crushing tablets is not an option or is unsuitable. Care should be taken with prescribing to ensure an appropriate formulation with acceptable excipients is chosen (see below).
Intended indication:	Sleep aid for children over 2 years of age with neurodevelopmental disorders and insomnia
Status of medicine or treatment:	A NHS GGC Paediatric Formulary medicine Licensed products are available. Different formulations have differing licensed indications. Some formulations are licensed for use in insomnia in children and adolescents from 6 -17 years of age. Other formulations are licensed in adults, and their use in children for sleep management represents off-label prescribing. Please consult the relevant Summary of Product Characteristics.

RESPONSIBILITIES OF ACUTE CARE/SPECIALIST SERVICE

- To assess the suitability of patients for treatment.
- To undertake any baseline investigations and monitoring.
- To initiate prescribing of melatonin, monitor response and recommend any dose adjustments as necessary.
- To check for possible complications.
- To discontinue treatment if it is ineffective.
- To advise the parent / carer / patient regarding the periodic discontinuation of melatonin to determine its on-going need e.g. on the length and frequency of treatment breaks, or how to improve efficacy in children who may be slow to metabolise.
- To report any suspected adverse events to the MHRA via Yellow Card Scheme.

Acute Care/Specialist Service will provide the GP with:

- A letter including diagnostic information and details of the dose and preparation of melatonin to prescribe, including the duration of treatment before Specialist review, if appropriate.
- A written report of outpatient consultations, ideally within 14 days from when the consultation occurred.

Acute care/specialist service will provide the patient / carer with relevant information to enable:

- Informed consent to therapy.
- Understanding of potential side effects and appropriate action.
- Understanding of the role of sleep hygiene and its monitoring.
- Understanding of changes in formulation if required.

RESPONSIBILITIES OF PRIMARY CARE (GENERAL PRACTITIONER):

- To prescribe melatonin treatment in collaboration with the Specialist.

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- To ensure that the patient's Primary Care medication records are updated to reflect advice from specialist services e.g. dose adjustments.
- Manage any adverse effects or refer to Specialist services as outlined in this agreement.

RESPONSIBILITIES OF PATIENT / PARENT / CARER:

- To attend hospital and GP clinic appointments.
- Failure to attend appointments may result in the medication no longer being prescribed.
- To report adverse effects to their Specialist or the GP.
- Adhere to the advice for periodic discontinuation of melatonin.
- To maintain good sleep hygiene practices alongside the use of melatonin.

ADDITIONAL RESPONSIBILITIES:

- Any serious reaction should be reported to the MHRA by whoever they are highlighted to. Use the Yellow Card System to report adverse drug reactions- http://yellowcard.mhra.gov.uk/

CAUTIONS:

Melatonin causes drowsiness- it should be used with caution if the effects of drowsiness are likely to cause a risk to safety.
Caution required in renal and hepatic impairment- Avoid in severe impairment.
Caution should be exercised in patients with epilepsy and autoimmune diseases.

Please see Summary of Product Characteristics for comprehensive information.

Melatonin modified release 2mg tablets

- Should be swallowed whole and not be broken, crushed or chewed as this affects the prolonged release properties.

Melatonin 1mg/ml oral solution

- Use of liquid preparations of melatonin should be limited. This is due to cost and content of excipients potentially harmful in children e.g. propylene glycol, making these products less suitable for children under 5 years.
- For children unable to swallow tablets, the first option is to crush melatonin 3mg immediate release tablets and to mix with soft food or liquid (unlicensed use). Melatonin oral solution should only be considered if there are compliance issues with crushed tablets or for patients with fine bore enteral feeding tubes.

To avoid delays, it is advised that other strengths and preparations of melatonin ARE NOT prescribed.

CONTRAINDICATIONS:

- Hypersensitivity to the active substance or to any of the excipients.

TYPICAL DOSAGE REGIMENS:

Dosage regimen for melatonin 3 mg immediate release tablets

Route of administration:	Oral – tablets swallowed or crushed (may be mixed with small amount of water / soft food)
Recommended starting dose:	One tablet (3mg) to be taken 1 hour before desired sleep time
Titration of dose:	Increase to 6 mg depending on response after 7 – 14 days
Maximum dose:	9mg daily but additional benefit limited above 6mg
Adjunctive treatment regimen:	Sleep hygiene (advice)
Conditions requiring dose adjustment:	Non response / side effects
Usual response time:	7 days
Duration of treatment	Indefinite but annual treatment breaks advised

Dosage regimen for melatonin 2mg modified release tablets

Route of administration:	Oral – to be taken whole.
Recommended starting dose:	One tablet (2mg) to taken 1 hour before desired sleep time after food
Titration of dose:	Increase by 2 mg depending on response every 7-14 days
Maximum dose:	8 mg but additional benefits limited above 6mg
Adjunctive treatment regimen:	Sleep hygiene (advice)
Conditions requiring dose adjustment:	Non response / side effects
Usual response time:	7 days
Duration of treatment	Indefinite but annual treatment breaks advised

Dosage regimen for melatonin 1mg/ml oral solution (see notes above for caution under 5 years of age)

Route of administration:	Oral
Recommended starting dose:	2- 3 ml (i.e. 2 – 3 mg) taken as a single dose 1 hour before desired sleep time.
Titration of dose:	Increase to 4- 6 mg depending on response after 7 – 14 days
Maximum dose:	9mg daily but additional benefits limited above 6mg
Adjunctive treatment regimen:	Sleep hygiene (advice)
Conditions requiring dose adjustment:	Non response / side effects
Usual response time:	7 days
Duration of treatment	Indefinite but annual treatment breaks advised

SIGNIFICANT DRUG INTERACTIONS:

The following list is not exhaustive; please see Summary of Product Characteristics for comprehensive information.

- Fluvoxamine – increases melatonin levels by inhibiting its metabolism. The manufacturer advises that this combination should be avoided.
- Benzodiazepines/non-benzodiazepine hypnotics - melatonin may enhance the sedative properties.
- Cimetidine, oestrogens - inhibit melatonin metabolism and therefore increases plasma melatonin levels
- CYP1A2 inducers, such as ciprofloxacin, carbamazepine and rifampicin - may reduce plasma levels of melatonin. Cigarette smoking may also reduce plasma melatonin levels.

UNDESIRABLE EFFECTS:

- Melatonin is generally well tolerated with only a few adverse side-effects having been reported. Most commonly reported side-effects include headaches, nausea and drowsiness. Melatonin may increase seizure frequency in patients with epilepsy.
- The following list is not exhaustive; please see Summary of Product Characteristics for comprehensive information.

Side effects	Management
Uncommon: Irritability, nervousness, restlessness, abnormal dreams, anxiety, migraine, lethargy, psychomotor hyperactivity, dizziness, somnolence, dermatitis, night sweats, hypertension, pruritus, rash, dry skin	Refer to specialist service and if serious / clinically significant discontinue medicine prior to referral.
Rare: leucopenia, altered mood, aggressive behavior, syncope, palpitations, hot flushes, reduced visual acuity mouth ulceration, dry mouth	Refer to specialist service and discontinue medicine immediately.

BASELINE INVESTIGATIONS / MANAGEMENT:

- Height and weight.
- Clinicians should determine if appropriate sleep hygiene measures have been used prior to initiating prescribing.

MONITORING (PRIMARY CARE):

- All routine monitoring relating to response is undertaken within the specialist service
- If the GP notes any concerns regarding height, weight or pubertal development, they should refer to the Specialist.

MONITORING (ACUTE SECTOR):

- Patients will be reviewed in line with the Specialist Children's Services standard operating procedure by Acute/Specialist services. This will usually be telephone review with the option of face to face if deemed necessary by the clinician.
- Patients will be monitored both for clinical efficacy and side effects.
- A letter will be sent and clinical efficacy will be monitored by asking patients to stop melatonin for the week leading up to review. Sleep should be monitored and sleep diaries may be used. This break will be discussed at the review and medication should be discontinued if patients sleep well without melatonin. Melatonin should also be discontinued if no benefit on the maximum dose.
- Some children who are slow metabolisers may initially respond well to melatonin but the benefit wears off over time and increasing the dose is not helpful. In this situation melatonin should be stopped for 2 weeks and then restarted at a low dose (1-2mg).
- Clinicians will ask about possible side effects at each review. There is no current evidence that long term melatonin effects pubertal timing or growth but there are theoretical concerns related to animal models. Growth and puberty will not be monitored routinely but clinicians will ask about these areas at review (especially for patients on treatment for over 3 years and teenagers). If there are concerns about growth or pubertal development then face to face review will follow.

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TRANSITION:

Patients who remain on melatonin at 18 years of age should have their annual review as previously. Patients may wish to stop melatonin at transition and a 1-2 week break before review is important. If melatonin is no longer needed then it should be stopped and this will be communicated to the GP.

If the patient requires transition to adult services e.g. complex physical disability, ADHD on medication, then on going follow up for melatonin will be provided by these services as per adult guidelines.

If young adults are on melatonin at the point of transition with no other needs that require input from secondary care, then they will be discharged to primary care for ongoing prescription. Discharge should be accompanied by a robust discharge letter which should include:

- Ongoing treatment plan
- Anticipated length of treatment (including whether it may be long term)
- Options for de-prescribing

PHARMACEUTICAL ASPECTS:

Melatonin immediate release tablets 3mg.

- Film coated tablets.
- May be crushed if required and preferred to the use of liquid formulations. (Can then be administered via a NG tube or gastrostomy if required – unlicensed use).

Melatonin modified release 2mg tablets.

- The tablets must be swallowed whole.
- These can be useful for children who have a fragmented sleeping pattern and wake up through the night.

Melatonin oral solution 1 mg / ml (immediate release):

- Some brands contain higher amounts of the excipient propylene glycol, making it less suitable for use in children under 5 years of age.
- Propylene glycol free formulations of melatonin 1 mg/ml oral solutions include Consilient Health Ltd and Aspire Pharma Ltd - it is suggested that this detail be checked prior to dispensing.
- This product should only be considered if crushing licensed 3mg standard release tablets is unsuitable.

To avoid delays, it is advised that other strengths and preparations of melatonin ARE NOT prescribed.

COST:

Melatonin 3mg tablets x 30 = £18.27, Melatonin 2mg modified-release tablets x 30 = £2.69, Melatonin 1mg/ml oral solution sugar free x 150 ml = £25.56 (Scottish Drug Tariff, accessed March 2025).

INFORMATION FOR COMMUNITY PHARMACIST:

Melatonin 3mg immediate release tablets, melatonin 2mg modified release tablets and the 1mg/ml oral solution should be available for ordering from regular wholesalers.

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION:

Name	Designation	Acute Site	Department phone number
Dr Allyson Ramsay	Consultant Paediatrician	Specialist Children's Services	0141 277 7475
Dr Jeremy Fellick	Consultant Paediatrician	Specialist Children's Services	0141 201 5665
Caroline Brown	Clinical Pharmacist	Leverndale Hospital/Royal Hospital for Children	0141 211 6525
Dr Joanna Young	Consultant Psychiatrist	Specialist Children's Services	

SUPPORTING DOCUMENTATION:

- A Royal College of Paediatrics & Child Health approved information leaflet regarding melatonin (is available at https://www.medicinesforchildren.org.uk/melatonin-sleep-disorders)