Powys Teaching Health Board

Shared Care Agreement: Melatonin for the Treatment of Sleep Disorders in Children and Adolescents

Specialist Responsibilities

- Ensure that non-pharmacological treatments are discussed and trialled with the patient and carer/parent/guardian.
- Complete full assessment: diagnose and assess eligibility for drug therapy as part of a treatment programme that includes psychological, behavioural and educational advice and interventions.
- Provide patient/carer with relevant information on use. Obtain consent for any unlicensed use.
- Advise patient/carer on side effects and the action to be taken should they occur.
- Undertake the baseline clinical evaluations (as detailed in *Section 6 below*).
- **Provide initial treatment for 3 months or until the patient has been reassessed.**
- **Communicate with the GP and request shared care using the *Shared Care Agreement Form* (Appendix 1), advising if the prescribing request is outside of license, and, where appropriate, specifying the BRAND of the medication prescribed.**
- Prescribing responsibility will only be transferred when:
    - Treatment is for a specified indication and duration.
    - Treatment has been initiated and established by the secondary care specialist.
    - The patient's initial reaction to and progress on the drug is stable.
    - The GP has agreed in writing in each individual case that shared care is appropriate.
    - The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.
- **Advise discontinuation of medication if no improvement is seen after a reasonable trial.**
- Consider drug holidays as indicated in Section 4.
- After each appointment inform the GP of dosage schedule, monitoring measurements and progress of treatment.
- Inform the GP if the patient fails to attend clearly indicating that the patient is taking melatonin.
- Provide any other advice or information for the GP if required including rapid referral arrangements and contacts.
- Consider a trial of withdrawal of medication when the condition is stable. The need to continue melatonin therapy should be reviewed at least every 12 months, sending a written summary and updated treatment plan to the GP.

Primary Care Responsibilities

- Return the Shared Care Agreement (SCA) Form (Appendix 1) to the requesting specialist within 14 days of receipt.
- Issue ongoing prescriptions for melatonin as per dose and BRAND adjusting in line with specialist recommendations (continued prescribing is appropriate for patients attending specialist review), taking into any account potential drug interactions in Section 5.
- Adjust the dose of melatonin prescribed as advised by the specialist.
- Manage adverse effects as detailed in Section 7 and discuss with specialist team when required.
- Monitor for the risk of diversion, misuse and abuse of melatonin and alert the specialist team if there are any concerns.
- Refer to specialist if patient's condition deteriorates and if there are any side effects or concerns.
- Oversee treatment cessation on the advice of the specialist or request of the patient.

Patient and/or Carer Responsibilities

- Attend hospital and GP clinic appointments. Failure to attend may result in the medication being stopped (on specialist advice).
- Take melatonin as prescribed.
- Store the medication appropriately and take according to the prescribed directions.
- Report any adverse events immediately to their specialist team or GP. Seek immediate medical attention if they develop any symptoms as detailed in Section 7.
- Keep contact details up to date with specialist team and GP.
- Report the use of any over the counter medications to their specialist team or GP and be aware they should discuss the use of melatonin with their pharmacist before purchasing any OTC medicines.

1. Background

This Shared Care Agreement (SCA) outlines shared care arrangements for patients taking melatonin for the treatment of sleep disorders in children and adolescents.

The SCA should be read in conjunction with:

- The Shared Care Agreement Form (Appendix 1).
- The Summary of Product Characteristics for the formulation/brand of melatonin prescribed http://www.medicines.org.uk/

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. Melatonin plays an important role in setting the correct timing of sleep-wake cycles.

Sleep disorders are very common in children with neurological and neuro-developmental disorders. 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 wakening and day-night reversal patterns. Improving sleep patterns generally leads to an improvement in health, behaviour and well-being.

Clinical experience suggests that when appropriate behavioural sleep interventions fail, melatonin may be of value for treating sleep onset insomnia and delayed sleep phase syndrome in children with conditions such as visual impairment, cerebral palsy, attention deficit hyperactivity disorder (ADHD), autism, and learning difficulties. It is also sometimes used before magnetic resonance imaging (MRI), computed tomography (CT), or EEG investigations. 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 in children and adolescents should be initiated and supervised by a specialist, but may be continued by general practitioners under a SCA.

2. Prescribing Information

Several brands of melatonin are now licensed for treating insomnia and unlicensed preparations are also still warranted in certain circumstances. It should be noted that licenses granted do not cover treating insomnia in all cohorts of patients.

Prescribers should prioritize licensed preparations and restrict unlicensed products to where there is need for dose titration, where patients have previously been stabilized on treatment or where patients are unable take solid dosage forms (e.g. swallowing difficulties).

Liquid preparations should be reserved for patients who cannot tolerate solid oral preparations.

Prescriptions should state the drug (and brand name), strength, form, frequency, and quantity to be supplied.

Prescribers are asked to prescribe melatonin as per the following table:

Place in Therapy	Powys Formulary Option	Licensing Information	Dosing
First line for insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient.	Melatonin (Adaflex®) 1mg, 2mg, 3mg, 4mg and 5mg ***standard release*** tablets*	Licensed	1-2mg nocte increased to 5mg if needed. Maximum 10mg. (*Locally agreed off-label use*) Dose to be taken 0.5 – 1 hour before bedtime at least 2 hours after food.†
	*These tablets are also licensed to be crushed and should be added to water directly before administration. †It is recommended that food is not consumed 2h before and 2h after intake of Adaflex© tablets.		
First line for children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis Syndrome, where sleep hygiene measures have been insufficient	Melatonin (Slenyto®) 1mg and 5mg ***prolonged release*** tablets*	Licensed	2mg nocte increased to 5mg if needed. Maximum 10mg. Dose to be taken 0.5 – 1 hour before bedtime.
	*These micro-tablets can be added to foods such as yoghurt, orange juice or ice-cream to facilitate swallowing and improve compliance.		
Second Line for those patients previously initiated on melatonin 2mg modified release tablets	Melatonin (Circadin®) ***modified release*** 2mg tablets	"Off-label" use	2mg nocte increased to a maximum of 10mg as needed. Dose to be taken 1-2 hours before bedtime.
Reserved for children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient who are unable to tolerate solid / crushed formulations	Melatonin (Ceyesto®) 1mg/ml Oral Solution SF*	Licensed	Initially 1-2 mg nocte increased to 5mg if needed. Maximum 10 mg per day. (*Locally agreed off-label use*) Dose to be taken 1-2 hours before bedtime.
	*Licensed available preparations contain concentrations of benzyl alcohol and propylene glycol which make them unsuitable for children under six years of age.		

3. Contraindications and Cautions

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNFc & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to the active ingredient or any excipients.

Cautions:

- Autoimmune disease: avoid—limited information available in patients with autoimmune disease; exacerbation reported occasionally.
- Epilepsy/susceptibility to seizures (risk of increased seizure frequency).
- Not recommended for women who are pregnant or breastfeeding.
- Drowsiness - melatonin may cause drowsiness and should therefore be used with caution when the risk of drowsiness may lead to harm.
- Renal impairment:
  - For modified-release tablets, caution (no information available).
  - For immediate-release formulations, caution (increased risk of exposure; limited information available); avoid in severe impairment.
- Hepatic impairment:
  - For modified-release tablets, avoid (risk of decreased clearance; limited information available).
  - For immediate-release formulations, avoid in moderate or severe impairment (risk of decreased clearance; limited information available).
- Patients with rare hereditary problems of galactose intolerance, LAPP lactase deficiency or glucose-galactose malabsorption should not take this product. Relevant to some formulations therefore check individual SPC if relevant.

4. Deprescribing / Drug Holidays

- Review children on melatonin after three months and deprescribe melatonin if there is no clinically relevant treatment effect seen (in liaison with specialist).
- All suitable patients should undergo a drug holiday to assess their need for ongoing treatment. This should take place three months after the commencement of treatment and every six months thereafter. If sleep improvements are maintained without melatonin, therapy should be stopped.

- If there is a consistent correlation of sleep deterioration during a drug holiday, patients should be advised to continue melatonin without a break unless they are suspected to be a poor metaboliser of melatonin (in which case regular washout with ongoing drug holidays when the benefit wanes, is recommended).
- For patients where caution should be exercised with drug holidays and deprescribing, refer to the patient's specialist for advice on managing this, including where melatonin is prescribed under a formal shared care arrangement.

5. Significant Medicine Interactions

Fluvoxamine: BNFc lists as a 'severe' interaction; fluvoxamine very markedly increases the exposure to Melatonin. Manufacturer advises avoid.

Other interactions are listed as 'moderate' severity or below. Please see BNFc & SPC for comprehensive information regarding brand prescribed and recommended management.

6. Baseline Investigations and Ongoing Monitoring

Baseline investigations:

- Standard clinical assessment, to include monitoring of growth and sexual development (Specialist).

Ongoing monitoring:

- The patient should be assessed every 6-12 months to ensure the continuing benefit of melatonin and to confirm that behavioural measures and sleep hygiene recommendations are maintained (Specialist).
- Standard monitoring of growth and sexual development is recommended to ensure that height, weight and pubertal development are as expected (Specialist).
- Follow the guidance on deprescribing / drug holidays, as described in Section 4 (Specialist).
- Because the effect of melatonin on seizure control in patients with epilepsy is unpredictable, seizure frequency should be closely monitored in patients with epilepsy. (All prescribers).

7. Adverse effects

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme.

www.mhra.gov.uk/yellowcard. See SPC for specific adverse effects relevant to formulation prescribed.

The following adverse effects are reported for melatonin. This list is not exhaustive. A detailed list of adverse reactions is available in the BNFc & SPC for individual preparations.

Common or Very Common

Arthralgia; behaviour abnormal; drowsiness; feeling abnormal; increased risk of infection; mood altered; pain; sleep disorders

Uncommon

Anxiety; asthenia; chest pain; dizziness; dry mouth; gastrointestinal discomfort; headaches; hyperbilirubinaemia; hypertension; menopausal symptoms; movement disorders; nausea; night sweats; oral disorders; skin reactions; urine abnormalities; weight increased

Rare or Very Rare

Angina pectoris; arthritis; concentration impaired; crying; depression; disorientation; electrolyte imbalance; excessive tearing; gastrointestinal disorders; haemorrhage; hot flush; hypertriglyceridaemia; leukopenia; memory loss; muscle complaints; nail disorder; palpitations; paraesthesia; prostatitis; seizures; sexual dysfunction; syncope; thirst; thrombocytopenia; urinary disorders; vertigo; vision disorders; vomiting

Frequency not known

Angioedema; appetite decreased; constipation; dyspnoea; galactorrhoea; hyperglycaemia; neutropenia

8. Advice to patients and carers

- The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

  Patient information:

  Medicines for Children leaflet: Melatonin for sleep disorders

- Patients, or their representatives, must be counselled on the current relevant licensed indication for melatonin and its intended treatment duration.
- Patients, or their representatives, must be made aware that this agreement is solely for children and adolescents and that patients may need to be referred into a different service if melatonin is still needed when they no longer meet the service criteria e.g. become an adult.

9. Specialist Contact Information

Advice can be requested from the local Child and Adolescent Mental Health Service (CAMHS) and Community Paediatric Services 9am to 4pm, Monday to Friday.

Please allow 5-7 working days for a call back or any prescription requests.

CAMHS: 01874 615662 01686 617401 PowysCAMHS.Admin@wales.nhs.uk	**Community Paediatrics:** 01874 615684 01686 617455 powys.communitypaediatrics@wales.nhs.uk

10. Additional Information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

11. Local Arrangements for Referral

Referral from primary care to secondary care should follow usual guidelines.

Ideally, sleep hygiene advice and support should have already been provided by primary care clinicians such as health visitors with input from other services or charities such as Early Help or Cerebra as appropriate.

It is likely that sleep may be only one factor in a referral with comprehensive information on the need for further diagnostic or other assessment being essential to ensure appropriate and timely triage to the correct service.

Referral back to primary care, other than to follow the SCA, will only occur if medication is no longer required or the patient no longer meets service criteria e.g. become an adult.

12. References

- BNF for Children
- PrescQipp Briefing 318 Melatonin 2.0. January 2023
- Electronic Medicines Compendium containing Summaries of Product Characteristics for all formulations/brands
- All Wales Medicines Strategy Group (AWMSG) Final Appraisal Recommendation 4694: melatonin (Slenyto®)