BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Melatonin
Amber ***three months***	
Indication	**Intrinsic sleep disorder in adults and children who have exhausted all behavioural sleep hygiene options and have either:** • **Autism Spectrum Disorder (ASD) diagnosis,** • **Learning Disability (LD) diagnosis,** • **a neurodevelopmental disorder / disability (e.g. cerebral palsy) (excluding those with Attention Deficit Hyperactivity Disorder as a standalone diagnosis*).** *Criteria for use:* At least one criteria from section A and B below must be satisfied to consider melatonin as a treatment option. A. Sleep disturbances can be manifested by (any of the following or in combination) • Early insomnia (getting off to sleep / delayed onset) • Problem with continuity of sleep (frequent night time waking) • Reduction in overall duration of sleep • Reversal of circadian rhythm (day night sleep pattern) B. Resulting in (any of the following or in combination to compromise quality of life) • Day time drowsiness • Unable to concentrate and engage in pleasurable activities and other activities of daily living • Increase in challenging behaviour** *For the purposes of clarity for this shared care protocol, standalone diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) has not been approved by the BNSSG Joint Formulary and is not included. Patients with Attention Deficit Hyperactivity Disorder who also have an Autism Spectrum Disorder or Learning Disability or additional neurodevelopmental disorder / disability diagnosis are covered by the formulary, but those patients with only an ADHD diagnosis would not be covered and prescribing is non-formulary.

	Challenging Behaviour – 'Behaviour can be described as challenging when it is of such an intensity, frequency or duration as to threaten the quality of life and/or the physical safety of the individual or others and is likely to lead to responses that are restrictive, aversive or result in exclusion.' **REM sleep disorder in adult patients diagnosed by neurologist, or physician / psychiatrist specialising in the care of older adults. *Criteria for use:* One criteria from section A **and** all criteria in section B below must be satisfied to consider melatonin as a treatment option. A. Diagnosis of REM sleep disorder: • REM sleep behaviour disorder (diagnosed according to International classification of sleep disorders version 3 criteria) on the basis of specialist sleep clinic assessment including inpatient sleep study. **OR** • Established alphasynucleinopathy (Parkinson's Disease, Lewy Body Dementia, multi-system atrophy) or other neurodegenerative condition who presents clearly with clinical features of REM sleep behaviour disorder, with no evidence of other secondary causes). **AND** B. All of the following: • Secondary causes of REM sleep behaviour disorder have been considered and treated appropriately. • Sleep hygiene and environmental safety have been discussed with the patient. • Symptoms of REM sleep behaviour disorder are of a severity requiring medical treatment – sleep related injuries to self/partner, or disrupted nocturnal sleep resulting in impaired functioning or quality of life. **Definitions** **Learning disability** is defined as arrest or incomplete development of the mind characterized by: • lower intellectual ability (usually an IQ of less than 70) • significant impairment of social or adaptive functioning • manifested during developmental period A person's learning disability may be described as mild, moderate, severe or profound. Learning disabilities are different from specific learning difficulties such as dyslexia, which do not affect intellectual ability. It is also different from Specific Developmental Disorders and Pervasive Developmental Disorders for example Autism etc.

	Autism Spectrum Disorder/ Condition Autism is a complex neuro-developmental spectrum condition involving persistent challenges with, for example, communication and social interaction. While autism is considered a lifelong disorder, the degree of impairment in functioning because of these challenges varies between individuals with autism. **Neurodevelopmental disorders/ disability** are a heterogenous group of disorders causing behavioural and cognitive alterations in sensory and motor symptoms and language. Examples may include autism and cerebral palsy.

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed and any relevant dosing information)*	**Children:** Oral: 0.5mg-6mg at night (off label for this indication) Most people will see maximum clinical benefits up to 6 mg. Very little clinical benefits are seen at doses between 6 mg - 10 mg. Up to 10 mg can be tried in cases where patients may need a referral to tertiary sleep centres. Maximum BNF (Adults and Children) dose is 10mg per day). **Adults:** Oral: 2-6mg at night (off label for this indication) REM Sleep disorder indication only - Melatonin MR 2mg-8mg at night but in special circumstances up to 12mg can be used. Higher doses most likely to be used in REM sleep disorder.
Route and formulation	Oral **Melatonin 2mg modified release tablets (generic)** are the most cost-effective formulation to BNSSG and should be used first-line for all indications. If new branded generic versions become available and are more cost-effective, GP Practices should be guided by Script Switch messages. The most cost-effective product should be used first line even if this is used on an off-label basis. Local specialists have experience of using melatonin off-label. If a faster release is thought to have an advantage for a particular individual where the modified release profile has been ineffective, the modified release tablet can be crushed to exert this immediate release effect. Alternatively, Melatonin immediate release tablets may also be considered but may be more expensive. For patients who cannot swallow tablets, the following should be considered: 1) Advise parents to start pill training prior to consideration of alternative formulations: https://www.nenc-

	healthiertogether.nhs.uk/parentscarers/medicine-children/pill-swallowing-kidzmed Helping your child to swallow tablets – Medicines For Children 2) historically, melatonin 2mg modified release tablets have been quartered, halved or crushed (changing the release profile to immediate release) and mixed in 15-30ml of water) or mixed with a small amount of soft food (unlicensed). This option remains the most cost-effective option. 3) Adaflex immediate release tablets can be crushed and mixed with water directly before administration. It is recommended that food is not consumed 2 hours before and 2 hours after intake of Adaflex tablets. (AGB-Pharma, 2022). 4) Slenyto prolonged release tablets can be put into food such as yoghurt, orange juice or ice cream to facilitate swallowing and improve compliance. If the tablets are mixed with food or drink, they should be taken immediately and the mixture not stored (Flynn Pharma, 2021). 5) **Any liquid formulation will be more expensive than a solid dosage form and should only be considered as a last resort for the shortest period of time required.** Locally, Consilient Health is the preferred brand of melatonin 1mg/1ml oral solution sugar free as this is now licensed for some paediatric cohorts aged 6 years and over. It does not contain propylene glycol or alcohol which may present concern for children, especially of younger ages. Where the Consilient Health brand is unavailable due to supply issues, reconsider whether solid oral dosages are appropriate (see steps 1-3 above). If an alternative liquid preparation is required, see appendix 1 for further information. The use of licensed liquid preparations (even off-label i.e. has a UK marketing authorisation for a different indication) should be trialled in preference to unlicensed liquids as per MHRA recommendations. **Caution** If melatonin 1mg/1ml oral solution sugar free liquid is written generically, the licensed brand Colonis may be supplied. Melatonin 1mg/1ml oral solution (Colonis Pharma Ltd) should not be used in children under 6 years old due to safety and efficacy concerns (Colonis, 2022) . The levels of propylene glycol also exceeds the recommended safety limits for some children based on their weight. To supply unlicensed formulations in line with Specials supplier policies, community pharmacies may need a letter from the prescriber confirming why the patient requires an unlicensed product where there are licensed alternatives. Furthermore, prescribers should

	make it clear to the dispensing pharmacy that an alternative liquid preparation is needed. For patients with an enteral feeding tube, the preferred first line option is melatonin 2mg modified release tablets that have been crushed (changing the release profile to immediate release) and mixed in 15-30ml of water prior to administration (unlicensed). If this is unsuitable for an individual, discuss alternative options with the specialist team.
Duration of treatment	Trial of 3 months initially prescribed and managed by specialist team. Only to be continued by primary care where an improvement in sleep disorder has been assessed by specialist team. Regular review of benefit should take place to ensure ongoing benefit. Techniques could include: weekend/school holiday melatonin breaks, considering dose reduction/weaning or trialling 1-2 weeks off melatonin periodically with the aim of eventually stopping. Specialist teams to specify which tools should/will be used to support review and to ensure patient/parents are aware of information in 'Advice to patient' section. Sleep diaries such as the SNappD app and https://thesleepcharity.org.uk/information-support/children/sleep-diary-for-kids/ are the primary tools used. For intrinsic sleep disorder a drug holiday may be considered if: - Prolonged period (6 months) with much improved (normalised) sleep pattern. - The weekend or school holiday period. - Improved Wellbeing and reduced Functional Impairment, as measured by WEMWBS and Weiss Functional Impairment rating scale https://www.intermed.com/content/uploads/Weiss-Adult-ADHD-Rating-Scale.pdf **Transition to adult services/ discharge from paediatric services** Specialist teams should consider a planned trial from melatonin prior to discharge from the paediatric services to ensure continued benefit.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate

Baseline clinical evidence of disrupted sleep disturbance prior to commencing melatonin (such as at least 2 weeks of sleep diaries or clinician decision based on reported symptoms and impact on life, which may include reports and interventions from school nurse/health visitor).

Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results)*

Response to treatment and whether it is appropriate to continue treatment to be reviewed by a specialist before referring patient to primary care.
Treatment response to be assessed clinically by:

a. reported improvement in subjective sleep quality, improved behaviour and quality of life using tools such as https://flynnforum.com/education_training/snappd-the-sleep-nap-diary-app/ and sleep diaries such as https://thesleepcharity.org.uk/information-support/children/sleep-diary-for-kids/
b. reported reduction in daytime sleepiness
c. REM sleep disorder - reported benefit in reduction of nocturnal awakenings, reduction of sleep related incidents, reduction in sleep related injuries. Collateral history of bed partner reporting reduction in frequency and severity of dream enactment behaviour at night.
d. Intrinsic sleep disorder - improved Wellbeing and reduced Functional Impairment, as measured by WEMWBS and Weiss Functional Impairment rating scale.
e. Re-assess suitability of most cost-effective and suitable formulation where patients have previously had difficulties swallowing tablets and are prescribed alternative formulations.

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNF or SPC.

Side effects and management

Side effect	Frequency/severity	Action/management
See BNF/ SPC for full side effects		
Nocturia	Rare	Stop if problematic and seek advice from specialist
Daytime Drowsiness/over sedation	Sometimes (anecdotal)	Stop if problematic and seek advice from specialist

Referral back to specialist

If melatonin is reported to be ineffective and/or side effects intolerable

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent action for GP to take (For full list please see BNF or SPC)

Issues	**Caution** If melatonin 1mg/1ml oral solution sugar free liquid is written generically, the licensed brand Colonis may be

	supplied. Melatonin 1mg/1ml oral solution (Colonis Pharma Ltd) should not be used in children under 6 years old due to safety and efficacy concerns (Colonis, 2022) . The levels of propylene glycol also exceed the recommended safety limits for some children based on their weight. To supply unlicensed formulations in line with Specials supplier policies, community pharmacies may need a letter from the prescriber confirming why the patient requires an unlicensed product where there are licensed alternatives. Furthermore, prescribers should make it clear to the dispensing pharmacy that an alternative liquid preparation is needed.
Reminder to ask patient about specific problems	N/A

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

1. Melatonin prolonged release should be initiated at 2 mg taken one hour before bedtime and after food.
2. Tablets should be swallowed whole but can be halved using a tablet cutter, maintaining the prolonged release profile.
3. Tablets can be crushed and dispersed in water or mixed with a small amount of soft food for those with swallowing difficulty / too young to swallow(unlicensed).

For intrinsic sleep disorder:

A. "Treatment breaks" are an important component of prescribing this product, and best practice supports the use of treatment breaks. Stopping melatonin does not mean that it will be less effective when restarting. From local specialist experience when restarting, a slightly lower dose may be as effective as that which was last used.

B. Ensure that the following behavioural interventions/sleep hygiene measures continue to be implemented even whilst on medication:
   - Ensuring that there is an established bedtime routine and that a realistic sleep-wake schedule has been agreed.
   - Ensuring that the room conditions (temperature, light and noise) are at an optimum level to promote sleep (e.g. minimise background noise, use of a blackout blind).
   - Ensuring no late afternoon / evening caffeine consumption.
   - Removing television and electronic devices from the patient's room or advising patients to avoid using screens/phones, since it is known that the blue green light emitted by these screens can disturb sleep and could reduce melatonin efficacy. Patients should avoid looking at bright screens beginning 2-3 hours before bed.
   - Physical activity - minimum 60 minutes / day where there is a raise in heart rate / breathing rate (struggles to complete a sentence) as per UK Physical Activity Health guidelines. In addition, stretching and relaxation like yoga and mindfullness help to improve sleep.
   - Good hydration. No sugar drinks ,/caffeine / fatty foods and processed / ultra processed foods - have impact on sleep.

Patient Resources/ leaflets

- Medicines for Children: Melatonin for sleep disorders
- Medicines for Children: Helping your child to swallow tablets

- Swallowing pills (Kidsmed)
- Choice and Medication (Avon and Wiltshire Mental Health Partnership NHS Trust)
  Melatonin information
- Sleep toolkits (South Gloucestershire Council One You website)
  -Special Educational Needs and Disability
  -Early Years 0-5 years
  -Childhood 5-13 years
  -Adolescence 13-18 years
- Teen Sleep hub
- Cerebra charity sleep advice
- Sleep Charity which includes links to sleep diaries https://thesleepcharity.org.uk/information-support/children/sleep-diary-for-kids/
- SNappD: The Sleep Nap Diary App
- BNSSG Remedy Insomnia Page (adults)- includes link to two week sleep diary
- British Society of Lifestyle Medicine 'The importance of good quality sleep' page (adults)
- UK Physical Activity Guidelines includes guidance for:
  - under 5s
  -5-18 years
  -disabled children and disabled young people
  -adults and older adults
  -disabled adults
  -pregnancy and after childbirth
- https://humble.info/

Section 7: Generic principles of shared care for SECONDARY CARE

Please do not amend.

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Please do not amend.

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

Name	Organisation	Telephone Number	E mail address
Care of the Elderly Consultants	North Bristol Trust	N/A	COTEConsultants@nbt.nhs.uk
Neurology team	North Bristol Trust	N/A	NMSKNeurologyConsultants@nbt.nhs.uk neurologypharmacists@nbt.nhs.uk
Dr Emma Stratton	University Hospitals Bristol and Weston	0117-3420790	N/A
Initiating clinician at AWP/Sirona teams	AWP/Sirona	As provided on patient's individual correspondence/ clinic letters	As provided on patient's individual correspondence/ clinic letters

Section 10: Document Details

Date prepared	April 2024
Prepared by	BNSSG Formulary team
Date approved by JFG	September 2024
Date of review	September 2027
Document Identification: Version	V1

Section 11: Collaboration

All shared care protocols should be BNSSG wide where possible. Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

This shared care protocol incorporates and replaces all existing shared care protocols for both adult and paediatric patients.
Comments/input received from:

1. AWP CAMHS consultant team
   Sarah Steel, Highly Specialised Clinical Pharmacist, Lead for CAMHS.
2. Sirona Care and Health Community Paediatric team- Dr Saraswati Hosdurga, Consultant Community Paediatrician, CCHP Bristol,
   Kate Ellis, Head of Medicines Optimisation, Sirona Care and Health
   Sandra Williams, Pharmacist, Sirona Care and Health
3. NBT Neuro/neuropsych teams (Adult-REM indication)
4. UHBW Care of Elderly team (Adult-REM indication)

Shared with AWP Adult Learning Disability team and BNSSG GP ICB representatives.

Section 12: References

Please list references

1. AGB-Pharma (2022) Summary of Product Characteristics: Adaflex 1mg tablets. Available from: https://www.medicines.org.uk/emc/product/13628/smpc [accessed 1/8/24]
2. Colonis Pharmacy (2022) Summary of Product Characteristics: Melatonin 1mg/1ml oral solution. Available from: https://www.medicines.org.uk/emc/product/10419#PHARMACODYNAMIC_PROPS [accessed 1/8/24]
3. Flynn Pharma (2021) Summary of Product Characteristics: Slenyto 1mg prolonged-release tablets. Available from: https://www.medicines.org.uk/emc/product/10023/smpc [accessed 1/8/24]
4. Newcastle upon Tyne Hospitals NHS Trust, North East and North Cumbria, Child Health and Wellbeing Network- North East and North Cumbria, Royal College of Paediatrics and Child Health (2020) Swallowing pills (Kidzmed). Available at: Swallowing pills (Kidzmed) :: North East and North Cumbria Healthier Together (nenc-healthiertogether.nhs.uk) [accessed 1/8/24]

BNSSG Shared Care Guidance
Please complete all sections

Appendix 1

Product manufacturer	Indication	Propylene Glycol (E1520)	Alcohol	Sugar	Sweetener	Shelf-life	Price
Melatonin 1mg/ml (Consilient Health)	Licensed 6-17 for insomnia in ADHD	Free Unflavoured / bitter taste	Free	Free	Glycerol	6 months after first opening	Drug tariff (June 24)- fixed price for the liquids 1mg/1ml sf £124.10 150ml (0.82/ml)
Ceyesto 1mg / ml (Alturix Ltd)	Licensed 6-17 for insomnia in ADHD	52mg / ml Strawberry flavour	Benzyl alcohol 6mg/ml	Free	Sucralose	Use within 1 month of opening	Drug tariff (June 24)- fixed price for the liquids 1mg/1ml sf £124.10 150ml (0.82/ml)
Melatonin 1mg/1ml (colonis)	Licensed for 6-17 insomnia in ADHD	150.50mg/ml Strawberry flavour Melatonin 1mg/1ml oral solution (Colonis Pharma Ltd) should not be used in children under 6 years old due to safety and	140mg sorbitol/ ml	Free	Sucralose	2 months after first opening	Drug tariff (June 24)- fixed price for the liquids 1mg/1ml sf £124.10 150ml (0.82/ml)

		efficacy concerns (Colonis, 2022) . The levels of propylene glycol also exceed the recommended safety limits for some children based on their weight.					
Kidmel 1mg/ml (Veriton Pharma)	Special (unlicensed) To supply unlicensed formulations in line with Specials supplier policies, community pharmacies may need a letter from the prescriber confirming why the patient requires an unlicensed product where there are licensed alternatives. Furthermore, prescribers should make it clear to the dispensing pharmacy that an alternative liquid preparation is needed.	52mg / ml	Free	Free	Aspartame 0.5mg/ml	24 months	~£138 200ml (0.69/ml)