NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT (SCA) FRAMEWORK

Shared care guidelines - Melatonin for Sleep Disorders in Children	
Monitoring level	**Level Amber 0 – prescribe the drug and perform basic monitoring, such as annual review.**

Generic and Proprietary/Brand Name

The Medicines and Healthcare products Regulatory Agency (MHRA) advice is to prescribe licensed products in preference to off-label and unlicensed preparations.

Immediate-release formulations of melatonin that are covered by this shared care agreement:

- Adaflex®[1] tablets (**Prescribe by brand**)

Adaflex® is licensed for the treatment of insomnia in children and adolescents aged **6-17 years with attention deficit hyperactivity disorder (ADHD)**, where sleep hygiene measures have been insufficient. Use outside of this licensing would be off-label. **Adaflex® tablets are licensed to be crushed and mixed with water directly before the administration.**

- Ceyesto®[2] 3mg tablets (**Prescribe by brand**)

Ceyesto® 3mg tablets are licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient. Use outside of this licensing would be off-label.

- Syncrodin®[3] 3mg film-coated tablets (**Prescribe by brand**)

Syncrodin® does not have a UK marketing authorisation for the indication covered by this shared care, the use of Syncrodin® is therefore **off-label**.

Modified-release formulations of melatonin that are covered by this shared care agreement:

- Melatonin 2mg modified-release tablets (generic)

Off-label use for this indication.

Restricted formulations that are covered by this shared care agreement but are reserved for use as follows:

- Ceyesto® 1mg/ml oral solution[4] (**Prescribe by brand**)

*Ceyesto® 1mg/ml oral solution is **restricted** for use in Norfolk & Waveney; it should be reserved for children that are aged **≥ 3 years and ≥15kg** who:*

- *have a **fine bore enteral feeding tube,***
- *or who are unable to tolerate other solid oral dosage forms.*

Ceyesto® 1mg/ml oral solution is licensed for insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient.

Important points of note if prescribing Ceyesto® 1mg/ml oral solution:

- ✓ *Ceyesto® 1mg/ml oral solution **should only be prescribed for children ≥ 3 years of age and ≥15kg** due to the presence of the excipient's benzyl alcohol and propylene glycol in the formulation.*

- ✓ *If prescribing for a child who is between the ages of **3 – 6 years** (off-label), the **maximum daily dose** should be **capped at 5mg**. This is to ensure safety limits for the excipient propylene glycol are not exceeded.*
- ✓ *Ceyesto 1mg/ml oral solution is licensed for administration via silicone gastric, duodenal or nasal feeding tubes. The use of tubes made of polyurethane is not recommended as compatibility has not been demonstrated.*
- ✓ *Please note that any prescribing outside of the medicines licensing is off-label.*

*N.B. whilst other licensed liquid formulations of melatonin are available this particular brand has been approved on formulary, due to its favourable excipient profile, and should be prescribed by **brand name** where a liquid formulation is indicated.*

- Circadin® 2mg prolonged release tablets (**Prescribe by brand**)

Circadin® is restricted for use in Norfolk & Waveney and should be reserved for children with enteral feeding tubes. Whilst this use would be off-label NEWT guidelines[20] state the tablets can be crushed (note this would change the release profile from modified-release to immediate-release) and mixed with 15-30mL of water for administration via enteral feeding tubes.

See Appendix 1 for Summary Table of melatonin formulations.

Indication for shared care

1. Autistic spectrum conditions with severe sleep problems not amenable to behaviour management strategies.[6,7]
2. Insomnia in children with ADHD, which is not responsive to sleep hygiene intervention.[8, 14, 15]
3. Insomnia in children with neurodevelopmental disabilities not responsive to sleep hygiene intervention.[9]

For all other specialist requests please email the medicines optimisation team at nwicb.medsqueries@nhs.net for further guidance.

Melatonin is indicated for the treatment of sleep onset disorders in patients under 18 years where no physical cause is identified and it has not responded to behavioural advice, including sleep hygiene which should be offered initially.
Patients **under 18 years of age with sleep disorders** do not need to remain under regular specialist follow-up, however specialists will be available to discuss drug therapy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Melatonin should not be initiated in patients 18 years and above; however, treatment can be continued in patients aged 18 years and over if initiated when the patient was a child. This is providing the continued need for treatment is reviewed regularly and 6 monthly drug holidays introduced.

Specialist Prescribing and Monitoring Responsibilities	GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities
1. Assess suitability of the patient for treatment. 2. Discuss treatment options with the patient, the parent(s) and carer(s). Obtain appropriate consent to treatment and to share care with the GP. 3. Initiate treatment, ensuring that the patient is stabilised on the dose before the patient is transferred back to the care of the GP. 4. Send a letter to the GP suggesting that initial shared care is agreed for this patient. 5. Prescribe melatonin, please see the summary table and pathway in Appendix 1. Only the formulations named can be prescribed under this shared care agreement. 6. Review the patient regularly and monitor their response to treatment; a drug holiday is recommended after the initial three months of treatment, and then every six months thereafter. This involves a trial withdrawal of treatment for two weeks to test ongoing need (See Duration of Therapy section below for more information on melatonin drug holidays). Most patients will be under more regular secondary care review for underlying neurodevelopmental condition. 7. Report adverse events and suspected adverse drug reactions to the MHRA through the Yellow Card reporting scheme. 8. Ensure clear arrangements for GP back up advice and support. 9. If no adverse effects, clear benefits to child, and no other medical issues requiring ongoing specialist review (i.e. ADHD medication), the patient can be discharged to primary care. 10. Once discharged if primary care need advice this can be offered. Regularly monitor height, weight, pubertal maturation progress and seizure frequency in epileptic patients in first year of use. If well tolerated and no adverse side effects continued need for treatment can be assessed in primary care, every 12 months.	1. Prescribe melatonin after communication with specialist about the need for treatment. 2. GP to take on prescribing following written confirmation from the specialist within 3 months. 3. Ask patient/carer about side effects and general well-being and report back to the Specialist. 4. Ask carer about effectiveness. 5. Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment. 6. Report adverse events and suspected adverse drug reactions to the MHRA through the Yellow Card reporting scheme. 7. Stop treatment if patient no longer needs it or has unacceptable side effects. 8. Stop or adjust treatment if necessary (e.g. side effects) on discussion child and if necessary, can discuss with the specialist.

Patient Information

Families will be provided with relevant patient information leaflets.

Specialist Contact Details

- Jenny Lind Clinic, NNUH, Colney Lane, Norwich NR4 7UY, Tel 01603 286343
- The Child Development Unit, Norwich, Tel 01603 505581
- Newberry Child Development Centre, Lowestoft Road, Gorleston, NR31 6SQ, Tel 01493 442322
- CAMHS Central and West Norfolk, Tel 0330 790 0371.
- CAMHS East Norfolk, Great Yarmouth and Waveney, Tel 0300 123 1882.

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment

Children with neurodevelopmental disabilities which include Autistic Spectrum Disorder, learning disabilities and ADHD, are at increased risk of having a sleep disorder. These tend to be longstanding, resistant to treatment and adversely affect development and health. Co-morbid sleep problems exacerbate the burden of neurodevelopmental disability on caregivers.[5]

Melatonin is a hormone produced by the pineal gland in a circadian manner, in response to darkness. The link with circadian rhythms has led to its use in the treatment of sleep disorders underpinned by learning disability, Autistic Spectrum Disorders and ADHD. Melatonin is classified as a medicine in the UK and is only available on prescription. In contrast, it is readily available to purchase in some countries, e.g., USA.

In practice, the use of melatonin for the treatment of paediatric sleep-wake cycle disorders is widespread. There are a number of published trials [6, 7, 8, 9,10,11] although these are often small and of short duration, they have come to similar conclusions. Children with ADHD treated with melatonin have been shown to fall asleep earlier and sleep for longer when compared to controls.[8] Generally no significant change in behaviour or attention has been demonstrated. It would appear that there is wide variability in response. Melatonin may be most effective in those children whose sleep patterns indicate that their circadian rhythm is disrupted, and in whom sleep hygiene methods have been ineffective.

Melatonin is recommended for use in these disorders in the BNFC.

Licensed Use

Immediate release formulations of melatonin:

- Adaflex® is licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient.
  The recommended starting dose of Adaflex® is 1-2 mg 30-60 minutes before bedtime. The dose of Adaflex® can be increased by 1 mg every week until effect up to a **maximum 5 mg per day**, independent of age. The lowest effective dose should be sought. **Adaflex® tablets are licensed to be crushed and mixed with water directly before the administration.**
- Ceyesto® 3mg tablets are licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient[2]. The dose is 3mg to be taken 30-60 minutes before bedtime. The **maximum licensed dose is 3mg**[2].
- Syncrodin® is only licensed for the short-term treatment of jet-lag in adults[3].

Modified-release formulations of melatonin:

- Melatonin 2mg modified-release tablets (generic) are licensed for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over. They are not licensed for children.

Restricted formulations of melatonin reserved for use:

- Ceyesto® 1mg/ml oral solution is licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient. The recommended starting dose is 1-2 mg, 30-60 minutes before bedtime.
  The dose of melatonin should be adjusted individually until effective up to a **maximum of 5 mg per day**, independent of age. The lowest effective dose should be sought and taken for the shortest period. If necessary, this medicinal product can be administered via a silicone gastric, duodenal or nasal feeding tube. Rinse the tube twice with at least 10 ml of water following administration.
  Please note the use of tubes made of polyurethane is not recommended as compatibility has not been demonstrated.
- Circadin® 2mg prolonged release tablets are licensed as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over. They are licensed for oral administration.

Please note that Slenyto® prolonged-release tablets are not recommended for prescribing by the East of England Priorities Advisory Committee, as the case for cost-effectiveness has not been proven. Therefore, Slenyto® are not included in this shared care agreement.

Criteria for Patient Selection

1. Autistic spectrum conditions with severe sleep problems not amenable to behaviour management strategies.[6,7]
2. Insomnia in children with ADHD, which is not responsive to sleep hygiene intervention.[8, 14, 15]
3. Insomnia in children with neurodevelopmental disabilities not responsive to sleep hygiene intervention.[9]

For all other specialist requests please email the medicines optimisation team at nwicb.medsqueries@nhs.net for further guidance.

Form and strength of preparation

Product	Strength	Pack size	Price[A]	
Immediate release formulations				
Adaflex® tablets	1mg tablet 2mg tablet 3mg tablet 4mg tablet 5mg tablet	30 30 30 30 30	£10.89 £10.89 £10.89 £10.89 £10.89	
Ceyesto® 3mg tablets	3mg tablet	30	£10.99[B]	
Syncrodin® 3mg film-coated tablets	3mg film-coated tablet	30	£14.95[B]	
Modified-release formulations				
Melatonin 2mg modified-release tablets (*if prescribed generically*)	2mg modified-release tablet	30	£2.71	
Restricted formulations				
Ceyesto® 1mg/ml oral solution	1mg/ml oral solution	100ml 150ml	£17.10 £25.65	
Circadin® 2mg prolonged-release tablets	2mg prolonged-release tablets	30	£15.39[B]	

[A] Price based on Drug Tariff, April 2025
[B] Price from dm+d, April 2025

Side Effects – Please refer to BNFC and SPCs

1. Melatonin is generally well tolerated with only mild adverse effects similar to placebo such as: headaches, drowsiness, gastrointestinal disturbances, drowsiness, arthralgia, sleep disorders and pain. [9,16]
2. Delay in sexual maturity and alterations in hormone levels have been reported in animal studies. The effect of melatonin on onset of puberty in children is uncertain.[14]
3. Vivid dreaming has been reported which may be dose related and diminishes with time.
4. Adverse events, interactions and precautions for the different formulations can be found in the SPC. Melatonin 2mg modified-release tablets (generic) and Circadin® 2mg prolonged-release tablets are only licensed for adults aged 55 years or over for the short-term treatment of primary insomnia. Syncrodin® is only licensed for short-term treatment of jet lag in adults. Therefore, the information presented in the SPC for these products cannot be presumed to apply to paediatric patients.
5. **Other:** Itching, tachycardia, dizziness, see BNFC for further information
6. **Children with epilepsy:** Melatonin has some anti-convulsant properties, but some reports have shown that children may have more seizures. Melatonin should be used with caution, see below.

Drug Interactions - Please refer to BNFC and SPCs

Possible interactions with other medicinal products have not been fully characterised. Interaction of melatonin with selective serotonin re-uptake inhibitors has been observed. Melatonin may potentiate the effectiveness of warfarin or other oral anticoagulants and may increase the effectiveness of other monoamine oxidase inhibitors. Melatonin may reduce the effectiveness of nifedipine and other calcium channel blockers.[17]
Sodium valproate and GABAergic antiepileptics reported to suppress nocturnal levels of melatonin.[18]

Cautions and Contraindications - Please refer to BNFC and SPCs

Ensure that obstructive sleep apnoea is ruled out.
Caution in autoimmune disease. BNFC states to avoid use to limited information available for patients with autoimmune disease; exacerbation reported occasionally.
Melatonin studies have shown possible adverse immunomodulatory effects on rheumatoid arthritis and asthma. However, some studies have shown that patients with asthma showed that their sleep difficulties improved with melatonin without side effects.[18]

Caution susceptibility to seizures; BNFC states risk of increased seizure frequency. Increased seizure activity has been reported in patients with epilepsy, but there is also anecdotal evidence that seizure activity improves as a result of improved sleep. Much of the clinical trial data with melatonin does not report an increase in seizure frequency, but data must be treated cautiously due to the short-term nature, size, and heterogeneous nature of the populations studied. Until more is known, prescribers need to approach melatonin use in children with epilepsy cautiously and be alert for alterations in seizure activity.

Hepatic impairment: BNFC states to avoid modified-release tablets as risk of decreased clearance, limited information available. For immediate-release formulations the BNFC states to avoid in moderate or severe hepatic impairment as risk of decreased clearance, limited information available.

Renal impairment: BNFC states caution with use in renal impairment. To avoid immediate release formulations in severe renal impairment.

Initiation of therapy

1. Paediatric consultant or paediatric registrar under supervision of consultant.
2. Consultant child psychiatrist or child psychiatry registrar under supervision of the consultant.

Initial dose and method of administration and supply

Immediate release formulations of melatonin:

- Adaflex® is licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient. The recommended starting dose of Adaflex® is 1-2 mg 30-60 minutes before bedtime. The dose of Adaflex® can be increased by 1 mg every week until effect up to a **maximum 5 mg per day**, independent of age. The lowest effective dose should be sought. Use outside of this licensing would be off-label.
  Adaflex® tablets are licensed to be crushed and mixed with water directly before the administration. Food can enhance the increase in plasma melatonin concentration. Intake of melatonin with carbohydrate-rich meals may impair blood glucose control for several hours. It is recommended that food is not consumed 2 hours before and 2 hours after Adaflex tablets[1].

- Ceyesto® 3mg tablets are licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient[2]. The dose is 3mg to be taken 30-60 minutes before bedtime. The **maximum licensed dose is 3mg**[2]. Use outside of this licensing would be off-label.

- Syncrodin® is only licensed for the short-term treatment of jet-lag in adults[3]. The standard licensed dose for the short-term treatment of jet-lag in adults is 3mg daily for a maximum of 5 days. The SPC states the dose can be increased to 6mg daily if the standard dose does not alleviate symptoms.

  Whilst not licensed to be dissolved in water the manufacturer Pharma Nord Medical confirms that from UK clinical practice (post-marketing) they have received feedback from various clinical settings that Syncrodin® 3mg Film-Coated Tablets disintegrate very quickly when in contact with even few ml of water (e.g. on a 2.5ml measuring spoon, or in saliva within the mouth). Croscarmellose sodium (an excipient of Syncrodin® 3mg Film-Coated Tablets) plays an important role in dissolving the tablet quickly. However please note Syncrodin® 3mg Film-Coated Tablets are not designed as soluble tablets.

Modified-release formulations of melatonin:

- Melatonin 2mg modified-release tablets (generic) are off-label for children. They are licensed for short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 years or over. The recommended dose for this indication in adults is 2mg once daily, 1-2 hours before bedtime and after food. Manufacturers recommend that tablets are swallowed whole; this is essential to maintain the modified-release properties.

Restricted formulations reserved for use as follows:

- Ceyesto® 1mg/ml oral solution is licensed for the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient.

  *Ceyesto® 1mg/ml oral solution is **restricted** for use in Norfolk & Waveney; it should be reserved for children that are aged **≥ 3 years and ≥15kg** who:*
  - *have a **fine bore enteral feeding tube,***
  - *or who are unable to tolerate other solid oral dosage forms.*

  The recommended starting dose is 1-2 mg, 30-60 minutes before bedtime. The dose of melatonin should be adjusted individually until effective; the maximum licensed dose is **5 mg per day**, independent of age. The lowest effective dose should be sought and taken for the shortest period.

  Important points of note if prescribing Ceyesto® 1mg/ml oral solution:
  - ✓ *Ceyesto® 1mg/ml oral solution **should NOT be prescribed for children < 3 years of age** due to the presence of the excipient **Benzyl alcohol** in the formulation.*
  - ✓ *If prescribing for a child who is between the ages of **3 – 6 years,** the **maximum daily dose** should be **capped at 5mg**. This is to ensure safety limits for the excipient Propylene glycol are not breached.*
  - ✓ *Please note that any prescribing outside of the medicines licensing is off-label.*

If necessary, this medicinal product can be administered via a silicone gastric, duodenal or nasal feeding tube. Rinse the tube twice with at least 10 ml of water following administration.
Please note the use of tubes made of polyurethane is not recommended as compatibility has not been demonstrated.

N.B. whilst other licensed liquid formulations of melatonin are available this particular brand has been approved on formulary, due to its favourable excipient profile, and should be prescribed by brand name where a liquid formulation is indicated.

- Circadin® 2mg prolonged release tablets (**Prescribe by brand**)

Circadin® 2mg prolonged release tablets are licensed as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over. They are licensed for oral administration. Use in children and administration via enteral feeding tubes is off-label. The standard licensed dose for adults is 2mg once daily, 1-2 hours before bedtime and after food.

Circadin® is restricted for use in Norfolk & Waveney and should be reserved for children with enteral feeding tubes. Whilst this use would be off-label NEWT guidelines[20] state the tablets can be crushed (note this would change the release profile from modified-release to immediate-release) and mixed with 15-30mL of water for administration via enteral feeding tubes. The tube should be flushed well after administration.

Maintenance Dose and Administration

See above.
Consultant responsible for prescribing until stable dose achieved. This would usually be within 1 month. Once stable dose achieved consultant to request GP to take on prescribing. GP to take on prescribing following written confirmation from the specialist within 3 months. It is important to continue to review the need for ongoing treatment. A drug holiday is recommended after the initial three months of treatment, and then six monthly thereafter. This involves a trial withdrawal of treatment for 2 weeks to test ongoing need (See Duration of Therapy section below for more information on melatonin drug holidays).

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

Treatment should be stopped when there is evidence of lack of effect from a sleep diary or patient/parent perception.
Treatment may need to be long term. Patients should be instructed to withdraw melatonin for a period known as a 'drug holiday' to assess on-going need.
Ideally a drug free holiday will take place 3 months after the commencement of treatment and 6 monthly thereafter. The patients should undergo a drug free holiday for 2 weeks. Patients and their carers can choose a suitable time to undertake a drug free holiday and do not have to inform their GP or specialist. An opportunity to undertake the drug free holiday could be two to four weeks before the specialist's annual review; recording the outcomes on and off treatment in a sleep diary. Alternatively, patients could try having a drug free holiday during the school holidays to avoid adverse effects on school days and their sleep diary reviewed at their next specialist review. If the break from melatonin has resulted in no deterioration in sleep cycle, the young person can remain off melatonin. The specialist and GP should be informed if the drug withdrawal trial has been successful, and that melatonin is no longer required.
If withdrawal of medication has impacted the young person's sleep cycle they should restart treatment, at the same dose they were stable on prior to the drug holiday.

If there is a consistent correlation of sleep deterioration during a drug holiday, patients should be advised to continue 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).
If requiring further advice relating to drug holidays the GP should contact the patient's specialist

Initial monitoring / baseline assessment – by Specialist

Monitor effectiveness for the first 4 weeks with a sleep diary or patient/parent perception.

Specialist monitoring responsibilities

Regularly monitor height, weight, pubertal maturation progress and seizure frequency in epileptic patients in first year of use. If well tolerated and no adverse side effects continued need for treatment can be assessed in primary care, every 12 months.

GP / Community Team or other Primary Care monitoring responsibilities

Ask patient/carer about side effects and general well-being and report back to the specialist.

Consultant / Specialist prescribing responsibilities

1. Assess suitability of patient for treatment.
2. Discuss treatment options with the patient, the parent(s) and carer(s). Obtain appropriate consent to treatment and to share care with the GP.
3. Initiate treatment, ensuring that the patient is stabilised on the dose before the patient is transferred back to the care of the GP.
4. Send a letter to the GP suggesting that initial shared care is agreed for this patient.
5. Prescribe melatonin, please see the summary table and pathway in Appendix 1. Only the formulations named can be prescribed under this shared care agreement.
6. Review the patient at least annually to monitor response to treatment, with trial withdrawal of treatment for 2 weeks to test ongoing need. Most patients will be under more regular secondary care review for underlying neurodevelopmental condition.
7. Report adverse events to the MHRA (Yellow Card reporting scheme).
8. Ensure clear arrangements for GP back-up advice and support.
9. If no adverse effects and clear benefits to the child and no other medical issues requiring ongoing specialist review (i.e. ADHD medication) can be discharged to primary care.
10. Once discharged, if primary care need advice this can be offered.

GP prescribing responsibilities

1. Prescribe melatonin after communication with specialist about the need for treatment.
2. GP to take on prescribing following written confirmation from the specialist within 3 months.
3. Ask patient/carer about side effects and general wellbeing and report back to the Specialist.
4. Ask carer about effectiveness.
5. Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6. Report adverse events to the MHRA via the Yellow Card reporting scheme.
7. Stop treatment if patient no longer needs it or has unacceptable side effects.

8. Stop or adjust treatment if necessary (e.g. side effects) on discussion child and if necessary, can discuss with the Specialist.

Indications for referral back to Specialist

Uncommon, severe, or unexpected side effects. Lack of efficacy. If there are concerns or queries, telephone consultation will usually be available at short notice.

References

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16. *BNFC 2020 Melatonin Side effects*
17. Summary of product characteristics – Bio-melatonin 3 mg tablets.

18. Monteleone P, Tortorella A, Borriello R, et al. Suppression of nocturnal plasma melatonin levels by evening administration of sodium valproate in healthy humans. *Biol Psychiatry 1997:41:336-41*
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Author(s) and Organisation	NHS Norfolk & Waveney Medicines Optimisation Team (NC)
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Reviewed by	Therapeutics Advisory Group
Last review date	May 2025
Date of next review	May 2027

Appendix 1: Formulations of Melatonin Summary Table

Immediate-release formulations				
Name of formulation & strength	**Licensing**	**Price per Pack**[A]	**How to Prescribe**	**Administration**
Adaflex® tablets; 1mg, 2mg, 3mg, 4mg, and 5mg	For the treatment of insomnia in children and adolescents **aged 6-17 years with ADHD**. Use outside of this licensing would be off-label.	£10.89 for 30 tablets - all strengths	Prescribe by **brand**	Adaflex® tablets are **licensed** to be **crushed and mixed with water** directly before the administration.
Ceyesto® 3mg tablet	For the treatment of insomnia in children and adolescents aged **6-17 years with ADHD**. Use outside of this licensing would be off-label.	£10.99[B] for 30 tablets	Prescribe by **brand**	Tablets to be swallowed whole.
Syncrodin® 3mg film-coated tablet	Syncrodin® does **not** have a UK marketing authorisation for the indication covered by this shared care, the use of Syncrodin® is therefore **off-label**. Not licensed in children.	£14.95[B] for 30 tablets	Prescribe by **brand**	Tablets disintegrate very quickly when in contact with even few ml of water (e.g. on a 2.5ml measuring spoon, or in saliva within the mouth). This is an off-label use.
Modified-release formulations				
Name of formulation & strength	**Licensing**	**Price per Pack**[A]	**How to Prescribe**	**Administration**
Melatonin 2mg modified-release tablets (Generic)	**Off-label** use for this indication. Not licensed in children.	£2.71 for 30 tablets	Prescribe **generically**	Tablets to be swallowed whole to maintain the modified-release properties**.**
Restricted formulations reserved for use				
Name of formulation & strength	**Licensing**	**Price per Pack**[A]	**How to Prescribe**	**Administration**
Ceyesto® 1mg/ml oral solution	For the treatment of insomnia in children and	100ml = £17.10	Prescribe by **brand**	If necessary, this medicinal product can be

*Note reserved for children aged **≥3 years and ≥15kg** who have a fine bore enteral feeding tubes, or for children and young people who are unable to tolerate other solid oral dosage forms. If prescribing for a child who is between the **ages of 3 – 6 years,** the **maximum daily dose** should be **capped at 5mg**. This is to ensure safety limits for excipients are not breached.*	adolescents aged **6-17 years with ADHD**, where sleep hygiene measures have been insufficient.	150ml = £25.65		administered via a **silicone gastric, duodenal or nasal feeding tube**. Rinse the tube twice with at least 10 ml of water following administration. Please note the use of tubes made of polyurethane is **not** recommended as compatibility has not been demonstrated.
Circadin® 2mg modified-release tablets *Note reserved for administration via enteral feeding tubes only.*	**Off-label** use for this indication. Not licensed in children.	£15.39 for 30 tablets	Prescribe by brand if administering via enteral feeding tube only.	Circadin® is restricted for use in Norfolk & Waveney and should be reserved for children with enteral feeding tubes. Whilst this use would be off-label NEWT guidelines[20] state the tablets can be crushed (note this would change the release profile from modified-release to immediate-release) and mixed with 15-30mL of water for administration via enteral feeding tubes. The tube should be flushed well after administration.
[A] Price based on Drug Tariff, April 2025				[B] Price from dm+d, April 2025

Document history:

Version	Date	Author/Editor	Status	Comment
1.	Mar11	Dr R Adiga, Dr Z Iqbal, Dr R Hoogkamer, Dr S Steel. Edited by F Marshall	Superseded	Therapeutics Advisory Group (TAG) approved
2.	Feb12	Dr R Hoogkamer Edited by F Marshall	Superseded	Updated manufacturer, pack size and price following transfer of product licence / marketing authorisation
3.	Sept 13	Dr R Adiga (NCH&C), Dr Z Iqbal (NSFT), Dr R Hoogkamer (NSFT), Dr S Steel (NCH&C) / Edited by F Marshall, TAG Lead Pharmacist (CSU)	Superseded	Use of current version extended to March 2014 pending results of audit of prescribing and monitoring by local providers, NCH&C and NSFT. January 2014 – Contact details for Drs Hoogkamer and Iqbal updated.
4.	July 14	Edited by F Marshall, TAG Lead Pharmacist (NEL CSU Anglia) on behalf of the TAG.	Superseded	Shared Care Agreement reviewed and approved by the TAG following presentation of a report of audit results from NCH&C.
5.0	Feb – March 17	Dr R Hoogkamer (NSFT) and Dr S Steel (NCH&C) / F Marshall, TAG Lead Pharmacist (CSU).	Superseded	Reviewed by authors. Sleep disorders in depression and anxiety, and delayed sleep phase disorder added under criteria for use – considered and supported by the TAG.
6.	Nov 20	Dr S Steel	Superseded	Reviewed by authors. Request that after 1 year no longer needs specialist review as safety of medication is good
6.1	March 2021	Jen Carroll, TAG Lead Technician	Superseded	Supported by TAG and D+TC. Ratified by CCG Governing Body
6.2	March 2022	Jen Carroll, TAG Lead Technician	Superseeded	Added Syncrodin as immediate release option. Supported by TAG and D+TC. Ratified by CCG Governing Body May 2022. Also amended title
6.3	September 2022	Natalie Cunningham Medicines	Superseded	Addition of Adaflex as first line treatment option.

		Optimisation Pharmacist		Addition of information relating to the dissolution of Syncrodin® by manufacturer. Request that treatment can be continued in patients aged over 18 years, if initiated as a child, and reviews have been conducted.
7	April 2023	Natalie Cunningham Medicines Optimisation Pharmacist	Superseded	Addition of Ceyesto® and generic 2mg modified release melatonin tablets. Liquid melatonin changed to Double Red from Black to reflect change in status. Addition of Appendix 1, Summary Table, and Appendix 2 Pathway.
7.1	July 2023	Natalie Cunningham Medicines Optimisation Pharmacist	Superseded	Recommendation for 6 monthly drug holidays.
7.2	October 2023	Natalie Cunningham Medicines Optimisation Pharmacist	Superseded	Amendment to Specialist Prescribing and Monitoring Responsibilities section, now refer to pathway in Appendix 2 rather than specify here the brands/formulations that are covered by shared care.
7.3	January 2024	Natalie Cunningham Medicines Optimisation Pharmacist	Superseded	Title changed from '*Shared care guidelines for Melatonin for Sleep Disorders*' to '*Shared care guidelines - Melatonin for Sleep Disorders in Children*'. Indications for shared care section expanded; to make it clearer which indications melatonin is commissioned for in primary care. In criteria for patient selection wording changed from '*Autistic spectrum conditions **and** severe sleep problems not amenable to behaviour management strategies*' to '*Autistic spectrum conditions **with** severe sleep problems not amenable to behaviour management strategies.*' Caution in autoimmune disease added to cautions and contraindications section. Links to the BNFC and SPC also added to the following sections – side effects, drug interactions and

				cautions/contraindications section. Hepatic and renal impairment also added to the cautions and contraindications section as per BNFC.
7.4	January 2024	Natalie Cunningham Medicines Optimisation Pharmacist	Superseeded	Indications for shared care reviewed. The following indications for shared care have been removed: i) Sleep disorders in depression and anxiety (Not provided by NCHC), and ii) Delayed sleep phase syndrome when appropriate behavioural sleep interventions fail (NCHC are not commissioned to provide this service unless child has neurodevelopmental disorder). Removed to reflect current service provisions; unclear if these services are still commissioned. Note added to Indication for Shared Care and Criteria for patient selection sections which states, '*For all other specialist requests please email the medicines optimisation team at nwicb.medsqueries@nhs.net for further guidance*.' Note also added to Adaflex and Ceyesto® to say '*Use outside of this licensing would be off-label prescribing*'. In the Initial dose and method of administration and supply section a note has been added to state that '*Use of Syncrodin® in children is off-label prescribing*'. For melatonin 2mg modified release tablets (generic) a note was also added to state '*Use of melatonin 2mg modified release tablets (generic) in children is off-label prescribing*'.
8	May 2025		Current	Addition of Ceyesto® 1mg/ml oral solution; restricted for children aged ≥3 years and ≥15kg who have a fine bore enteral feeding tubes, or for children and young people who are unable to tolerate other solid oral dosage forms. Due to the excipient profile further information added; *'Ceyesto® 1mg/ml oral solution should NOT be prescribed for children < 3 years of age due to the presence of the excipient Benzyl alcohol in the formulation'*, and *'If prescribing for a*

				child who is between the ages of 3 – 6 years the maximum dose should be capped at 5mg. This is to ensure safety limits for the excipient Propylene glycol are not breached.' Information on the administration of Circadin® 2mg prolonged-release tablets via enteral feeding tubes added as per NEWT guidelines. Both Ceyesto® 1mg/ml oral solution and Circadin® 2mg modified release tablets named as restricted formulation reserved for use. Under the 'Form and Strength of Preparation' section I have removed the box in the table for manufacturer name. Prices updated. Appendix 2 removed. Specialist contact details updated.