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| **INFORMATION SHEET – Blue Traffic Light Classification** | | | |
| **Name of medicine** | | Melatonin 2mg MR tablets, melatonin 1,2,3,4,5mg immediate release tablets, or melatonin 1mg/ml oral solution sugar free | |
| **Indication**  **(including whether for adults and/or children)** | | For the treatment of persistent sleep disorders in Children over 3 years old with Neurodevelopmental Disorders | |
| **APC policy statement reference**  **(if applicable)** | | n/a | |
| **Author(s):** Alison Marshall  **Organisation(s):** Surrey and Borders Partnership NHS Foundation Trust | | | |
| **Version: 1.1** | **APC recommendation date:** | | **Review date: Dec 2022** |

The information sheet is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface for medicines classified by Area Prescribing Committee (APC) as **BLUE**

**BLUE** drugs are considered suitable for prescribing in primary care, following initiation and stabilisation by a specialist as ongoing monitoring can be undertaken in primary care without specialist support and WITHOUT the need for a formal shared care guideline.

For each drug classified as **BLUE**, the Area Prescribing Committee will recommend the minimum supply and whether an information sheet is required or not. A minimum of one month supply of medication will be provided by the initiating consultant.

This information sheet sets out the patient pathway relating to this medicine and any information not available in the British National Formulary and manufacturer’s Summary of Product Characteristics. Prescribing must be carried out with reference to those publications. A GP or Primary Care Prescriber must ensure they are familiar with the prescribing responsibilities. This information sheet is available on the internet [**http://pad.res360.net/**](http://pad.res360.net/) forming part of the Prescribing Advisory Database (PAD) giving GPs appropriate advice / guidance and is not required to be sent to the GP with the clinic letter.

**RESPONSIBILITIES and ROLES**

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| **Consultant / Specialist responsibilities** |
| 1. To assess the suitability of patient for treatment |
| 1. To discuss the aims, benefits and side effects of treatment with the patient and/or carer as well as their role |
| 1. To consider melatonin where non-pharmacological strategies have failed, and underlying physical causes are managed where they exist. |
| 1. To consider melatonin only where parents, carers or, where appropriate the patient, has completed a sleep questionnaire and sleep diary highlighting problems with sleep latency. |
| 1. Explain to the patient and/or carer the treatment plan including the dosing schedule and request for transfer of care to GP |
| 1. Baseline monitoring undertaken |
| 1. Monitor and evaluate response to treatment, including adverse drug reactions, with the patient and to continue / discontinue treatment in line with agreed treatment plan |
| 1. Supply GP with summary of patient review (including anticipated length of treatment) and a copy of any information sheet available |
| 1. Advise GP if treatment is to discontinue at any point |
| 1. Inform GP if patient does not attend planned follow-up |
| 1. Prescribe melatonin for a minimum of one month. Initiate off label melatonin 2mg MR tablets.   If an immediate release preparation is required, the licensed melatonin 1,2,3,4, or 5mg tablets should be prescribed. The licence for these tablets permits them to be crushed if patient is unable to swallow a whole tablet. Note that the modified release formulation of melatonin will assist with *maintenance* of sleep, whereas the immediate release formulation will assist with promoting the *onset* of sleep. |
| 13 If necessary, only where the patient has a feeding tube or significant swallowing difficulties, the use of the licensed melatonin 1mg/mL oral solution may be considered. In some cases, this may be an off-label use due to variation in licensing of the product from different manufacturers. Consideration should be given when dispensing to the excipients present in the licensed melatonin oral solution, with particular reference to propylene glycol and sorbitol.  For information on the suitability of excipients see http://nppg.org.uk/wp-content/uploads/2020/12/Position-Statement-Liquid-Choice-V1-November-2020.pdf |
| 14. Provide dose titration schedule (if differs from Summary of Product Characteristics), and whether all actions are taken in secondary care, or may require Primary Care prescriber to titrate dose |
| 1. Perform baseline checks of physical health (including height, weight) |
| 1. Assess and monitor the patient’s response to treatment and make dose adjustments where necessary. |
| 1. If treatment is ineffective and discontinued check for possible complications following discontinuation. |
| 1. Obtain informed consent for the off-label prescribing of melatonin if melatonin 2mg MR tablets are prescribed, or if immediate release tablets are used in children below the age of 6 or if the licensed liquid formulation is prescribed for an off-label indication. |
| 1. Assess the continuing need for melatonin at 6 monthly review and consider stopping melatonin, e.g. 14 day break every 6 months using an appropriate sleep monitoring tool, and advise GPs on this for patients discharged from specialist care. |
| 1. Whilst the patient remains under the care of the specialist, monitor continued positive impact on sleep and review every 6 months by discontinuing the medicine to assess continued benefit. (This will be undertaken by the GP once the person is discharged from specialist care) |
| 1. Monitor weight and standard monitoring of growth and sexual development (this has been seen in animals but not in human use of melatonin). |
| 1. Although leukopenia is a known (rare) side effect, regular FBCs are not specifically required |
| 1. Maintain good communication with the GP. A written letter should be sent to the GP after each clinic visit. Keeping the GP fully informed about the patient’s condition and medication. The specialist will be available to answer queries from the GP and carers. |
| 1. To take responsibility for reviewing the need for ongoing treatment and stop treatment or agree aftercare when the patient reaches 18 years of age. |

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| **General Practitioner (GP) or Primary Care Prescriber responsibilities** |
| 1. Subsequent prescribing of melatonin as melatonin 2mg MR tablets; melatonin immediate release 1,2,3,4, or 5mg tablets, or occasionally the licensed 1mg/1ml oral solution sugar free, once the treatment has been established, the patient stabilised and the care of the patient has been transferred and accepted.   In some cases this may be an off-label use of the liquid due to variation in licensing of the product from different manufacturers. Consideration should be given when dispensing to the excipients present in the licensed melatonin oral solution, with particular reference to propylene glycol and sorbitol.  For information on the suitability of excipients see http://nppg.org.uk/wp-content/uploads/2020/12/Position-Statement-Liquid-Choice-V1-November-2020.pdf |
| 1. For patients discharged from specialist care, undertake any necessary monitoring including height and weight every 6 months |
| 1. Refer patients back to the specialist if there is delayed sexual development or failure to gain weight and height for the expected age and familial characteristics. |
| 1. For patients no longer under specialist care, assess the continuing need for melatonin at least 6 monthly and consider stopping melatonin e.g., 14-day break using an appropriate sleep monitoring tool |
| 1. Re-refer the patient or seek advice from the specialist if there are on-going sleep problems, side-effects or other difficulties |
| 1. To report any adverse drug reactions to the specialist and to the Medicines and Healthcare Products Regulatory Authority (MRHA) as part of the Yellow Card Scheme. https://yellowcard.mhra.gov.uk/ |

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| **Patient / Carer role** |
| 1. Informing the specialist team, primary care prescriber or other healthcare professional if he or she has further questions or wants more information about the treatment |
| 1. Tell the consultant / specialist or GP or Primary Care Prescriber of any other medication being taken, including over-the-counter products. |
| 1. Sharing any concerns about their treatment and problems they are having taking their medicines with the specialist team, primary care prescriber or other healthcare professional involved in their care |
| 1. Supported to know how to report any adverse effects to the specialist team, primary care prescriber or other healthcare professional involved in their care, and how adverse effects can be managed |
| 1. To be available for monitoring as required |
| 1. Attend follow-up appointments with the consultant / specialist / GP. **Non-attendance of appointments may result in treatment being stopped** |

**Key information on the medicine**

Please refer to the current edition of the British National Formulary (BNF), available at [www.medicinescomplete.org](http://www.MEDICINESCOMPLETE.org), and Summary of Product Characteristics (SPC), available at [www.medicines.org.uk](http://www.medicines.org.uk) for detailed product and prescribing information and specific guidance.

Insomnia is a widespread problem in children with neurodevelopmental or psychiatric disorders such as autistic spectrum disorder and attention deficit hyperactivity disorder (ADHD).Behavioural therapy can be very effective in some forms of paediatric insomnia however children with neuropsychiatric disorders tend to have a lower response rate to behavioural therapy and may require drug treatment.

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced by the pineal gland during the dark hours of the day and night which appears to support the normal circadian rhythm and aid sleep onset. It is used as a treatment of sleep disorders in children. It is most helpful where sleep onset is a significant problem, but is rarely useful to maintain sleep if a child is waking during the night. Melatonin should not be used in isolation but should be combined with a behavioural programme, involving Clinical Psychology where necessary.

The use of a weekly sleep diary before and during treatment will assist the monitoring of response.

With regards to its use in children and adolescents with autism spectrum disorders, the British Association for Psychopharmacology guidelines on assessment and treatment of autism spectrum disorder (2017) recommends melatonin, if possible in combination with a behavioural intervention, for the management of sleep disorders in children.

Short term use of melatonin may also occasionally be useful in a range of isolated circumstances where other methods have failed. It should not be considered in the management of sleep problems in otherwise normal children.

Once a regular sleep pattern has successfully been achieved and maintained, there should be a trial withdrawal of treatment. In some children with neurodevelopmental / psychiatric problems, longer term treatment may be needed, but intermittent trials off treatment should be considered.

If tablets cannot be swallowed whole, the licence for some immediate release melatonin (eg Adaflex®) tablets permits crushing of the tablets. The details of the conditions to be treated included in the licence should be confirmed to establish whether this would be an off-label indication

Where the use of a whole or crushed immediate release melatonin tablet is not possible, the use of melatonin oral solution 1mg/mL sugar free (this may be an off-label use) may be considered with due attention paid to the excipients present.

**Indication**

Sleep disorders in children and adolescents over three years old with neurodevelopmental disorders.

**Dosage and Administration**

* Initiate at melatonin 2mg (formulation selected according to guidance above) 1-2 hours before bedtime.
* Increase dosage according to response.
* Maximum BNF-C dose 10mg
* If the child wakes during the night, an extra dose of melatonin should not be given.
* If an immediate release preparation is required, the licensed melatonin 1,2,3,4,or 5mg tablets should be prescribed. These may be crushed if required (check licensing of formulation selected).

- **No** other solid dose formulations of melatonin are supported for use

- **No** other liquid formulations of melatonin are supported for use

- Melatonin for use in jet lag is **not** supported for use

- The Slenyto® brand (1mg and 5 mg prolonged release tablets) has been assigned a **NON FORMULARY** status for all indications - see link for further information

https://surreyccg.res-systems.net/PAD/Search/DrugConditionProfile/6243

**Expected outcome**

*Improvement in sleep pattern*

**Monitoring**

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| **Monitoring requirements including frequency and appropriate dose adjustments** | **Responsible clinician** |
| **Pre-treatment**:   * Sleep diary | Specialist Clinician |
| **Initiation**:   * Nil required |  |
| **Maintenance**:   * Monitor continued positive impact on sleep and review every 6 months by discontinuing the medicine to assess continued benefit. * Weight and Growth velocity * Sexual development | Specialist Clinician until care taken over by primary care prescriber |
| **If dose change when on maintenance**:   * Nil specific required |  |

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| Test | Frequency | Abnormal Result | Action if Abnormal Result |
| Effect on sleep | Ineffective at promoting or maintaining sleep | Refer to specialist clinician | Effect on sleep |
| Weight, growth velocity, sexual development | Outside normal parameters | Refer to specialist clinician | Weight, growth velocity, sexual development |

**Cautions, contraindications -** Refer to current Summary of Product Characteristics (SPC): [www.medicines.org.uk](http://www.medicines.org.uk)

**Adverse effects -** Refer to current Summary of Product Characteristics (SPC): [www.medicines.org.uk](http://www.medicines.org.uk)

**Drug interactions -** Refer to current Summary of Product Characteristics (SPC): [www.medicines.org.uk](http://www.medicines.org.uk)

Appendix

**Sleep Questionnaire**

Using these tools will help you and the specialist review your child’s sleep and develop the care plan. Complete for two weeks.

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| Name: DOB: Patient ID/NHS number: | |
| List any current medications, total daily doses or allergies: | |
| Do you find that your child has trouble getting off to sleep at bedtime? | Yes/No |
| Do you find that your child wakes up after bedtime? | Yes/No  If yes, how many times? |
| Does your child have any trouble getting back to sleep when they wake during the night? | Yes/No |
| Does your child experience any sleepwalking, nightmares (wakes up from a ‘bad’ dream but can be comforted) or night terrors (waking up screaming/distressed/confused/frightened and difficult to get back to sleep after comforting)? | Yes/No  If yes, which ones and what happens? |
| What time does your child normally go to bed? | School days:  Weekends: |
| What time does your child wake up? | School days:  Weekends: |
| Does your child experience any breathing difficulties (e.g. gasping, pause in breathing) at night? | Yes/No |
| Do you find that your child snores loudly at night? | Yes/No |
| Do you think your child has enough sleep? | Yes/No |
| Do you find that your child has difficulty waking up in the morning? | Yes/No |
| Do you find that your child is sleepy during the daytime? | Yes/No |
| Do you find that your child naps during the day? | Yes/No |
| Do you find that your child tires easily during the day? | Yes/No |

With thanks to South West London and St George’s Mental Health NHS Trust for sharing this work.

**Sleep Diary**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Day:**  **Date:** | **Monday** | **Tuesday** | **Wednesday** | **Thursday** | **Friday** | **Saturday** | **Sunday** |
| Sleepy during the  day (Yes/No) |  |  |  |  |  |  |  |
| Duration of any  daytime sleep |  |  |  |  |  |  |  |
| Time of any snacking. (e.g. chocolate, fizzy drinks, tea,  coffee, sweets) |  |  |  |  |  |  |  |
| Daytime activities |  |  |  |  |  |  |  |
| Activities 1 hour before bedtime |  |  |  |  |  |  |  |
| Time to bed |  |  |  |  |  |  |  |
| Times woke up in the night |  |  |  |  |  |  |  |
| How long did your child stay up for when waking in the  night? |  |  |  |  |  |  |  |
| Time awake in the morning |  |  |  |  |  |  |  |
| Mood on waking |  |  |  |  |  |  |  |
| Night time sleep duration |  |  |  |  |  |  |  |
| What did you do to aid your child’s sleep?  Give a score of 0-5  0 = Did not help  5 = most helpful |  |  |  |  |  |  |  |