

Melatonin Prescribing Support in Children and Adolescents

Prescribing of melatonin should only be considered where other sleep hygiene methods alone have been unsuccessful.

- 1. Melatonin is generally prescribed locally for children with sleep disturbances associated with learning difficulties, Attention Deficit Hyperactivity Disorder (ADHD) or autism.*
- 2. Melatonin should only be prescribed in Primary Care on the advice of a specialist clinician. See Quick Reference Guide.*
- 3. Adaflex immediate release tablets (licensed in children and adolescents aged 6 to 17 years old with ADHD, where sleep hygiene measures have been insufficient) is the first line formulary choice of melatonin across Cambridgeshire and Peterborough.*
- 4. Adaflex tablets can be crushed and mixed with water directly before the administration (licensed).*
- 5. Where a modified release formulation is required, generic melatonin 2mg modified release tablets can be considered where a modified release formulation is required.*
- 6. Licensed melatonin 1mg/1ml oral solution manufactured by Consilient Health, can be considered and is the preferred brand of oral solution for patients who are unable to tolerate crushed tablets (this may include patients with learning difficulties/autism and issues with texture) who require an immediate release formulation.*
- 7. There is no routine ongoing monitoring required specifically for melatonin in primary care other than monitoring for possible adverse effects and continued need.*
- 8. If treatment is successful, a trial reduction in the dose should be attempted after 6 months as some patients would have settled into a regular sleep pattern and may not need to continue at the same dose or may even be able to maintain sleep with no medication.*
- 9. Efficacy of melatonin may be lost if prescribed for longer than two years continuously. It suggests that if melatonin is withdrawn prior to this, sensitivity may be re-established, and melatonin successfully re-introduced at a lower dose if still required.*
- 10. If further advice or support is required, the Community Paediatrics Team or Community Child and Adolescent Mental Health Services can be contacted (contact details under Advice and Support).*

Indications and prescribing good practice

Whenever possible the patient (and their parents/guardian) should be involved in the decision making about initiating treatment and should be given information about melatonin in order to make an informed choice. Printable leaflets including information about good sleep hygiene can be found on the [NHS website – Healthy Sleep Tips for Children](#) and on the [Cambridgeshire Community Services NHS Trust website](#).

Melatonin is a pineal hormone which may affect sleep pattern. Melatonin is generally prescribed locally for children with sleep disturbances associated an underlying neurodevelopmental condition. Occasional reports of its use for children with chronic fatigue syndrome or Asperger's syndrome have also been noted.

Slenyto® prolonged release tablets should only be considered for children who meet the indications covered by the license specifically a confirmed diagnosis of Autism Spectrum Disorder and/or Smith-Magenis syndrome and require a modified release formulation.

The formulations of melatonin which can be prescribed across Cambridgeshire and Peterborough are:

- Immediate release preparation: Adaflex® tablets (licensed) (available as 1mg, 2mg, 3mg, 4mg, 5mg).
 - For use in patients aged 6 to 17 years, who require an immediate release formulation (licensed).
 - For use in patients under 6 years, who require an immediate release formulation (off-label).
 - Adaflex tablets can be crushed and mixed with water directly before the administration (licensed).
 - 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 intake of Adaflex tablets.
- Licensed melatonin 1mg/1ml oral solution by Consilient Health is available for patients who require an immediate release formulation and are unable to tolerate crushed tablets (this may include patients with learning difficulties/autism and issues with texture).
- Where a modified release preparation is required: Generic melatonin 2mg modified release tablets (off-label) should be prescribed.
 - Tablets should not be crushed as this will result in loss of the modified release property of the tablets.
- *All other formulations of melatonin are considered non-formulary and not suitable for prescribing including:*
 - *Melatonin 1mg/1ml oral solution by Colonis Pharma Ltd.*
 - *All strengths of unlicensed special solutions and suspensions of melatonin.*
 - *All strengths and brands of melatonin tablets (apart from Adaflex).*
 - *All strengths of melatonin capsules.*

For more information on melatonin formulations and the rationale for choices across Cambridgeshire and Peterborough see '[Melatonin prescribing for Paediatric Patients \(Formulation Choice\)](#)'.

On the advice of a Specialist Clinician

Treatment with melatonin should only be started on the advice of a specialist clinician, which may include paediatric consultant, child psychiatrist or non-medical prescriber with a specialist interest in paediatric sleep disorders, in-line with this prescribing guidance.

Prescribing and monitoring melatonin will usually be the responsibility of the primary care clinician.

Dosage

Consult the latest edition of the [British National Formulary for Children](#).

Initially 2 mg once daily, increased to 4mg once daily after 5 days if required. The dose should be taken before bedtime.

If treatment at 4mg daily remains ineffective at controlling sleep, advice of a specialist clinician should be sought as daily doses of 6mg and above are rarely required.

Patients and carers should be advised on initiation that treatment with melatonin and the need for continued use, will be reassessed every six months via a treatment holiday (see [Monitoring and Treatment Holidays in Primary Care](#)).

Renal impairment: The effect of any stage of renal impairment on melatonin pharmacokinetics has not been studied. Caution should be used when melatonin is administered to such patients.

Hepatic impairment: There is no experience of the use of melatonin in patients with liver impairment. Published data demonstrates markedly elevated endogenous melatonin levels during daytime hours, due to decreased clearance in patients with hepatic impairment. Therefore, melatonin is not recommended for use in patients with hepatic impairment.

Monitoring and Treatment Holidays in Primary Care

There is no pathology monitoring generally required for melatonin.

A melatonin treatment holiday should be attempted every 6 months as some children/adolescents will have settled into a regular sleep pattern and may not need to continue at the same dose or may even be able to maintain sleep with no melatonin.

This could be considered during school holidays or over an extended weekend. However, timing of a treatment holiday should be in discussion with the patient/guardian and consider individual circumstances where the impact of potential sleep disruption can be minimised.

If sleep patterns are maintained during the treatment holiday, stopping melatonin permanently should be considered. Alternatively, if treatment with melatonin is still required, dosing can be reduced by 2mg. If the difficulties recur, the original dose should be reinstated. A further trial reduction/treatment holiday should be attempted six months later, and every six months thereafter.

Some clinical experience from the National Child and Adolescent Learning Disability Psychiatry Network suggests that the efficacy of melatonin may be lost if prescribed for longer than two years continuously. It suggests that if melatonin is withdrawn prior to this, sensitivity may be re-established, and melatonin successfully re-introduced at a lower dose if still required. Reinforcement of good sleep hygiene should be discussed at each six-monthly review and should be continued by the child/adolescent, in conjunction with melatonin prescribing.

Individual patients may require additional monitoring based on co-morbidities or interacting medicines. It is likely these patients would remain within secondary care or community services, and any primary care monitoring will be agreed on a case-by-case basis.

[Prescribing of melatonin as patients transition to adult services](#)

The Cambridgeshire and Peterborough Joint Prescribing Group (CPJPG) is currently reviewing the prescribing of melatonin in adult patients. Melatonin is not currently recommended across Cambridgeshire and Peterborough for adult patients (any indication).

Young people who are transitioning towards adult services or reach 18 years should be reviewed in conjunction with advice from children's specialist services before transition where applicable. It isn't appropriate to refer patients to adult specialist services solely for melatonin review.

Whilst the melatonin prescribing review is being undertaken, treatment with melatonin should not be stopped for patients with learning disabilities, or additional needs, solely due to the patient's age or transfer to adult services due to the clinical impact this may have on the patient. Prescribing may continue in primary care for these patients.

For other patient cohorts, until the review is completed, if sleep concerns remain, treatment should follow standard guidance for adults with sleep problems:

- [Clinician information: Insomnia.](#)
- [Cambridgeshire and Peterborough NHS Foundation Trust Patient Information Leaflet: Coping with sleep difficulties.](#)
- [NHS UK website: Insomnia.](#)
- [Patient video \(TED talk\): What causes insomnia?](#)

Contraindications and Cautions

Melatonin may cause **drowsiness**. Therefore the product should be used with caution if the effects of drowsiness are likely to be associated with a risk to safety.

No clinical data exists concerning the use of melatonin in individuals with **autoimmune diseases**. Therefore, melatonin is not recommended for use in patients with autoimmune diseases.

In view of the lack of clinical data, use in **pregnancy** and by women intending to become pregnant is not recommended. **Breast-feeding** is not recommended in women under treatment with melatonin.

Adverse effects

Short-term use of melatonin appears to be safe for most people. Documented long term studies, greater than two years are lacking, however, adverse effects associated with melatonin are generally uncommon.

Possible side-effects include:

Uncommon ($\geq 1/1,000$ to $< 1/100$): Irritability, nervousness, restlessness, insomnia, abnormal dreams, nightmares, anxiety, migraine, headache, lethargy, psychomotor hyperactivity, dizziness, somnolence, hypertension, abdominal pain, abdominal pain upper, dyspepsia, mouth ulceration, dry mouth, nausea, hyperbilirubinaemia, dermatitis, night sweats, pruritus, rash, pruritus generalised, dry skin, pain in extremity, glycosuria, proteinuria, asthenia, chest pain, liver function test abnormal, weight increased.

Drug Interactions

Melatonin interacts specifically with the following drugs:

- Caution should be exercised in patients on **fluvoxamine**, which increases melatonin levels. The combination should be avoided.
- Caution should be exercised in patients on **5- or 8-methoxypsoralen** (5 and 8-MOP), which increases melatonin levels.
- Caution should be exercised in patients on **cimetidine** a CYP2D inhibitor, which increases plasma melatonin levels.
- Caution should be exercised in patients on **oestrogens** (e.g. contraceptive or hormone replacement therapy), which increase melatonin levels.
- CYP1A2 inhibitors such as **quinolones** may give rise to increased melatonin exposure.
- CYP1A2 inducers such as **carbamazepine and rifampicin** may give rise to reduced plasma concentrations of melatonin.

Melatonin also belongs to the class of anxiolytics/hypnotics, which may interact with:

- ACE inhibitors, adrenergic neurone blockers, alcohol, alpha-blockers, anaesthetics, angiotensin-II receptor antagonists, tricyclics or tricyclic-related antidepressants, opiates, antihistamines, antipsychotics, baclofen, beta-blockers, calcium-channel blockers, clonidine, diazoxide,

diuretics, hydralazine, lofexidine, methyldopa, minoxidil, mirtazapine, moxonidine, nitrates, opioid analgesics, ritonavir, tizanidine.

Cigarette smoking may decrease melatonin levels.

For further information on cautions, contraindications, adverse effects and interactions please consult the latest edition of the [British National Formulary for Children \(BNFC\)](#) or [Summary of Product Characteristics \(SPC\)](#) for full details.

Patient information

- [Healthy Sleep Tips for Children.](#)
- [Cambridgeshire and Peterborough NHS Foundation Trust Paediatric Psychology Team Toolkit - Sleep Difficulties.](#)
- [Cambridgeshire Community Services NHS Trust Patient Information Leaflet.](#)

Advice and Support

Community Paediatrics (Cambridgeshire Community Services NHS Trust) are available, Monday-Friday 09:00 to 17:00, to provide general advice and support on the prescribing of melatonin
Telephone: 0300 029 50 50.

North Cambridge, South Cambridge, Cambridge City and Ely Community Paediatrics
The Peacock Centre, Brookfields Hospital, 351 Mill Road, Cambridge, CB1 3DF.
Telephone number: 01223 218072.
Email: ccs-tr.communitypaediatricssouth@nhs.net.

Huntingdon and Fenland Community Paediatrics
The Oak Tree Centre, 1 Oak Drive, Huntingdon, PE29 7HN.
Telephone number: 01480 425300
Email: ccs-tr.clinicalsupport@nhs.net.

For patients who are receiving treatment under the **Community Child and Adolescent Mental Health Services** in Cambridgeshire and Peterborough, contact Single Point of Access Clinicians on 01480 428115, Monday to Friday 09:00 to 17:00 or via e-mail accesscamhs@nhs.net.

References

1. Summary of Product Characteristics (SPC). Accessed 14/09/2020 via [Medicines Complete](#).
2. British National Formulary for Children. Accessed 14/09/2020 via the [BNF-C](#).
3. National Children and Adolescent Learning Disability Psychiatry Network, 2008.

Document ratification details

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Quick Reference Guide to the Prescribing of Melatonin for Children and Adolescents where other sleep hygiene methods alone have been unsuccessful

