# National clinical recommendations for melatonin treatment of sleep disturbances in children and adolescents

Quick guide

## Melatonin for children and adolescents with idiopathic sleep disturbances

### Consider use of melatonin for children and adolescents with persistent idiopathic sleep disturbances and with impaired daytime functioning, where sleep hygiene measures have not had a sufficient effect

*Weak recommendation for*

The recommendation covers children and adolescents aged 5 to 20.

Children and adolescents with autism and ADHD are not covered by the recommendation, as the Danish Health Authority has separate recommendations for use of melatonin for these patient groups.

Before treatment with melatonin, sleep hygiene measures must have been tried for minimum four weeks, and the sleep pattern must be registered using a sleep diary for 14 days.

Sleep hygiene measures include a comprehensive action plan with advice on behaviour, routines and conditions for better sleep, and should comprise guidance within the following three points:

- Routines and circadian rhythm regulating measures (e.g. fixed bedtime and rising time)
- Physical surroundings of the sleeping environment (e.g. temperature, sound, light, disturbances)
- Emotional regulation and parental support measures (e.g. avoiding conflicts)

In addition, other non-pharmacological treatment, such as weighted products, should be considered before melatonin is tried.

In case of psychiatric and somatic comorbidity or social problems/burdens, this must have been examined and treatment of underlying illness must have been initiated.

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If a primary sleep disorder is suspected, referral to a centre for sleep medicine for further examination is recommended.

Initiation of treatment with melatonin (immediate- or extended-release form) may be considered at a dosage of 1-3 mg per day (approx. 0.05 mg per kg body weight). The dosage may be increased by 1 mg per week. The maximum dosage is 5 mg per day. Treatment with melatonin must be short term and must always be reassessed after 14 days and again after three months. Treatment must be discontinued in case of little or no effect. In case of good efficacy and need of continued treatment, the effect and treatment plan must be reassessed using a sleep diary at minimum every six months. Correspondingly, after pausing or tapering, the sleep pattern should also be assessed using a sleep diary. On discontinuation, melatonin must be tapered over time.

Commencement and treatment with melatonin of children and adolescents with idiopathic sleep disturbances can be handled by a specialist in general medicine. Treatment should be done in collaboration with a specialist in child and adolescent psychiatry or a paediatrician with special knowledge of sleep disorders in children and adolescents. Treatment of young people over the age of 18 should be done in collaboration with specialists in corresponding medical specialties.

Melatonin treatment for children and adolescents who are not diagnosed with Smith-Magenis syndrome, autism and ADHD is off label. In connection with melatonin treatment, the child/adolescent/parents must be informed that treatment with melatonin is outside the approved therapeutic indication, and therefore the indication cannot be found in the package leaflet.

## Rationale for the recommendation

In the formulation of the recommendation, it was considered important that there may be a small net benefit from treatment with melatonin, as it may improve total sleep time and reduce sleep latency, while melatonin is unlikely to affect the occurrence of serious adverse events. However, there is no or only little effect on the critical outcomes sleep quality and level of function, and the use of melatonin is likely to increase the incidence of adverse events. Melatonin may not affect pubertal development, but there is a general uncertainty concerning the long-term effects and harms that are insufficiently described in the literature.

The guideline panel assesses that families, who have not had sufficient effect of well-tested sleep hygiene advice and actions will predominantly want to try treatment with melatonin. Combined with the low confidence in the evidence, the Danish Health Authority provides a weak recommendation for treatment with melatonin in children and adolescents aged 5 to 20 years, with persistent idiopathic sleep disturbances and impaired daytime functioning, where sleep hygiene measures have not had a sufficient effect.

The guideline panel assesses that non-pharmacological treatment should be considered before treatment with melatonin is initiated.

# Melatonin for children and adolescents with sleep disturbances due to other illness

## Consider use of melatonin for children and adolescents with persistent sleep disturbances due to other illness and with impaired daytime functioning, where sleep hygiene measures have not had a sufficient effect

*Weak recommendation for*

The recommendation covers children and adolescents aged 2 to 20.

Children and adolescents with autism and ADHD are not covered by the recommendation, as the Danish Health Authority has separate recommendations for use of melatonin for these patient groups.

Before treatment with melatonin, sleep hygiene measures must have been tried for minimum four weeks, and the sleep pattern must be registered using a sleep diary for 14 days.

Sleep hygiene measures include a comprehensive action plan with advice on behaviour, routines and conditions for better sleep, and should comprise guidance within the following three points:

- Routines and circadian rhythm regulating measures (e.g. fixed bedtime and rising time)
- Physical surroundings of the sleeping environment (e.g. temperature, sound, light, disturbances)
- Emotional regulation and parental support measures (e.g. avoiding conflicts)

In addition, other non-pharmacological treatment, such as weighted products, should be considered before melatonin is tried.

In case of psychiatric and somatic comorbidity or social problems/burdens, this must have been examined and treatment of underlying illness must have been initiated.

If a primary sleep disorder is suspected, referral to a centre for sleep medicine for further examination is recommended.

Initiation of treatment with melatonin (intermediate- or in extended-release form) may be considered at a dosage of 1-3 mg per day (approx. 0.05 mg per kg body weight). The dosage may be increased by 1 mg per week. The maximum dosage is 5 mg per day. Treatment with melatonin must be short term and must always be reassessed after 14 days and again after three months.

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Treatment must be discontinued in case of little or no effect. In case of good efficacy and need of continued treatment, the effect and treatment plan must be reassessed using a sleep diary minimum every six months. Correspondingly, after pausing or tapering, the sleep pattern should also be assessed using a sleep diary. On discontinuation, melatonin must be tapered over time.

Commencement and treatment with melatonin of children and adolescents with sleep disturbances due to other illness must be handled by a specialist in child and adolescent psychiatry or by a paediatrician with special knowledge in neurological disorders, developmental disorders and/or congenital syndromes. Maintenance treatment can be handled by a specialist in general medicine, provided that it is done by specific, mutual agreement and in collaboration with a specialist in child and adolescent psychiatry and/or a paediatrician with special knowledge of neuropsychiatric disorders, developmental disorders and/or congenital syndrome disorders. Specialists in corresponding relevant adult departments should be consulted in connection with treatment of adolescents aged over 18.

Melatonin treatment of children and adolescents with severe chronic paediatric or psychiatric conditions should be handled by the clinics responsible for the patient's course of treatment.

Melatonin treatment for children and adolescents who are not diagnosed with Smith-Magenis syndrome, autism and ADHD is off label. In connection with melatonin treatment, the child/adolescent/parents must be informed that treatment with melatonin is outside the approved therapeutic indication, and therefore the indication cannot be found in the package leaflet. Patients with Smith-Magenis syndrome should be treated with the melatonin product approved for this disorder.

## Rationale for the recommendation

In the formulation of the recommendation, it was considered important that there may be a small net benefit from treatment with melatonin, as it may improve total sleep time and reduce sleep latency, while melatonin is unlikely to affect the occurrence of serious adverse events. However, there is no or only little effect on the critical outcomes sleep quality and level of function, and the use of melatonin is likely to increase the incidence of adverse events. The effect on quality of life is uncertain. Melatonin may not affect pubertal development, but there is a general uncertainty concerning long-term effects and harms, that are insufficiently described in the literature.
The guideline panel assesses that families who have not had sufficient effect of well-tested sleep hygiene advice and actions will predominantly want to try treatment with melatonin. Combined with the low confidence in the evidence, the Danish Health Authority provides a weak recommendation for treatment with melatonin in children and adolescents aged 2 to 20 years with persistent sleep disturbances due to other illness and with impaired daytime functioning where sleep hygiene measures have not had a sufficient effect.

The guideline panel assesses that non-pharmacological treatment should be considered before treatment with melatonin is initiated.

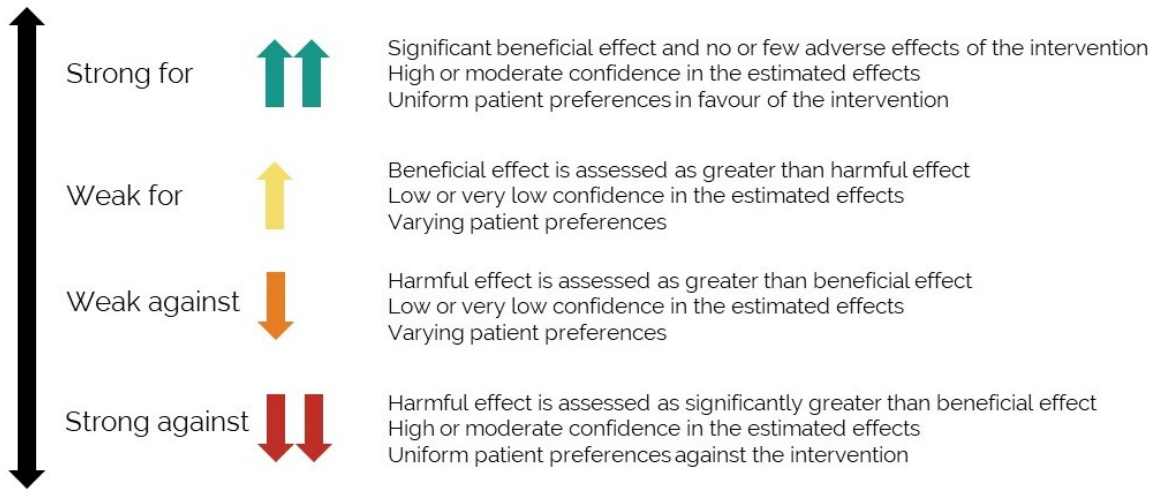
## Delimitation

The population comprises children and adolescents both with and without other illness where sleep hygiene measures have not had a sufficient effect. In case of psychiatric and somatic comorbidity, as well as social problems/burdens, examination and any treatment must be initiated. Persistent sleep disturbances are defined as repeated difficulties with falling asleep, uninterrupted sleep, duration or quality of sleep despite ensuring age-relevant settings for achieving sleep. The sleeping problems must be related to impaired daytime functioning and be present minimum three times a week and for minimum three months.

Children and adolescents with autism and ADHD are not covered by these national clinical recommendations, as the Danish Health Authority has separate recommendations for use of melatonin for these patient groups.

A full-length version of the national clinical recommendations is available at the Danish Health Authority's website (www.sst.dk), including a detailed review of the underlying evidence on which the recommendations are based.

## What does a weak or strong recommendation mean?



## What is a national clinical recommendation?

A national clinical recommendation is delimited to a specific problem in the course of the patient's treatment. Therefore, a national clinical recommendation cannot stand alone, but is complemented and supplemented by other guidelines and treatment guides. This may, for example, be interdisciplinary and intersectoral guidelines for other parts of the course of the patient's treatment or other patient populations, guidelines prepared by societies and professional organisations, as well as regional and municipal guidelines and instructions.

National clinical recommendations are classified as professional advice, which means that the Danish Health Authority recommends that the relevant professionals adhere to the recommendations. The national clinical recommendations are not legally binding, and a professional assessment in the specific clinical situation will always be of decisive importance to the decision on appropriate and correct healthcare services.

## Collaboration

The recommendations have been drawn up in collaboration with a guideline panel with representatives from:

- Child and Adolescent Psychiatric Association in Denmark
- Danish Society of Clinical Pharmacology
- Danish Society for Physiotherapy
- Danish Paediatric Society
- Danish Association of Occupational Therapists
- Danish Psychological Association
- Danish Psychiatric Society
- Danish College of General Practitioners
- Danish Society for Sleep Medicine
- Danish Nursing Society