NICE advice

# Melatonin for treating sleep disorders in adults who are blind

Evidence summary
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## Product overview

The content of this evidence summary was up to date in August 2021. See summaries of product characteristics (SPCs), British National Formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites for up-to-date information.

Melatonin is a hormone that occurs naturally in the body. It is involved in regulating sleep and circadian rhythms. Melatonin can be given as a medicine to treat sleep problems.

Several melatonin products are available that are taken by mouth. Marketing authorisations differ depending on the product (see the summaries of product characteristics for more information).

The use of melatonin for treating sleep disorders in adults who are blind is off-label. See NICE's information on prescribing medicines.

# Likely place in therapy

Limited evidence from 3 very small studies suggests that melatonin might improve total night sleep duration, and reduce the amount of time spent awake after falling asleep in adults with sleep disorders who are totally blind. However, it is not possible to say what dose should be used and how long treatment should be continued.

# Factors for decision making

## Effectiveness and safety

Evidence was from 1 randomised controlled trial (Roth et al. 2015; n=13) and 2 crossover studies (Hack et al. 2003; n=10 and Sack et al. 2000; n=7) in adults who were totally blind.

Roth et al. (2015) found that mean total night sleep duration (the primary outcome) increased by 43 minutes from baseline with melatonin 2 mg prolonged release compared with 16 minutes with placebo (mean difference 27 minutes; 95% confidence interval [CI] −14.4 to 69.0 minutes; p=0.18). Although this was not statistically significant, the authors report that it was clinically relevant. Hack et al. (2003) found that mean total night sleep duration was statistically significantly greater with melatonin 0.5 mg (6.64 hours) compared with placebo (5.99 hours; p<0.01). Sack et al. (2000) found no statistically significant difference in total time asleep with melatonin 10 mg compared with placebo.

Hack et al. (2003) found no statistically significant difference in the number of night awakenings with melatonin 0.5 mg compared with placebo. However, the duration of night awakenings was statistically significantly less. Sack et al. (2000) found that time spent awake after the onset of sleep was statistically significantly less with melatonin 10 mg compared with placebo.

None of the studies found a statistically significant difference between melatonin and placebo in the time it takes to fall asleep (sleep latency).

Roth et al. (2015) reported on quality of life and found no difference between melatonin and placebo in the Clinical Global Impression of Change score for severity of illness and global improvement and the WHO-Five Well-being Index (no statistical analyses were reported).

In the study that reported safety outcomes (Roth et al. 2015), 1 out of 5 (20%) people in the melatonin 2 mg prolonged-release group and 2 out of 8 (25%) people in the placebo group experienced 1 or more treatment-emergent adverse events. These were all considered to be mild in severity and none led to withdrawal from the study.

The BNF states that common and very common adverse effects reported with melatonin include arthralgia, headaches, increased risk of infection, and pain (see the BNF for more information).

# Limitations of the evidence

The evidence for using melatonin to treat sleep disorders in adults who are blind is limited. Only one of the studies (Roth et al. 2015) was randomised. The other studies (Hack et al. 2003 and Sack et al. 2000) were crossover studies and the authors did not report if they were randomised, and as such are subject to potential bias.

The studies were small, including between 7 and 13 people, and so were underpowered to detect a statistically significant difference between melatonin and placebo.

The dose and formulation of melatonin used in the studies varied. Roth et al. used a 2 mg prolonged-release formulation of melatonin whereas Hack et al. and Sack et al. used immediate-release formulations at dosages of 0.5 mg and 10 mg daily, respectively. The durations of treatment varied from around 3 to 12 weeks. This makes it difficult to determine what dose should be used for treating sleep disorders in adults who are blind.

Safety data for using melatonin to treat sleep disorders in adults who are blind is limited. Roth et al. (2015) reported safety data but only provided overall numbers of people who experienced treatment-emergent adverse events, rather than the types of events experienced. No safety information was reported in the other studies.

Overall, the limitations of the available evidence make it difficult to determine the clinical effectiveness and safety of melatonin for treating sleep disorders in adults who are blind.

# Person-centred factors

Safety data was poorly reported in the studies and long-term safety data is lacking.

Melatonin is taken once a day, usually between 30 minutes and 2 hours before a person's usual bedtime, depending on which product is prescribed.

Melatonin is taken by mouth as tablets, capsules, prolonged-release tablets, and oral solution, depending on the person's needs and preferences.

# Related NICE guidance

NICE has not published any guidance on treating sleep disorders in adults who are blind.

Some NICE guidelines include recommendations for considering melatonin (often off-label) for treating sleep disorders in people with other underlying conditions in certain circumstances. These are NICE guidelines on:

- autism spectrum disorder in under 19s
- chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy)
- cerebral palsy in under 25s
- challenging behaviour and learning disabilities
- Parkinson's disease in adults.

There was insufficient evidence to make recommendations on using melatonin for sleep disorders in the NICE guidelines on:

- attention deficit hyperactivity disorder
- autism spectrum disorder in adults
- dementia (except Alzheimer's disease, when melatonin should not be offered to manage insomnia in adults with Alzheimer's disease).

# Resource implications

The cost of prescribing melatonin for treating sleep disorders in adults who are blind will vary depending on the dose and product prescribed. The cost of a year's treatment with melatonin is estimated to be between £187 and £1,278. See the resource impact assessment accompanying this evidence review for more information.

See the full evidence review for more information.

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