NHS
Pan Mersey
Area Prescribing Committee

Melatonin prolonged release tablets (Circadin® and Slenyto®) for the treatment of persistent chronic sleep disorders in adults and children

The Pan Mersey Area Prescribing Committee recommends the prescribing of melatonin prolonged release tablets (Circadin® and Slenyto®) for the treatment of persistent chronic sleep disorders in the circumstances below where sleep hygiene measures have been insufficient.

AMBER following specialist initiation

The patient and or parent must be offered a structured sleep behavioural intervention programme if appropriate and available prior to consideration of melatonin. If a structured sleep behavioural intervention programme is not available, sleep hygiene must be optimised first.

Melatonin should only be considered if the patient experiences

- <6 hours of continuous sleep persistently for at least 3 months AND/OR
- >0.5 hour sleep latency on at least 3 out of 5 work/school nights per week for 2 weeks.

There must be evidence that the patient has been diagnosed with a persistent chronic sleep disorder (e.g. insomnia or delayed sleep phase syndrome) associated with at least one of the following:

- Attention Deficit Hyperactivity Disorder (ADHD)
- Autistic Spectrum Disorders (ASD)
- Cerebral Palsy
- Chronic fatigue syndrome (CFS)/ myalgic encephalomyelitis (ME) (or encephalopathy)
- Complex neurodevelopmental disorders (i.e., Angelman's syndrome, Rett's syndrome, Smith Magenis syndrome (SMS), tuberous sclerosis complex, fragile X syndrome, foetal alcohol spectrum disorder (FASD))
- Global developmental delay / learning disability
- Parkinson's disease with REM sleep disorder.

Slenyto® is licenced for the treatment of insomnia in children and adolescents ages 2-18 with ASD and/or SMS. Slenyto® should only be used in these indications, or for patients unable to swallow Circadin® with persistent chronic sleep disorder associated with conditions specified in this statement (off label).

This statement does not include other forms of licensed melatonin such as melatonin 2mg capsules (Colonis®), melatonin 3mg tablets (Colonis®) or melatonin 1mg/ml liquid (Colonis®) which are licensed in jet lag for short term use. The melatonin 1mg/ml liquid has been assessed and the quantities of propylene glycol may be excessive for some children. Other unlicensed melatonin preparations or melatonin food supplements remain RED due to the variation in quality, cost to primary care and lack of evidence regarding suitability of excipients in children. **For certain patients, unlicensed melatonin may be required i.e., patients with feeding tubes. In this circumstance prescribing, monitoring and review responsibilities will be held by specialist.**

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness

Melatonin is a pineal hormone that may affect sleep pattern. Clinical experience suggests that when appropriate behavioural sleep interventions fail, melatonin may be of value for treating sleep disorders secondary to conditions listed above [1].

There are multiple randomised controlled trials, meta-analyses and systematic reviews which assess the safety and efficacy of melatonin. The evidence for the use of melatonin varies in quality depending on the condition being studied. There is good quality evidence supporting the use of melatonin in sleep disorders secondary to ASD and learning disabilities [2-9]. The evidence for treating sleep disorders secondary to other neurodevelopmental disorders supports the use of melatonin [10-17], the studies however have low patient numbers due to the heterogeneity of the conditions studied and their rare nature. Evidence for the use of melatonin in sleep disorders caused by visual impairment, acquired brain injury and epilepsy is poor and/or lacking.

The National Institute of Health and Care Excellence (NICE) CG53[18], NG62[19], NG11[20] supports melatonin use for sleep problems secondary to chronic fatigue syndrome/myalgic encephalomyelitis, cerebral palsy and learning disability respectively in children and young people.

NICE CG170 and The Scottish Intercollegiate Guidelines Network (SIGN) SIGN 145[21-22] recommend melatonin to aid sleep for autistic children following consultation with a specialist paediatrician or psychiatrist with expertise in the management of autism or paediatric sleep medicine. It should be used in conjunction with non-pharmacological interventions and be regularly reviewed to evaluate the ongoing need for a pharmacological intervention and to ensure that the benefits continue to outweigh the side effects and risks.

The All Wales Medicines Strategy Group (AWMSG) have recommended the use of Slenyto® in line with its marketing authorisation only where the approved Wales Patient Access Scheme is utilised [23].

Safety

Melatonin therapy is well tolerated from primary literature and from clinical experience. The most commonly reported side effects tend to be mild and transient.

A study by Malow et al showed that long term melatonin therapy continues to be effective and has shown that there are no significant effects on growth or pubertal development [24]. This has also been corroborated by Van Geijlswijk et al [25] in an earlier study. These studies followed up children after 2 and 3.1 years of melatonin therapy respectively.

Cost

Slenyto®: £0.69/mg. Available as 1mg (60 pack) or 5mg tablets (30 pack)

Circadin®: £0.26/mg. Available as 2mg tablets (30 pack)

Estimated current total Pan Mersey spend per annum: £2,203,318.

Projected spend[1]: Between £3,772,729[2] and £5,835,505[3] plus cost of sleep behavioural intervention service.

1. Projected spend based on drug tariff price. Cost range given as unable to accurately predict number of children who will be on Slenyto® due to inability to swallow Circadin®. Hospital contract prices and rebate schemes available.
2. Based on adults on unlicensed formulations changing to Circadin® tablets. Slenyto® used in children who fit its licensed indications. All other children switched or remain on Circadin ®
3. Based on adults on unlicensed formulations changing to Circadin®MR tablets and all children switched to Slenyto®

For comparison
Melatonin 3mg tablets (Colonis Pharma Ltd): £0.72/mg
Melatonin 1mg/ml oral solution (Colonis Pharma Ltd): £0.87/mg
Melatonin 2mg capsule (Colonis Pharma Ltd): £0.95/mg

The Scottish Medicines Consortium (SMC) has not recommended Slenyto® for the treatment of insomnia in children and adolescents ages 2-18 with ASD/SMS [26]. The SMC also commented on the fact that they did not receive sufficiently robust clinical and economic analysis to gain acceptance by the SMC.

Patient factors

Melatonin prolonged release therapy should always be recommended over instant release (or crushed prolonged release tablets) as instant release therapy can cause sleep phase shifting [27]. Longer term safety data only exists for prolonged release melatonin.

Prescribing should reflect the **STOMP/STAMP** pledge that children and young people with a learning disability, autism or both are able to access appropriate medication but are not prescribed inappropriate psychotropic medication. Regular and timely reviews should be undertaken.

See prescribing support documentation for more extensive information to guide formulation choice.

Prescribing information

See prescribing support documentation

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