



THE PAEDIATRIC SOCIETY OF NEW ZEALAND

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20 May, 2014

Dr Geraldine MacGibbon
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PHARMAC
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Dear Geraldine

Proposal to fund Melatonin 2mg modified-release tablets (Circadin)

We would like to comment on the proposal for melatonin 2mg modified-release tablets to be funded from 1 July 2014 for secondary insomnia in children and adolescents with neurodevelopmental disorders.

We are grateful that PHARMAC has gained an agreement with Aspen to fund melatonin for this group of children and wish to make the following comments:

Appropriate preparations for children

Children are entitled to safe, efficacious and age-appropriate medicines¹. Many children with neurodevelopment disabilities, also have problems swallowing tablets. In fact, children without neurodevelopment difficulties also have problems swallowing tablets. Although swallowing whole tablets can be taught to the majority of young children with techniques, this is often not applicable to children with various neurodevelopmental conditions.

The 2mg modified-release tablet (Circadin) is intended to be swallowed whole. There are no oral liquid preparations of melatonin available in New Zealand. At present, immediate release tablets are crushed into soft food or mixed into solution prior to administration. This is important for children being administered medicines via PEG tubes. We are concerned if SR tablets are crushed there may be blockage of PEG tubes.

Retention of immediate release preparations

We have the ability to adjust doses using the tablets currently available on the HML (1mg, 2mg and 3mg tablets and 2mg and 3mg capsules). There is now an understanding that doses as low as 0.5mg can be effective for some children^{5,6}. We would ask PHARMAC to consider having even one of these available beyond October 2014 so that children, who require their doses to be administered in liquid for administration or dosing reasons, can have a tablet which is readily crushable instead of having to crush a SR product which is not intended for this purpose.

Registration of the immediate-release forms of melatonin on the HML is important for DHB respite facilities such as The Wilson Centre.

The immediate release form is more often studied in placebo controlled studies²⁻⁴ and more physiologically appropriate for reducing sleep-onset latency, which is the more common symptom with lower potential for daytime somnolence.

Extended Approval

Approval should be extended for primary sleep disorders and delayed sleep-phase syndrome in children with no learning difficulties and those with visual impairment. Placebo controlled trials⁷⁻¹⁰ also demonstrate beneficial effects in these children and alternatives have less evidence for efficacy and more potential side effects¹¹.

We would like clarification of what happens when adolescents turn 18 years of age and require melatonin for insomnia due to their neurodevelopmental disorders. Other options are often not appropriate. Melatonin will be funded on this proposal only to the age of 18 years.

In summary, we would like PHARMAC to consider the following:

1. Retention of an immediate release melatonin on the HML
2. Funding of an immediate release product under special authority
3. Extended approval of melatonin to include disorders mentioned above
4. Extended approval of melatonin for adults between 18 and 55 years

We look forward to discussing this further with you if more clarification is needed.

Kind regards,



Dr David Newman
President
Paediatric Society of NZ



Louise McDermott
Chairperson
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SIG
Paediatric Society of NZ



Dr Janine Thomson
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This letter includes comments from the following members of the Paediatric Society of New Zealand

Dr Bobby Tsang, Specialist Paediatrician, Northshore Hospital, WDHB

Jenny Crawford, Paediatric Pharmacist, WDHB

Dr Barry Taylor, Dean, Dunedin School of Medicine, University of Otago

Dr Kate Robertshaw, Child Development Service, HBDHB

Dr Alison Leversha, Community Paediatrician, Greenlane Clinical Centre, ADHB

Dr Sneha Sadani, Gateway Assessment Consultant Paediatrician, WaikatoDHB

References

1. Priority Medicines for Europe and the World 2013 Update http://www.who.int/medicines/areas/priority_medicines/Ch7_1Children.pdf
2. Shamseer L and Vohra S. Complementary, Holistic and Integrative Medicine. Melatonin *Pediatr Rev* 2009 Jun 30(6): 223-8
3. Braam W et al Exogenous melatonin for sleep problems in individuals with intellectual disability: a meta-analysis. *Developmental Medicine & Child Neurology* 2009 51: 340-349
4. Appleton RE et al. The use of MELatonin in children with Neurodevelopmental Disorders and impaired Sleep: a randomised, double-blind, placebo-controlled, parallel study (MENDS). *Health Technol Assess* 2012;16(40):i-239
5. Appleton RE et al. Melatonin: helping to MEND impaired sleep. *Arch Dis Child*. 2013 Mar;98(3):216-7
6. Van Geijlswijk IM et al. Dose finding of melatonin for chronic childhood sleep onset insomnia: an RCT. *Psychopharmacology (Berl)*. 2010 Oct;212(3) : 379-91
7. Szeinberg A et al Melatonin treatment in adolescents with delayed sleep phase syndrome. *Clin Pediatr (Phila)* 2006 Nov: 45(9): 809-18
8. Smits MG et al Melatonin for chronic sleep onset insomnia in children: a randomized placebo-controlled trial *J Child Neurol* 2001 Feb;16(2):86-92
9. Jan JE et al Melatonin treatment of sleep-wake cycle disorders in children and adolescents. *Developmental Medicine & Child Neurology* (1999) 417: 491-500
10. Pelayo Rafael and Kin Yeun. Pediatric Sleep pharmacology. *Child Adolesc Psychiatric Clin Am* 21 2012 861-883
11. Merenstein D et al The trail of infant response to Diphenhydramine. The TIRED Study – A Randomised, Controlled, Patient-Oriented Trial. *Arch Pediatr Adolesc Med* 2006 Jul: 160(7): 707-712