

Melatonin: Cost-effective formulary choices

Context

Melatonin is mainly used to treat insomnia and sleep disorders in people aged 55 and over and children and adults with neurodevelopmental disorders.

There are many different strengths and formulations available with many being unlicensed or licensed for specific populations. Melatonin comes as both immediate release (IR), modified release (MR) tablets and capsules. Capsules are costlier than tablets.

Various liquid solutions and suspensions are available with varying excipients including sugar, alcohol and propylene glycol (PEG) excipient content. Significant amounts of the PEG (50mg/kg/ day or more in children 1month – 4 years) is considered above the EU safety limits and is not advised.

https://www.ema.europa.eu/en/documents/scientific-guideline/questions-answers-propylene-glycol-used-excipient-medicinal-products-human-use_en.pdf

In recent years there has been a significant increase in both different formulations, strengths, specials liquids and corresponding costs. In 2021/22 prescribing melatonin products in children accounted for £757.5k with a third of this being unlicensed liquids costing £286.5k. adult prescribing (>55yrs) cost the NEL ICB £200k.

The aim of this is to rationalise array of unlicensed products to a few cost-effective formulary choices. These choices will cover use in both adults and children.

Formulary choices:

Formulation	Product name	Formulary position	Licensing	Notes
Immediate release (IR) preparation required	Adaflex® IR tablets 1mg, 2mg, 3mg, 4mg and 5mg tablet	First line formulary choice of melatonin	<ul style="list-style-type: none"> Insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient Use < 6yrs (off-label) Use in other age groups is off-label Insomnia in children and adolescents aged 6-17 years with ADHD, where 	Tablets can be crushed and mixed with water directly before the oral administration (licensed).
	Cyesto® IR tablets 3mg	Second line choice (if stock issues. Chosen as has similar licensed indication to adaflex®)		Off-label use for administration via PEG enteral feeding tubes. Use restricted to give alternate choice if stock issues arise with preferred choice. NB: some generic IR preparations are unlicensed in some indications.

			<p>sleep hygiene measures have been insufficient</p> <ul style="list-style-type: none"> • Use < 6yrs (off-label) • Use in other age groups is off-label 	
Modified release (MR) preparation required	Generic melatonin MR 2mg or Circadin® (where previously established).	Formulary choice where a MR preparation is required	Licensed >55yrs short term primary insomnia	<p>Crushing the MR tablet render the modified release properties making it immediate release (IR) and off-label use.</p> <p>Unlicensed use for administration via PEG enteral feeding tubes.</p>
Modified release preparation required	Slenyto® MR 1mg and 5mg	Formulary choice where patients on high (10mg) doses only	Licensed for insomnia aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, (first line preparation for these patients) where sleep hygiene measures have been insufficient	Formulated as a microtab to facilitate adherence
Liquid formulation required	Crushed and dispersed Adaflex immediate release tablets	First line formulary choice of melatonin	Licensed in use 6-17yrs Off-label in other populations	
Liquid formulation (alternative) *NB: only to be considered where clinically excluded from using other products (e.g. PEG)	<p>Kidmel® melatonin 1mg/1ml oral solution</p> <p>Ceyesto® 1mg/ml oral liquid (Branded generic - from Phoenix & Alliance)</p>	2 nd line formulary position	Unlicensed Special	<p>Prescribe by brand so as to get the SF and alcohol product</p> <p>NB: Some products e.g. Colonisl® liquid (licensed 6-17yrs) has a PEG content deemed unsafe in children <5yrs as per EMEA</p> <p>Other liquids are very High cost</p>

QIPP recommendations:

- Use of tablets only. Switch patients on capsules
- New patients to be initiated on first line choices
- Where the MR preparation is being crushed or a liquid preparation is required consider using Adaflex®. This includes children who were initially initiated on liquid but can consider tablets as get older.
- Review children who were initially initiated on liquid but can consider tablets as they get older.
- When patients are being considered for switching, the opportunity should be used to review ongoing need for melatonin. particularly in young people approaching their 18th birthday
- Consider de-prescribing in adults where use for insomnia (short term) >55yrs exceeds 3months
- No prescribing for indications of jet-lag

Other immediate release formulations of melatonin are considered non-formulary and not recommended for prescribing due to licensing or cost:

- o Melatonin 1mg/1ml oral solution by Colonis Pharma Ltd
- o All other strengths except 1mg/ml of unlicensed special solutions and suspensions of melatonin
- o All other strengths and brands of melatonin tablets (apart from listed above)
- o All strengths of melatonin capsules.

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