

## **VI.2 Elements for a Public Summary**

### **VI.2.1 Overview of disease epidemiology**

#### **Children**

In children poor routines at bedtime and as a result, insufficient sleep may affect up to 20-30% of healthy school children. Sleep disturbances are also common in children with “Attention Deficit Hyperactivity Disorder (ADHD)”, one of the most common behavioural disorders in school age which is a development-related condition with a prevalence of 3-10% worldwide. ADHD is a condition where 25-50 % of the children have sleeping problems, such as difficulty with sleep onset, difficulty maintaining sleep, problems with sleep patterns, early awakening and poor sleep routines.

#### **Jet-lag**

Currently the prevalence of jet-lag is uncertain; however it is naturally dependent on the amount of travellers flying through several time zones therefore affecting millions of travellers worldwide.

### **VI.2.2 Summary of treatment benefits**

The intended purpose of the product, Melatonin AGB 1-5 mg tablets, is to prevent insomnia in adults and children.

Melatonin is an endogenously occurring hormone, sometimes designated the natural sleep hormone of the body, produced by the pineal gland. Endogenous melatonin production varies with age and declines during adulthood such that by age 70 years, nocturnal melatonin concentration may be less than a quarter of that seen in early adulthood. This is considered to contribute to impaired sleep in older individuals. Therefore it is thought that treatment with melatonin can substitute the age-related reduction in melatonin levels thereby restoring normal sleep patterns.

Available data suggest that melatonin is also a well-tolerated and efficacious treatment option for children with sleep problems, especially for children with ADHD.

Various strategies have been used to alleviate jet-lag such as bright light therapy, outdoor activity, special diets, and the use of addictive-hypnotics. Timed administration of melatonin could be a rather physiological way of solving such kind of sleep problems. Melatonin is remarkably effective in preventing or reducing jet-lag.

The advantages of melatonin and melatonergic drugs in relation to other sleep-inducing agents, mostly addictive, are: 1) the absence of hangover the morning after; 2) the absence of withdrawal symptoms; and 3) the absence of addiction.

Melatonin causes few and no serious adverse reactions. These adverse reactions are also common for placebo-treated patients in the clinical studies and no reported significant difference between patients who received active treatment and placebo is seen in these studies.

### **VI.2.3 Unknowns relating to treatment benefits**

None currently.

**VI.2.4 Summary of safety concerns****Important identified risks**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
None		

**Important potential risks**

<b>Risk</b>	<b>What is known (Including reason why it is considered a potential risk)</b>
Long-term safety in children and adolescents	Melatonin is a hormone that may have other effects than sleep regulation. It has been discussed if that could influence puberty development in long term use. Sleep disturbance in children with ADHD is considered more or less chronic since it is often related to the background disease. Thus, long-term treatment with melatonin in children and adolescents with ADHD could potentially effect sexual hormones and pubertal development in this population.
Effects on sexual maturation and development in children and adolescents	Melatonin is a hormone that may have other effects than sleep regulation. It has been discussed if that could influence puberty development in long term use. Sleep disturbance in children with ADHD is considered more or less chronic since it is often related to the background disease. Thus, long-term treatment with melatonin in children and adolescents with ADHD could potentially effect sexual hormones and pubertal development in this population.

**Missing information**

<b>Risk</b>	<b>What is known</b>
None	

**VI.2.5 Summary of risk minimisation measures by safety concern**

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the Package Leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package Leaflet for Melatonin AGB can be found in Annex 2.

This medicine has no additional risk minimisation measures.

**VI.2.6 Planned post authorisation development plan****List of studies in post authorisation development plan**

<b>Study/activity (including study number)</b>	<b>Objectives</b>	<b>Safety concerns /efficacy issue addressed</b>	<b>Status</b>	<b>Planned date for submission of (interim and) final results</b>
Post-authorisation safety study (PASS) on long-term safety in prepubertal and pubertal children (Non-interventional, 3)	To investigate long-term safety in prepubertal and pubertal children, considering the theoretical concern of effects of long-term melatonin treatment on hormones and sexual maturation.	Sexual maturation in children.	Planned	TBD

**Studies which are a condition of the marketing authorisation**

The study above is not a condition of the marketing authorisation.

**VI.2.7 Summary of changes to the Risk Management Plan over time**

Major changes to the Risk Management Plan over time

<b>Version</b>	<b>Date</b>	<b>Safety Concerns</b>	<b>Comment</b>
	At time of authorisation dd/mm/yyyy	Identified Risks Potential Risks Missing information	
1.0	11/10/2019	NA	This is the first version of the Risk Management Plan.