

Melatonin Vitabalans 3 mg and 5 mg tablet

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Public summary of the risk management plan

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Jet lag occurs to any individual (symptoms being susceptible to individual differences) travelling through several time zones [Herxheimer 2002]. Flight travel caused relatively sudden change in the surrounding light/dark cycle differs that from natural sleep-wake rhythm, and this contradiction (circadian misalignment) creates symptoms of jet lag. Typical symptoms of jet lag are fatigue, difficulty initiating and maintaining sleep, and general malaise. Currently the prevalence of jet lag is uncertain, however it is naturally dependent on the amount of travelers flying through several time zones therefore affecting millions of travelers worldwide [BMJ Best practices]. There appears to be no clear evidence or adequate studies of the role of age, gender or familial predisposition as potential risk factor for the development of jet lag [Sack et al. 2007].

VI.2.2 Summary of treatment benefits

Studies have found that jet lag symptoms have been reduced with the use of melatonin [Herxheimer 2002, Sack et al. 2007]. Melatonin has been shown to reduce sleep onset latency (the length of time it takes lying down for the night until sleep onset). According to the Finnish Current recommendation for the treatment (Käypä hoito suositus, 2015) melatonin is effective for the treatment of insomnia caused by jet lag [Käypä hoito 2015]. Melatonin has not been shown to cause dependence.

VI.2.3 Unknowns relating to treatment benefits

Safety and efficacy of Melatonin Vitabalans in children has not been established in children.

Caution is recommended when administered in patients with renal impairment. There is no evidence that renal insufficiency does not affect melatonin elimination. Melatonin Vitabalans is not recommended for use in patients with hepatic impairment.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Nightmares	Melatonin may cause nightmares.	Product should be used with caution if nightmares appear.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Retinal effects	Retinal toxicity has been reported in non-pigmented rats and thus visual disturbances are regarded as identified risks. However, the risk has not been detected in humans.
Infections	The SmPC of a prolonged release melatonin product Circadin contains adverse effect of Herpes zoster. No information about this was found in the literature but Herpes zoster is considered a potential risk based on the SmPC of Circadin.
Sperm motility decreased/spermatozoa morphology abnormal	Melatonin may have effects on male reproduction. Sperm quality may be decreased. However, there is no consistent evidence of that in the literature.
Suicide attempt/suicidal ideation/mood disturbance/depression/anxiety/depressed mood	Melatonin is involved in mood regulation. Even positive effects on mood have been observed but there is no clear evidence of neither positive nor negative effects.
Psychotic disorders, hallucinations	Single case report of melatonin causing psychotic episode has been described in the literature. Not any other information about melatonin causing psychosis is available. However, it is known that melatonin plays a role in various psychiatric states.
Panic attacks	Melatonin is involved in regulation of mood. There is no clear evidence in the literature whether melatonin would induce or relieve panic attacks.
Confusion/disorientation	A single case report of melatonin causing confusion has been described. On the contrary, melatonin deficiency has been suggested to be involved in delirium. No consistent evidence of melatonin causing confusion/disorientation is available.
Loss of consciousness	There is a possibility that melatonin may cause loss of consciousness, syncope perhaps due to its' sedative and alertness decreasing properties.
Dyspnoea	Melatonin may contribute to nocturnal worsening of asthma and may enhance contraction of trachea in response to contracting agents. However, no consistent evidence of these is available.
Hyperprolactinaemia/galactorrhoea	In literature melatonin has been described to increase prolactin levels. No consistent evidence of melatonin causing hyperprolactinaemia/galactorrhoea is available.
Interaction with levothyroxine	According to the information of the Finnish regulatory authority (Fimea) a risk management plan of a product with the same active ingredient has been approved on the EU with safety specification which includes this interaction as potential risk. No information

Risk	What is known (Including reason why it is considered a potential risk)
	available in the literature.
Interaction with warfarin	Melatonin has increased the effect of warfarin in single case reports. The mechanism of possible interaction is unknown.

Missing information

Off-label use	Information about off-label use is missing.
Use during pregnancy and breastfeeding and effects on fertility	There is no clinical information about using melatonin during pregnancy and breastfeeding. Melatonin is secreted to breast milk. In woman melatonin is suggested to inhibit ovarian function. Thus Melatonin Vitabalans is not recommended for use in patients that are pregnant, breastfeeding or trying to become pregnant.

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. This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

There are no planned studies in post authorisation development plan or as conditions of the marketing authorisation.

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

Not applicable. This is the first version of the risk management plan for Melatonin Vitabalans.