PUBLIC SUMMARY OF RISK MANAGEMENT PLAN (RMP)

MELATONIN ORION 3 MG, FILM-COATED TABLETS

ORION CORPORATION

DATE: 10-05-2016, VERSION 1.1

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

A flight over several time zones results in a desynchronisation of human circadian rhythms and periodic time cues in the environment. As a consequence of the disturbed biological cycles and sleep deprivation, most travellers experience a loss of well-being, sleepiness, sleep disorders and reduced performance for a few days. These symptoms are commonly known as jet-lag. The severity of jet-lag symptoms depends on the number of time zones crossed, whether the direction is east or west and on individual characteristics such as age, rhythm stability and motivation. The alleviation of the condition is of great importance for business people, military personnel, athletes and others who are required to perform complex tasks after arrival. Various strategies have been used to alleviate jet-lag such as bright light therapy, outdoor activity, special diets, and the use of hypnotics. Timed administration of melatonin could be a rather physiological way of solving such kind of sleep problems.

VI.2.2 Summary of treatment benefits

Melatonin Orion is indicated for short-term treatment of circadian rhythm sleep disorders caused by jet-lag in adults. Melatonin has a well-established medicinal use with recognised efficacy and an acceptable level of safety. Published clinical studies support the safety and efficacy aspects of melatonin. Studies have demonstrated that melatonin in daily doses of 3-6 milligrams may treat sleep disturbances after jet-lag in the majority of cases if taken before going to bed.

VI.2.3 Unknowns relating to treatment benefits

Melatonin Orion is not indicated in children and adolescents aged under 18 years. The safety and efficacy of melatonin in children and adolescents aged 18 years have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Nightmares	Nightmares have been reported with melatonin products.	If patient experiences intolerable nightmares, melatonin treatment should be discontinued.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Increases in the amount of prolactin hormone in the blood/abnormal milk secretion (Hyperprolactinaemia/galactorrhoea)	Melatonin may cause increases in the amount of the hormone prolactin in the blood. Adverse reactions reported for melatonin products in clinical studies/spontaneous reports include abnormal milk secretion.
Abnormalities in sperm (Sperm motility decreased/Spermatozoa morphology abnormal)	Reversible sperm abnormalities such as decreased sperm count and decreased sperm motility have been reported with melatonin products.
Suicide attempt/suicidal ideation/mood disturbance/depression/anxiety/depressed mood	Psychiatric disorders such as anxiety, altered mood and depression have been reported for melatonin products in clinical studies/spontaneous reports. Patients suffering from depression have a risk for suicidal ideation/suicide attempts.
Psychotic disorders	According to isolated reports, melatonin may induce psychotic symptoms such as paranoia and hallucinations at higher dose levels/during overdose.
Panick attacks	Psychiatric disorders such as anxiety, altered mood and depression have been reported for melatonin products in clinical studies/spontaneous reports. E.g. in cases of severe anxiety, occurrence of panic attacks cannot be excluded.
Confusion	Psychiatric disorders such disorientation have been reported for melatonin products in clinical studies/ spontaneous reports. Disorientation may be accompanied by confusion.
Hallucinations	Melatonin may induce psychotic symptoms such as paranoia and hallucinations at higher dose levels/during overdose.
Drug interaction with levothyroxine	Hormonal changes induced by higher doses of melatonin may affect especially women: decreases or increases in levels of thyroid hormones have been reported. Before taking melatonin, patients should inform their doctor if they are using any other medicines.

Potential interaction with warfarin	Concomitant use of melatonin and warfarin may result in potentiation of anticoagulation; INR monitoring is therefore recommended in concomitant use. Before taking melatonin, patients should inform their doctor if they are using any other medicines.
Loss of consciousness	Fainting (syncope) has been reported for melatonin products in clinical studies/spontaneous reports.
Infections	Herpes zoster has been reported for melatonin products in clinical studies/spontaneous reports. Also decreased level of white blood cells (leukopenia) has been reported. Leukopenia increases the risk of infections.
Retinal effects	Eye disorders such as reduced visual acuity and blurred vision have been reported for melatonin products in clinical studies/ spontaneous reports.
Breathing difficulty (Dyspnoea)	Isolated case of breathing difficulty has been reported. Hypersensitivity reactions may lead to breathing difficulties.

Missing information

Risk	**What is known**
Use for an unapproved indication or in an unapproved age group (Off-label use)	Melatonin Orion is indicated for short-term treatment of circadian rhythm sleep disorders caused by jet-lag in adults. The safety and efficacy of melatonin in children aged 0 to 18 years have not yet been established.
Fertility, pregnancy and breastfeeding	No adequate clinical data from the use of melatonin during pregnancy or lactation are available. In view of the lack of clinical data, use of melatonin is not recommended in pregnant or lactating women or in women planning to become pregnant. Effect of melatonin on human fertility is unknown.

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 Orion can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

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

Not applicable.