VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Insomnia (*i.e.* sleeplessness) is a common sleep disorder which may make a person hard to fall asleep, hard to stay asleep or both, despite the opportunity for adequate sleep.

Insomnia can be acute (short-term) or chronic (ongoing). Acute insomnia is common, lasts for days or weeks and often is brought on by situations such as stress at work, family pressures, or a traumatic event. Chronic insomnia lasts for a month or longer. Most cases of chronic insomnia are secondary, which means they are the symptom or side effect of some other problem *e.g.* medical conditions, medicines, sleep disorders, and use of substances like caffeine and nicotine.

For many people restful sleep can be restored back by changing one's sleep habits and addressing any underlying causes of insomnia, such as medical conditions or medications. If these measures don't work, medications (called hypnotic agents) which help with relaxation and sleep, may be recommended by the doctor.

VI.2.2 Summary of treatment benefits

Zopiclone is a benzodiazepine-like hypnotic agent/sleeping tablet which belongs to the group of cyclopyrrolones. The pharmacological properties are: sedation (calms down), anxiolysis (relieves anxiety), anticonvulsion (prevent or reduce the severity of epileptic fits or other convulsions), and muscle relaxation. It is used in adults as a sleeping drug for various kinds of sleeping problems, *e.g.* difficulty falling asleep, waking up too early or too many nightly awakenings.

Zopiclone Orion is used for the transient and short-term treatment of insomnia/sleeplessness and, for a limited time, for chronic insomnia in adults. Zopiclone Orion should only be prescribed if sleeping problem is severe, disabling or causing extreme distress.

VI.2.3 Unknowns relating to treatment benefits

Insufficient data are available on zopiclone to assess its safety during pregnancy and lactation.

The safety and efficacy of zopiclone in children and adolescents aged less than 18 years have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Breathing either slowed down or at risk of stopping (Respiratory depression)	Zopiclone may cause respiratory depression. Therefore, the use of zopiclone is not recommended in patients with diseases or conditions associated with compromised respiratory function like – myasthenia gravis (a serious muscle-weakness) – respiratory insufficiency (serious breathing problem)	The cause of the sleep disturbances should be clarified and the underlying diseases should be treated before starting treatment with zopiclone. The patient should always inform the doctor if he/she is suffering from anybreathing problems before starting treatment with zopiclone. In such cases, the doctor will decide whether to take

Risk	What is known	Preventability
	– severe sleep apnoea syndrome (a sleep disorder characterised by pauses in breathing during sleep) If zopiclone is used during the last three months of pregnancy or during labour, effects like very slow or shallow breathing (respiratory depression) on the newborn child may arise. This has been observed in children of mothers who have used zopiclone for long periods during the last months of pregnancy. Taking too much zopiclone/overdosage may cause shallow breathing or difficulty in breathing (respiratory depression).	Zopiclone Orion or not or may also reduce the dose. The patient is also closely monitored during the course of treatment.The newborn should be carefully watched for such symptoms. Doctor should be contacted immediately in case of zopiclone overdose.
Loss of memory for events after an incident (Anterograde amnesia)	Zopiclone may cause a short-term memory loss . This occurs particularly a few hours after taking the medicine. Sleep walking and other associated behaviours such as "sleep driving", preparing and eating food, or making phone calls, with memory loss of the event, have been reported in patients who have taken zopiclone and were not fully awake.	An uninterrupted sleep of 7–8 hours is must in order to reduce this risk. Doctor should be informed immediately if the patient develops any of the alongside listed symptoms. Doctor may discontinue treatment with zopiclone.
Mental, emotional, or behavioural effects and drug response opposite to the effect which would normally be expected from the drug (Psychiatric and paradoxical reactions)	Zopiclone may cause the following reactions: – restlessness, agitation – irritability, aggression, outbursts of anger – false beliefs, seeing, hearing or feeling things that do not really exist (hallucination) – nightmares – severe mental disorders characterised by disturbance of personality and loss of contact with reality (psychoses) – unsuitable behaviour The risk of these reactions is higher in elderly patients.	Zopiclone should be stopped and doctor should be informed immediately if the patient feels/develops any of the listed symptoms. Elderly should be given a reduced dose of zopiclone.

Risk	What is known	Preventability
State of progressively decreased responsiveness to a drug and a psychologic craving for physiologic/psychological dependence on drug (Tolerance and dependence)	The effect of zopiclone may decrease after repeated use for a few weeks. This is called tolerance. The use of zopiclone can lead to physical and psychological dependence. The risk of dependence increases with higher dose and long period of treatment. This risk is also higher in patients with a history of alcohol, drug or medicine abuse and/or those who have marked personality disorders. If physical dependence occurs, stopping the treatment suddenly may lead to withdrawal symptoms.	Doctor should be consulted if, the patient feels that the effect of zopiclone has decreased after repeated use for a few weeks. Treatment with zopiclone should be as short as possible. It should generally last between a few days to two weeks. The dose of zopiclone should be reduced gradually.
Group of symptoms that occur upon the abrupt discontinuation or decrease in intake of drug/ sleeplessness (Withdrawal symptoms/insomnia)	If physical dependence occurs, stopping the treatment suddenly may lead to withdrawal symptoms such as: headache, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases following symptoms may occur: an alteration in the perception of the world so that it seems strange or unreal, loss of your own personal identity followed by feelings of unreality and strangeness , oversensitivity to sound , numbness and tingling of arms and legs, hypersensitivity to light, noise or physical contact, seeing, hearing or feeling things that don't really exist (hallucinations) and epileptic seizures. After stopping zopiclone, a temporary syndrome called rebound insomnia may occur. Sleeplessness (insomnia) may return in a more severe form. Other symptoms may be mood changes, anxiety and restlessness. The risk of withdrawal or rebound symptoms is higher if the treatment is stopped suddenly. If zopiclone is used during the last three months of pregnancy or during labour, withdrawal symptoms may occur in	Treatment with zopiclone should be as short as possible. Later, the dose of zopiclone should be gradually reduced at the end of the treatment (tapering off). This measure lowers the risk of withdrawal or rebound symptoms like insomnia. Zopiclone should not be taken for longer than four weeks including the tapering off phase. If symptoms don't improve within this period, doctor's advice for alternative medicine should be sought for. The newborn should be carefully watched for such symptoms.

Risk	What is known	Preventability
	newborns. This has been observed in children of mothers who have used zopiclone for long periods during the last months of pregnancy.	

Important potential risk

Risk	What is known (Including reason why it is considered a potential risk)
Patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others and situation in which a medication prescribed for one person ends up in the hands of another (Abuse and diversion)	The use of zopiclone can lead to physical and psychological dependence and subsequent abuse. The risk of dependence or abuse increases with: – dose and duration of treatment – use with alcohol or other psychotropics – it is also greater in patients with a history of alcohol and or drug abuse – those patients who have marked personality disorders Benzodiazepines and benzodiazepine-like substances should be administered with extreme caution to patients with a previous history of alcohol or drug abuse.

Missing information

Risk	What is known
Use in pregnant women (Use during pregnancy)	Zopiclone Orion is not recommended for use during pregnancy. There are no or limited data from the use of zopiclone in pregnant women. If zopiclone is used during the last three months of pregnancy or during labour, some effects on the newborn child may arise. These include low body temperature, decreased muscle tone and very slow or shallow breathing (respiratory depression). Withdrawal symptoms may occur in the newborns. This has been observed in children of mothers who have used zopiclone for long periods during the last months of pregnancy.
Use in breastfeeding women (Use during lactation)	Zopiclone is excreted/passes into breast milk in a small amount. Therefore, its use is not recommended in breastfeeding women.

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 Zopiclone Orion medicinal product 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.