Summary of Risk Management Plan for Slenyto 1 mg and 5 mg prolonged-release tablets (melatonin)

This is a summary of the RMP for Slenyto 1 mg and 5 mg prolonged release tablets. The RMP details important risks of Slenyto, how these risks can be minimized, and how more information will be obtained about Slenyto's risks and uncertainties (missing information).

Slenyto's summary of product characteristics (SPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how Slenyto should be used.

This summary of the RMP for Slenyto should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Slenyto's RMP.

I. The Medicine and What it is Used For

Slenyto is authorized for insomnia in children and adolescents aged 2 to 18 years with Autism Spectrum Disorder (ASD) and and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient (see SPC for the full indication). It contains melatonin as the active substance and it is given by oral administration.

Further information about the evaluation of Slenyto's benefits can be found in Slenyto's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/slenyto.

II. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Slenyto, together with measures to minimize such risks and the proposed studies for learning more about Slenyto's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Slenyto is not yet available, it is listed under 'missing information' below.

IIA List of Important Risks and Missing Information

Important risks of Slenyto are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered/taken.

Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Slenyto. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of Important Risks and Missing Information	
Important Identified Risks	None
Important Potential Risks	None
Missing Information	Use in pregnancy and lactation Long-term safety in children (> 2 years)

IIB Summary of Important Risks/Missing Information

Missing Information: Use in pregnancy and lactation	
Evidence for Linking the Risk to the Medicine	Transfer via breast milk and/or physiological excretion of melatonin into maternal milk have been shown in different animal species and humans; additionally melatonin crosses the placenta and shows rhythmic variations in breast milk, in parallel with plasma, in both humans and goats.
Risk Factors and Risk Groups	Pregnant and lactating women
Risk Minimization Measures	Routine risk minimization measures: Indication in Section 4.6 of the SPC (Fertility, pregnancy and lactation) that there is not sufficient data relating to the use of Slenyto during breastfeeding and pregnancy. Inclusion of warning in the package leaflet that "If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine". Additional risk minimization measures: None.
Additional Pharmacovigilance Activities	Reports describing pregnancy shall be followed up and documented until the outcome is known. Additional pharmacovigilance activities: None.
Missing Information: Long term safety in children (>2 years)	
Evidence for Linking the Risk to the Medicine	There is no official data with the product for a duration longer than 2 years.
Risk Factors and Risk Groups	The target population and children that will be treated off label.
Risk Minimization Measures	Indication in Section 4.2 of the SmPC that "Data is available for up to 2 year's treatment"
Additional Pharmacovigilance Activities	Monitor any relevant post marketing safety reports. Reports related to long term use would be specifically followed up. Final report of the RTU has now been submitted.

Abbreviations: SPC = summary of product characteristics.
Data source: On file.

IIC Post-Authorization Development Plan

IIC.1 Studies Which are Conditions of the Marketing Authorization

None.

IIC.2 Other Studies in Post-Authorization Development Plan

None