# Part VI: Summary of the risk management plan

## Summary of risk management plan for Melatonin Unimedic Pharma

This is a summary of the risk management plan (RMP) for Melatonin Unimedic Pharma. The RMP details important risks of Melatonin Unimedic Pharma, how these risks can be minimised, and how more information will be obtained about Melatonin Unimedic Pharma's risks and uncertainties (missing information).

Melatonin Unimedic Pharma's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Melatonin Unimedic Pharma should be used.

## I. The medicine and what it is used for

Melatonin Unimedic Pharma is authorised for sleep disorders in children and adults (see SmPC for the full indication). It contains melatonin as the active substance and it is given orally.

## II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Melatonin Unimedic Pharma, together with measures to minimise such risks and the proposed studies for learning more about Melatonin Unimedic 's risks, are outlined below.

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

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised 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 minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Melatonin Unimedic Pharma, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly 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 Melatonin Unimedic Pharma is not yet available, it is listed under ‘missing information’ below.

## *II.A List of important risks and missing information*

Important risks of Melatonin Unimedic Pharma are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Melatonin Unimedic Pharma. 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 | Delay of sexual maturation and development |
| Missing information | Use in pregnancy and lactation<br>Long-term safety |

## *II.B Summary of important risks*

| Delay of sexual maturation and development | |
|---|---|
| Evidence for linking the risk to the medicine | Melatonin delays sexual development in rats in a transient and reversible manner. No evidence for delay in human. |
| Risk factors and risk groups | Children and adolescents that are between pre-pubertal to pubertal stages. |
| Risk minimisation measures | Indication in Section 4.2 of SmPC that the patient should be monitored at regular intervals (at least every 6 months) to check that Melatonin Unimedic Pharma is still the most appropriate treatment.<br><br>Inclusion in the package leaflet under section 3: "You or your child should be monitored by your doctor at regular intervals (recommended every 6 months) to check that Melatonin Unimedic Pharma is still the right treatment for you/them. |
| Additional pharmacovigilance activities | Monitor any relevant post marketing safety reports. Reports describing sexual maturation and development would be specifically followed up. |

| Missing information: Long term safety | |
|---|---|
| Evidence for linking the risk to the medicine | Possible long-term effects of melatonin have been inadequately studied. |

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|---|---|
| Risk factors and risk groups | The target population and children that will be treated off-label. |
| Risk minimisation measures | Indication in Section 4.4 of the SmPC that long-term effects have been inadequately studied. |

| Missing information: Use in pregnancy and lactation | |
|---|---|
| Evidence for linking the risk to the medicine | For melatonin there are no data from the treatment of pregnant women. Melatonin has been measured in breast milk and thus exogenous melatonin is probably secreted into breast milk. |
| Risk factors and risk groups | Pregnant and lactating women. |
| Risk minimisation measures | Routine risk minimisation measures. Indication in Section 4.6 of the SmPC that there is not sufficient data relating to the use of Melatonin Unimedic during breastfeeding and pregnancy. Inclusion of warning in the package leaflet. |

## *II.C Post-authorisation development plan*

### II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Melatonin Unimedic Pharma.

### II.C.2 Other studies in post-authorisation development plan

There are no studies required for Melatonin Unimedic Pharma.