Part VI: Summary of the risk management plan

Summary of risk management plan for Miacalcic (calcitonin-salmon)

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

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

I. The medicine and what it is used for

Miacalcic is authorised for prevention of acute bone loss due to sudden immobilisation, Paget’s disease, and hypercalcemia of malignancy (see SmPC for the full indication). It contains calcitonin-salmon as the active substance and it is given by subcutaneous or intramuscular injection and intravenous infusion.

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

Important risks of Miacalcic, together with measures to minimise such risks and the proposed studies for learning more about Miacalcic'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR 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 Miacalcic is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Miacalcic 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 Miacalcic. 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	Increased risk of malignancies with long-term use
Important potential risks	None.
Missing information	Use in pregnancy and during lactation. Use in paediatric population Use in patients with renal impairment Use in patients with hepatic impairment

II.B.1 Summary of important risks

Increased risk of malignancies with long-term use	
Evidence for linking the risk to the medicine	Meta-analysis of clinical trial data, provide evidence of a causal association between calcitonin and cancer. There are uncertainties surrounding the true magnitude of this risk.
Risk factors and risk groups	Patient with cancer (calcitonin promotes tumour progression rather than oncogenesis)
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2., 4.4. and 4.8.* *SmPC section 4.2 where advice is given to use calcitonin-salmon for shortest duration possible and consider individual risk-benefit balance if longer or periodic treatment is needed* *PL section 2 and 4.*

II.B.2 Summary of missing information

Use in pregnancy and during lactation	
Risk minimisation measures	Routine risk minimisation measures:

	SmPC section 4.6. *SmPC section 4.6 where advice is given to use calcitonin-salmon during pregnancy only if treatment is considered absolutely essential by the physician, and that breast-feeding is not recommended during treatment.* *.* *PL section 2.*

Use in paediatric population	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2.* *Use in children: There is insufficient evidence to support the use of salmon calcitonin in conditions associated with paediatric osteoporosis. Use of salmon calcitonin in children 0 to 18 years is therefore not recommended.* *PL section 2:* *Use of calcitonin is not recommended in patients under 18 years of age.*

Use in patients with renal impairment	
Risk minimisation measures	Routine risk minimisation measures: *In SmPC section 4.2* *The metabolic clearance is much lower in patients with end-stage renal failure than in healthy subjects. However, the clinical relevance of this finding is not known.* *In SmPC section 5.2.* *Salmon calcitonin is primarily and almost exclusively degraded in the kidneys, forming pharmacologically inactive fragments of the molecule. Therefore, the metabolic clearance is much lower in patients with end-stage renal failure than in healthy subjects. However, the clinical relevance of this finding is not known.*

Use in patients with hepatic impairment	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2.* *Experience with the use of calcitonin in patients with altered hepatic function has shown no evidence of reduced tolerability or altered dosage requirements.*

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 Miacalcic.

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

There are no studies required for Miacalcic.