Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for ZOLEDRONIC ACID 4 mg/ 100 ml solution for infusion

This is a summary of the risk management plan (RMP) for ZOLEDRONIC ACID 4 mg/ 100 ml solution for infusion, (hereinafter referred to as Zoledronic acid). The RMP details important risks of Zoledronic acid, how these risks can be minimised, and how more information will be obtained about Zoledronic acid's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Zoledronic acid is authorised for prevention of skeletal related events in patients with advanced malignancies involving bone, and tumour-induced hypocalcaemia (see SmPC for the full indication). It contains zoledronic acid as the active substance and it is given intravenously.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Zoledronic acid, together with measures to minimise such risks and the proposed studies for learning more about Zoledronic acid'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 Zoledronic acid, these measures are supplemented with additional risk minimisation measure mentioned under relevant important risk, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, 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 Zoledronic acid is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Zoledronic acid 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 Zoledronic acid. 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).

Table 8: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Osteonecrosis of the jaw (ONJ) • Hypocalcaemia • Renal function impairment • Acute phase reaction • Atrial fibrillation • Interstitial lung disease • Interaction with anti-angiogenic drugs • Anaphylaxis
Important potential risks	• Atypical femoral fractures • Cardiac arrhythmias • Fracture healing impairment • Cerebrovascular adverse events • Focal segmental glomerulosclerosis • Potential interaction with products that can significantly affect renal function • Medication errors • Off-label use in osteogenesis imperfecta
Missing information	• Fertility, pregnancy and lactation • Patients with severe renal impairment • Patients with hepatic insufficiency

II.B Summary of Important Risks

Table 9: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important potential risk: Osteonecrosis of the jaw (ONJ)	
Risk minimisation measures	**Routine risk minimisation measures** SmPC sections 4.2, 4.4, 4.5 and 4.8. PL sections 2 and 4. Prescription only medicine. **Additional risk minimisation measures** Patient reminder card.

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 Zoledronic acid.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Zoledronic acid.