Part VI: Summary of the risk management plan

Summary of risk management plan for Alendronic Acid 70 mg Oral Solution (Alendronic Acid)

This is a summary of the risk management plan (RMP) for Alendronic Acid 70 mg Oral Solution. The RMP details important risks of Alendronic Acid 70 mg Oral Solution, how these risks can be minimised, and how more information will be obtained about Alendronic Acid 70 mg Oral Solution's risks and uncertainties (missing information).

Alendronic Acid 70 mg Oral Solution's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Alendronic Acid 70 mg Oral Solution should be used.

I. The medicine and what it is used for

Alendronic Acid 70 mg Oral Solution is authorised for the treatment of post-menopausal osteoporosis (see SmPC for the full indication). It contains Alendronic Acid as the active substance, and it is given by oral administration.

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

Important risks of Alendronic Acid 70 mg Oral Solution, together with measures to minimise such 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 Alendronic Acid 70 mg Oral Solution is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

List of important risks and missing information	
Important identified risks	Osteonecrosis of the jaw (ONJ)
	Osteonecrosis of the external auditory canal
	Oesophageal adverse effects
Important potential risks	Atypical femoral fractures
Missing information	Use in children and adolescents

II.B Summary of important risks

Important identified risk: Osteonecrosis of the Jaw	
Evidence for linking the risk to the medicine	ONJ associated with bisphosphonate therapy in cancer patients was reported in 2003 and is now generally recognized as a very rare complication of long-term bisphosphonate therapy at doses used to treat osteoporosis.
Risk factors and risk groups	Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis), has been reported in patients with cancer receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates (class of medicines to which Alendronic Acid belongs). The following risk factors should be considered when evaluating an individual's risk of developing ONJ: - potency of the bisphosphonate, route of administration and cumulative dose - cancer, chemotherapy, radiotherapy, corticosteroids, smoking - a history of dental disease, poor oral hygiene, periodontal disease, invasive dental procedures and poorly fitting dentures
Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.4 Special Warnings and Precautions for Use SmPC Section 4.8 Undesirable Effects PL Section 2 and Section 4 Additional risk minimisation measures

	None

Important identified risk: Osteonecrosis of the external auditory canal	
Evidence for linking the risk to the medicine	A small number of cases of osteonecrosis of the external auditory canal have been reported in patients taking bisphosphonates for both cancer and osteoporosis indications.
Risk factors and risk groups	A small number of cases of osteonecrosis of the external auditory canal have been reported in patients taking bisphosphonates for both cancer and osteoporosis indications. Most cases were associated with long term bisphosphonate therapy and the majority of cases had possible risk factors including steroid use, chemotherapy and/or possible local risk factors such as local infection, or trauma.
Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.4 Special Warnings and Precautions for Use SmPC Section 4.8 Undesirable Effects PL Section 4 Additional risk minimisation measures None

Important identified risk: Oesophageal reactions	
Evidence for linking the risk to the medicine	In clinical trials, Upper Gastrointestinal (UGI) Adverse Events (AEs), including severe events such as oesophageal ulcer, oesophagitis and erosive oesophagitis, have been reported at similar frequencies in placebo- and active-treatment arms. However, post-marketing studies have highlighted UGI AEs as a concern. These studies show that a significant portion of patients are less compliant with administration instructions outside strict clinical trial supervision, and when oral bisphosphonates are not administered as directed, patients are more likely to experience UGI AEs.
Risk factors and risk groups	The risk of severe oesophageal adverse experiences appears to be greater in patients who fail to take alendronate properly and/or who continue to take alendronate after developing symptoms suggestive of oesophageal irritation.

Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.4 Special Warnings and Precautions for Use SmPC Section 4.8 Undesirable Effects PL Section 2 and Section 4 Additional risk minimisation measures None

Important potential risk: Atypical Femur Fractures	
Evidence for linking the risk to the medicine	Class effect for bisphosphonates. Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. These transverse or short oblique, fractures can occur anywhere along the femur from just below the lesser trochanter to just above the supracondylar flare. These fractures occur after minimal or no trauma and some patients experience thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femoral fracture. Fractures are often bilateral; therefore, the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures has also been reported.
Risk factors and risk groups	Atypical femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long term treatment for osteoporosis.
Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.4 Special Warnings and Precautions for Use SmPC Section 4.8 Undesirable Effects PL Section 4 Additional risk minimisation measures None

Missing Information: Use in children and adolescents	
Risk minimisation measures	Routine risk minimisation measures

	SmPC Section 4.2 Posology and method of administration PL Section 2 Additional risk minimisation measures None

II.C Post-authorisation development plan

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

Not applicable.

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

Alendronic Acid has been used for many years and no additional post authorisation studies are planned.