5. SUMMARY OF THE EU RISK MANAGEMENT PLAN

Summary of activities for each safety concern

Safety concern	Proposed pharmacovigilance activities (routine and additional)	Proposed risk minimization activities (routine and additional)
Important identified risks		
Renal function impairment	Routine pharmacovigilance including cumulative analysis in PSUR. **Additional Activities** - Targeted follow-up of all serious spontaneous and post marketing surveillance reports.	SPC Section 4.2 Posology and method of administration, 4.4 Special warnings and precautions for use, and 4.5 Interaction with other medicinal products and other forms of interaction Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects.
Osteonecrosis of the jaw	Routine pharmacovigilance including cumulative analysis in PSUR. **Additional Activities** Targeted follow-up of all serious spontaneous and post marketing surveillance.	Routine risk minimization activities SPC Section 4.4 Special warnings and precautions for use Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects. **Additional Activities:** **<u>Patient Reminder Card</u>** This reminder card contains important safety information that you need to be aware of before and during treatment with Zoledronic acid Fresenius Kabi injections for cancer-related conditions Your doctor has recommended that you receive Zoledronic acid Fresenius Kabi injections to help prevent bone complications (e.g. fractures) caused by bone metastases, or bone cancers and/or to reduce the amount of calcium in the blood in adult patients were it is too high due to a presence of tumor. A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported uncommonly (may affect up to 1 in 100 people) in patients receiving Zoledronic acid Fresenius Kabi injections for cancer-related conditions. ONJ can also occur after stopping treatment.

Safety concern	Proposed pharmacovigilance activities (routine and additional)	Proposed risk minimization activities (routine and additional)
		In order to reduce the risk of developing osteonecrosis of the jaw, there are some precautions you should take: **<u>Before starting treatment:</u>** — Ask your doctor to tell you about ONJ before you start treatment — Check with your doctor whether a dental examination is recommended before you start treatment with Zoledronic acid Fresenius Kabi. — Tell your doctor/nurse (health care professional) if you have any problems with your mouth or teeth. Patients undergoing dental surgery (e.g. tooth extractions), who do not receive routine dental care or have gum disease, are smokers, who get different types of cancer treatments or who were previously treated with a bisphosphonate (used to treat or prevent bone disorders) may have a higher risk of developing ONJ. **<u>While being treated:</u>** — You should maintain good oral hygiene, make sure your dentures fit properly and receive routine dental check-ups. — If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor and tell your dentist that you are being treated with Zoledronic acid Fresenius Kabi — Contact your doctor and dentist immediately if you experience any problems with your mouth or

Safety concern	Proposed pharmacovigilance activities (routine and additional)	Proposed risk minimization activities (routine and additional)
		teeth such as loose teeth, pain or swelling, non-healing of sores or discharge, as these could be signs of osteonecrosis of the jaw Read the package leaflet for further information.
Acute phase reaction	Routine pharmacovigilance including cumulative analysis in PSUR.	SPC Section 5.1 Pharmacodynamic properties Pediatric patients Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects.
Hypocalcemia	Routine pharmacovigilance including cumulative analysis in PSUR.	SPC Sections 4.2 Posology and Method of Administration, and 4.4 Special Warnings and Precautions for Use Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects
Ocular adverse events	Routine pharmacovigilance including cumulative analysis in PSUR. **Additional Activities** Targeted follow-up of all serious spontaneous and post marketing surveillance reports.	Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects
Atrial fibrillation	Routine pharmacovigilance including cumulative analysis in PSUR. **Additional Activities** Targeted follow-up of all serious spontaneous and post marketing surveillance reports and global clinical trial SAE reports.	Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects
Anaphylaxis	Routine pharmacovigilance including cumulative analysis in PSUR.	Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects
Important potential risks		
Atypical Fractures	Routine pharmacovigilance including cumulative analysis in	SPC Section 4.4 Special Warnings and Precautions for Use

Safety concern	**Proposed pharmacovigilance activities (routine and additional)**	**Proposed risk minimization activities (routine and additional)**
	PSUR. **Additional Activities** Targeted follow-up of all serious spontaneous and post marketing surveillance reports and global clinical trial SAE reports	Relevant preferred terms are included as ADRs in SPC Section 4.8 Undesirable effects
Cerebrovascular AEs	Routine pharmacovigilance including cumulative analysis in PSUR. **Additional Activities** Targeted follow-up of all serious spontaneous and post marketing surveillance reports and global clinical trial SAE reports.	Currently available data do not support the need for risk minimization.
Focal Segmental Glomerulosclerosis	Routine pharmacovigilance including cumulative analysis in PSUR.	Currently available data do not support the need for risk minimization.
Fracture healing impairment	Routine pharmacovigilance including cumulative analysis in PSUR.	Currently available data do not support the need for risk minimization.
Interstitial lung disease	Routine pharmacovigilance including cumulative analysis in PSUR.	Currently available data do not support the need for risk minimization.
Potential Interactions		
Products that can significantly affect renal function	Routine pharmacovigilance including cumulative analysis in PSUR.	SPC Sections 4.4 Special Warnings and Precautions for Use and 4.5 Interaction with other medicinal products and other forms of interaction
Important missing information		
Races other than Caucasian	Routine pharmacovigilance	Currently available data do not support the need for risk minimization.
Fertility, Pregnancy and Lactation	Routine pharmacovigilance	SPC Sections 4.3 Contraindications, 4.6 Pregnancy and lactation, and 5.3 Preclinical safety data.
Patients with severe renal impairment	Routine pharmacovigilance	SPC Sections 4.2 Posology and method of administration, 4.4 Special warning and precautions for use, and 4.5 Interaction with other medicinal products and other forms of interaction. Relevant preferred terms are included as ADRs in SPC section 4.8 Undesirable effects.

Safety concern	Proposed pharmacovigilance activities (routine and additional)	Proposed risk minimization activities (routine and additional)
Patients with hepatic Insufficiency	Routine pharmacovigilance.	This item is appropriately communicated through current labeling. SPC Section 4.4 Special warnings and precautions for use