Part VI Summary of Risk Management Plan for Levofloxacin Fresenius Kabi 5 mg/ml solution for infusion (Levofloxacin hemihydrate)

This is a summary of the RMP for Levofloxacin Kabi. The RMP details important risks of Levofloxacin Kabi and how these risks can be minimised.

Levofloxacin Kabi SmPC and its PL give essential information to healthcare professionals and patients on how Levofloxacin Kabi should be used.

Important new safety concerns or changes to the current ones will be included in updates of the Levofloxacin Kabi RMP.

I. The Medicine and What it is Used For

Levofloxacin Kabi solution for infusion is indicated in adults for the treatment of the following infections:

- Acute pyelonephritis and complicated urinary tract infections.
- Chronic bacterial prostatitis.
- Inhalation Anthrax: postexposure prophylaxis and curative treatment.

In the below-mentioned infections Levofloxacin Kabi should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

- Community-acquired pneumonia
- Complicated skin and soft tissue infections

It contains levofloxacin hemihydrate as active substance and is only intended for slow intravenous infusion; it is administered once or twice daily. The infusion time must be at least 30 minutes for 250 mg or 60 minutes for 500 mg Levofloxacin Kabi solution for infusion.

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

Important risks of Levofloxacin Kabi, together with measures to minimise such risks and the proposed studies for learning more about Levofloxacin Kabi 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 PL 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*.

II.A List of important Risks and Missing Information

Important risks of Levofloxacin Kabi 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 Levofloxacin Kabi. 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	- Prolonged, potentially irreversible, serious suspected adverse drug reaction that last 30 days or more - Aortic aneurysm and dissection and Heart valve regurgitation / incompetence
Important potential risks	- None
Missing information	- None

II.B Summary of Important Risks

Important identified risk - Prolonged, potentially irreversible, serious suspected adverse drug reaction that last 30 days or more	
Evidence for linking the risk to the medicine	Reports of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions with levofloxacin have been derived from spontaneous data sources, including published literature.
Risk factors and risk groups	Daily doses of 1,000 mg levofloxacin in older patients, patients with renal impairment,

	patients with solid organ transplants and those treated concomitantly with corticosteroids, are at higher risk of tendon damage. Patients with a history of tendon disease/disorder related to fluoroquinolone treatment. Patients with history of psychiatric disease. Patients with serious adverse reactions in past, associated with the use of quinolone or fluoroquinolone medicines.
Risk minimisation measures	*Routine risk minimisation measures* Guidance and safety information in section 4.3 "Contraindications", section 4.4 "Special warnings and precautions for use" and section 4.8 "Undesirable effects" of the SmPC. Guidance in PL section 2 "What you need to know before you are given Levofloxacin Kabi" and section 4 "Possible side effects". *Additional risk minimisation measures* DHPC letter to increase the awareness on the risk of disabling, long-lasting and potentially irreversible side effects and restrictions on use. For further details refer to Part V, sub-section V.2. Additional Risk Minimisation Measures.

Important identified risk - Aortic aneurysm and dissection and Heart valve regurgitation/ incompetence	
Evidence for linking the risk to the medicine	Reports of aortic aneurysm and dissection with levofloxacin have been derived from spontaneous data sources including published literature, while reports of heart valve regurgitation/ incompetence with levofloxacin have been derived from published literature.
Risk factors and risk groups	Elderly patients, patients with positive family history of aneurysm disease or congenital heart valve disease, patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection or heart valve disease and in

	patients treated concurrently with systemic corticosteroids. Presence of other risk factors or conditions predisposing: • for both aortic aneurysm and dissection and heart valve regurgitation/incompetence (e.g. connective tissue disorders such as Marfan syndrome or Ehlers-Danlos syndrome, Turner syndrome, Behcet's disease, hypertension, rheumatoid arthritis) or additionally • for aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu arteritis or giant cell arteritis, or known atherosclerosis, or Sjögren's syndrome) or additionally • for heart valve regurgitation/incompetence (e.g. infective endocarditis)
Risk minimisation measures	*Routine risk minimisation measures* Guidance in section 4.4 "Special warnings and precautions for use" and section 4.8 "Undesirable effects" of the SmPC. Guidance in PL section 2 "What you need to know before you are administered Levofloxacin Kabi" and section 4 "Possible side effects". *Additional risk minimisation measures* DHPC letters to increase the awareness on the risk of Aortic aneurysm and dissection (2018) and Heart valve regurgitation/ incompetence (2020). For further details refer to Part V sub-section V.2. Additional Risk Minimisation Measures.

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 Levofloxacin Kabi.

II.C.2 Other Studies in Postauthorisation Development Plan

There are no on-going or closed studies for Levofloxacin Kabi**.**