RMP version 0.2

Part VI: Summary of the risk management plan

Summary of risk management plan for Ciprofloxacin Kabi

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

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

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

I. The medicine and what it is used for

Ciprofloxacin Kabi solution for infusion is indicated for the treatment of the following infections. Special attention should be paid to available information on resistance to ciprofloxacin before commencing therapy.

Adults

- Lower respiratory tract infections due to Gram-negative bacteria
    - exacerbations of chronic obstructive pulmonary disease
    - broncho-pulmonary infections in cystic fibrosis or in bronchiectasis
    - pneumonia
- Chronic suppurative otitis media
- Acute exacerbation of chronic sinusitis especially if these are caused by Gram-negative bacteria
- Acute pyelonephritis
- Bacterial prostatitis
- Epididymo-orchitis including cases due to Neisseria gonorrhoeae
- Pelvic inflammatory disease including cases due to Neisseria gonorrhoeae

In the above genital tract infections when thought or known to be due to Neisseria gonorrhoeae it is particularly important to obtain local information on the prevalence of resistance to ciprofloxacin and to confirm susceptibility based on laboratory testing.

- Infections of the gastro-intestinal tract (e.g. travellers` diarrhoea)
- Intra-abdominal infections
- Complicated skin and skin structure infections / Complicated skin and soft tissue infections
- Malignant external otitis
- Infections of the bones and joints
- Ciprofloxacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection

- Inhalation anthrax (post-exposure prophylaxis and curative treatment)

Children and adolescents

- Broncho-pulmonary infections due to Pseudomonas aeruginosa in patients with cystic fibrosis
- Complicated urinary tract infections and acute pyelonephritis
- Inhalation anthrax (post-exposure prophylaxis and curative treatment)

Ciprofloxacin may also be used to treat severe infections in children and adolescents when this is considered to be necessary.

Treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.

It contains Ciprofloxacin hydrogen sulphate as active substance and is only intended for intravenous infusion; for children, the infusion duration is 60 minutes. In adult patients, infusion time is 60 minutes for 400 mg Ciprofloxacin Kabi and 30 minutes for 200 mg Ciprofloxacin Kabi. Slow infusion into a large vein will minimise patient discomfort and reduce the risk of venous irritation.

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

Important risks of Ciprofloxacin Kabi, together with measures to minimise such risks and the proposed studies for learning more about Ciprofloxacin 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 Ciprofloxacin 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 Ciprofloxacin 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 missinginformation	
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

The safety information in the proposed product information is aligned to the reference medicinal product.

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 ciprofloxacin have been derived from spontaneous data sources, including published literature.
Risk factors and risk groups	Older patients, patients with renal impairment, patients with solid organ transplants, patients with a history of tendon disease/disorder related to fluoroquinolone treatment and those treated concomitantly with corticosteroids are at higher risk of tendon damage. 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 4.4 "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 Ciprofloxacin 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 and heart valve regurgitation/ incompetence with ciprofloxacin have been derived from spontaneous data sources including 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. 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) The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated concurrently with systemic corticosteroids.
Risk minimisation measures	*Routine risk minimisation measures* Guidance in section 4.4 "Special warnings and precautions and section 4.8 "Undesirable effects" of the SmPC.

	Guidance in PL section 2 “What you need to know before you are given Ciprofloxacin 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 Ciprofloxacin Kabi.

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

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