Summary of risk management plan for Ciprofloxacin Orion 250 mg, 500 mg and 750 mg Film Coated Tablets (Ciprofloxacin) Orion Corporation Date: 13-03-2019, Version 2

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

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

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

I. The medicine and what it is used for

Ciprofloxacin Orion is authorised for certain bacterial infections (see SmPC for the full indication). It contains ciprofloxacin as the active substance and it is given by mouth.

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

Important risks of Ciprofloxacin Orion, together with measures to minimise such risks and the proposed studies for learning more about Ciprofloxacin Orion'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 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 Ciprofloxacin Orion is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Ciprofloxacin Orion are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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. 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	• Disabling and potentially long-lasting side effects • Aortic aneurysm and dissection
Important potential risks	• None identified
Missing information	• None identified

II.B Summary of important risks

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

Important identified risk: Disabling and potentially long-lasting side effects	
Evidence for linking the risk to the medicine	Post-marketing spontaneous and literature data together with non-clinical and clinical information related to the possible underlying mechanisms of long-lasting, disabling and potentially permanent adverse drug reactions (ADRs) provide evidence to support causal relationship between the fluoroquinolones and potentially disabling ADR.
Risk factors and risk groups	Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Information given in SmPC sections 4.4 and 4.8 and PL sections 2 and 4. <u>Additional risk minimisation measures:</u> Direct Healthcare Professional Communication letter to increase the awareness on the risk of long-term, persistent, potentially irreversible adverse drug reactions and the associated changes to the product information.

Additional pharmacovigilance activities	Additional pharmacovigilance activities: Not applicable.

Important identified risk: Aortic aneurysm and dissection	
Risk minimisation measures	Routine risk minimisation measures: Information given in SmPC section 4.4. and PL section 2. Additional risk minimisation measures: Direct Healthcare Professional Communication letter to increase the awareness on the risk of on the risk of aortic aneurysm and dissection.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Not applicable.

II.C Post-authorisation development plan

There are no studies required for Ciprofloxacin Orion.