Part VI: Summary of the risk management plan

Plan for Sodium Fusidate Essential Pharma 500 mg (Sodium fusidate)

This is a summary of the risk management plan (RMP) for Sodium Fusidate Essential Pharma 500 mg. The RMP details important risks of Sodium Fusidate Essential Pharma 500 mg, how these risks can be minimised, and how more information will be obtained about Sodium Fusidate Essential Pharma 500 mg's risks and uncertainties (missing information).

Sodium Fusidate Essential Pharma 500 mg's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Sodium Fusidate Essential Pharma 500 mg should be used.

I. The medicine and what it is used for

Sodium Fusidate Essential Pharma 500 mg is authorised for treatment of infections caused by sodium fusidate-susceptible staphylococci such as osteomyelitis, septicaemia, endocarditis, superinfected cystic fibrosis, pneumonia, skin infections; surgical and traumatic wound infections (see SmPC for the full indication). It contains sodium fusidate as the active substance and it is given by intravenous infusion.

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

Important risks of Sodium Fusidate Essential Pharma 500 mg, 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 Sodium Fusidate Essential Pharma 500 mg is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Sodium Fusidate Essential Pharma 500 mg 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 Sodium Fusidate Essential Pharma 500 mg. 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	Interaction with statins causing rhabdomyolysis (myotoxicity). Abnormal liver function and effect on patients with impaired transport and metabolism of bilirubin.
Important potential risks	Antibiotic resistance. Severe skin reactions (eosinophilia).
Missing information	Use in pregnancy.

II.B Summary of important risks

Important identified risk: Interaction with statins causing rhabdomyolysis (myotoxicity)	
Evidence for linking the risk to the medicine	The drug interaction with statins causing rhabdomyolysis was identified as an important identified risk during signal detection activities of the previous marketing authorisation holder and presented in post marketing data.
Risk factors and risk groups	No studies examining the mechanisms of the interaction between sodium fusidate and statins have been published, and the frequency and any risk factors are unknown. Predisposing factors for rhabdomyolysis in patients using statins are old age, renal impairment, hypothyroidism, personal or familial history of hereditary muscular disorders, previous history of muscular toxicity with a statin or fibrate and alcohol abuse, as well as concomitant use of medicinal products that may increase the plasma concentration of the statin. The risk of rhabdomyolysis is additionally dose-related; patients using a higher dose of statin have a higher risk of developing rhabdomyolysis
Risk minimisation measures	Routine risk minimisation measures Proposed text in SmPC section 4.3, 4.4, 4.5, 4.8 and in section 2, 4 of packaging leaflet

	Other routine risk minimisation measures • Prescription only medicine • Use restricted to clinical secondary care setting, prescribed by an infectious disease specialist • Not considered first line treatment option
Important identified risk: Abnormal liver function and effect on patients with impaired transport and metabolism of bilirubin	
Evidence for linking the risk to the medicine	Based on findings in previous periodic safety update reports the focus on the risk for developing abnormal liver function and effect on patients with impaired transport and metabolism of bilirubin has increased and the risk has been acknowledged as an identified risk in the post marketing data.
Risk factors and risk groups	The risk factors leading to abnormal liver function as a result of sodium fusidate include: treatment with high doses; prolonged periods of treatment; patients with existing liver dysfunction; patients taking potentially hepatotoxic medication; patients with biliary tract obstruction; and patients taking concurrent medication with a similar excretion pathway.
Risk minimisation measures	Routine risk minimisation measures: Proposed text in SmPC section 4.4, 4.8 and in section 2 and 4 of packaging leaflet Other routine risk minimisation measures • Prescription only medicine • Use restricted to clinical secondary care setting, prescribed by an infectious disease specialist • Not considered first line treatment option
Important potential risk: Antibiotic resistance	
Evidence for linking the risk to the medicine	Resistance to antibiotics in general is an increasing challenge. The most relevant issue regarding the efficacy of sodium fusidate is that of bacterial resistance. No change in the favourable risk-benefit balance of the product have been identified so far, however, this is an issue that needs to be monitored closely, wherefore the risk has been classified as an important potential risk.
Risk factors and risk groups	No specific studies have been carried out to examine the risk factors for resistance to sodium fusidate. However topical use of sodium fusidate is thought to have contributed to increasing resistance levels. General reasons for the development of antibiotic resistance include: use of an antibiotic as monotherapy; lack of a comprehensive and coordinated response to resistance; weak or absent antimicrobial resistance surveillance and monitoring

	systems; inadequate systems to ensure quality and uninterrupted supply of medicines; inappropriate use of antimicrobial medicines, including in animal husbandry; poor infection prevention and control practices; and insufficient diagnostic, prevention and therapeutic tools.
Risk minimisation measures	Routine risk minimisation measures: Proposed text in SmPC section 4.4 and in section 2 of packaging leaflet Other routine risk minimisation measures • Prescription only medicine • Use restricted to clinical secondary care setting, prescribed by an infectious disease specialist • Not considered first line treatment option
Important potential risk: Severe skin reactions (eosinophilia)	
Evidence for linking the risk to the medicine	Based on post marketing data, the Marketing Authorisation Holder have been requested to closely monitor severe skin reactions and drug reactions with eosinophilia. The cases in this category presented so far are associated with confounding factors such as co-suspect drugs known to have potential to cause DRESS syndrome, severe cutaneous hypersensitivity reactions, erythema multiforme, AGEP, and/or eosinophilia. Medical conditions such as hypersensitivity and for example in one case a reactivation of human herpes virus implicated in the occurrence of DRESS. Confounding co-suspect drugs were i.e. teicoplanin, vancomycin, piperacillin-tazobactam, ciprofloxacin, enoxaparin, fluconazole, levofloxacin, terbinafine, rifampicin, gentamycin, vancomycin, clindamycin, and amoxicillin. This potential risk is not addressed in the Summary of Product Characteristics, however, since the risk is considered to have an impact on the risk-benefit balance of the medicinal product if further characterized and confirmed, it is proposed as a new important potential risk. There is insufficient evidence to evaluate the potential risk-benefit impact.
Risk factors and risk groups	Since the association of the occurrence of eosinophilia with the use of sodium fusidate has not yet been established, information about the risk factors leading the severe skin reactions such as eosinophilia is insufficient.

Risk minimisation measures	**Routine risk communication:** None **Routine risk minimisation activities recommending specific clinical measures to address the risk:** None **Other routine risk minimisation measures beyond the Product Information:** **Legal status:** • Prescription only medicine • Use restricted to clinical secondary care setting, prescribed by an infectious disease specialist • Not considered first line treatment option
Missing information: Use in pregnancy	
Risk minimisation measures	Routine risk minimisation measures: Proposed text in SmPC section 4.6 and in section 2 of packaging leaflet Other routine risk minimisation measures • Prescription only medicine • Use restricted to clinical secondary care setting, prescribed by an infectious disease specialist • Not considered first line treatment option

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 Sodium Fusidate Essential Pharma 500 mg.

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

There are no studies required for Sodium Fusidate Essential Pharma 500 mg.