Part VI: Summary of the risk management plan

Summary of risk management plan for APROKAM (Cefuroxime sodium)

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

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

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

I. The medicine and what it is used for

APROKAM is authorised for antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery (see SmPC for the full indication). It contains cefuroxime sodium as active substance and it is given by intracameral route.

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

Important risks of APROKAM, together with measures to minimise such risks and the proposed studies for learning more about APROKAM'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;
- The authorised pack size — the amount of medicine in a pack (i.e. number of single-dose containers in the box or volume of solution in the multi-dose containers is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the fact that APROKAM requires a prescription to be 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 APROKAM is not yet available, it is listed under "missing information" below.

II.A List of important risks and missing information

Important risks of APROKAM 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 APROKAM. 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	None
Important potential risks	Retinal toxicity Medication errors Corneal endothelial toxicity
Missing information	Use in paediatric population

II.B Summary of important risks

Important identified risk – Retinal toxicity	
Evidence for linking the risk to the medicine	Cases of macular oedema were reported with standard and higher dose of cefuroxime in the literature and spontaneously.
Risk factors and risk groups	Risk factors included diabetes, age-related macular degeneration, retinal vein occlusion, genetic disorders (such as retinitis pigmentosa), inflammatory eye diseases (such as uveitis), eye injury, eye surgery, eye tumors, and medications (such as treatment with prostaglandins).
Risk minimisation measures	<u>Routine risk minimisation measures:</u> • SmPC section 4.8, 4.9 • PL section 4 • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

Important potential risk – Medication errors	
Evidence for linking the risk to the medicine	Case reports related to error in drug reconstitution (incorrect solvent) were reported.

Risk factors and risk groups	None
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.2, 6.6 • PL section 6 • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

Important potential risk – Corneal endothelial toxicity	
Evidence for linking the risk to the medicine	Corneal endothelial toxicity has not been reported at the recommended concentration of cefuroxime. However, literature data reported that the administration of incorrectly diluted cefuroxime (10-100 mg per eye) resulted in corneal toxicity including corneal oedema and loss of corneal endothelial cells *(Olavi et al, 2012 – Diez-Alvarez et al, 2021)*. A number of these patients had permanent and severe vision loss.
Risk factors and risk groups	Risk groups included patients with endothelial cell count <2000 cell/mm², corneal dystrophy, history of traumatism, acute glaucoma, anterior or posterior segments surgery, advanced age, hard nucleus density. Risk factors included cataract surgery (i.e. high ultrasound energy, long phacoemulsification time, phacoemulsification technique), and product dose.
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.4, 4.9 • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

Missing information – Use in paediatric population	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.2 • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

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 APROKAM.

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

There are no studies required for APROKAM.