SUMMARY OF SWISS RISK MANAGEMENT PLAN OF APROKAM (CEFUROXIME SODIUM)

Medicinal product: APROKAM (63029)
Active substance: Cefuroxime sodium
Marketing Authorisation Holder: THEA Pharma S.A.
RMP Version number: EU RMP Version number 3.1
Date: 06 September 2023

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of APROKAM is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the ”Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of APROKAM in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. Thea Pharma S.A. is fully responsible for the accuracy and correctness of the content of the published summary RMP of APROKAM.

I. The medicine and what it is used for

APROKAM is authorised for antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery (see Information for Health Professional 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.

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

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	Routine risk minimisation measures: • Information for Health professional: Undesirable effects and Overdose • 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: • Information for Health professional: Posology and method of administration and Special remarks • 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 – DiezAlvarez 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: • Information for Health professional: Warnings and precautions for use and Overdose. • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

Missing information – Use in paediatric population	
Risk minimisation measures	Routine risk minimisation measures: • Information for Health professional: Posology/Method of administration. • Prescription only medicine • Use only by ophthalmologist • Restricted use in hospital

C. Post-authorisation development plan

1. Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorisation or specific obligation of APROKAM.

2. Other studies in post-authorisation development plan

There are no studies required for APROKAM.