VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

The medicinal product APROKAM is a sterile ophthalmic powder for solution for injection in the anterior chamber of the eye, containing cefuroxime as active substance.

Cefuroxime (as cefuroxime sodium) belongs to a group of antibiotics called cephalosporins. Antibiotics are used to kill the bacteria or «germs» that cause infections.

This medicine will be used if the patient is undergoing eye surgery because of cataract (cloudiness of the lens) in order to prevent eye infection.

Cataract is the most important cause of visual impairment and decreased mobility in the elderly. Cataract extraction with intra-ocular lens implantation is the most commonly performed surgical procedure in the elderly population in Europe.

Cataract surgery is usually successful in restoring failing eyesight and technical advances have enhanced the efficacy of the procedure but it is also responsible for permanent and significant loss of vision resulting from severe postoperative eye infection such as endophthalmitis.

Endophthalmitis is an inflammatory reaction occurring as a result of intraocular colonisation by bacteria, fungi or rarely parasites.

The medicine can only be obtained with a prescription and used, after reconstitution, by an ophthalmic surgeon in the recommended aseptic conditions of cataract surgery.

The recommended dose is one injection in the anterior chamber of the eye of 1 mg cefuroxime in 0.1 mL saline solution at the end of cataract surgery.

VI.2.2 Summary of treatment benefits

The company provided complete review of the worldwide clinical experience with intracameral cefuroxime in the prophylaxis of endophthalmitis already used for more than 10 years. The particular Swedish experience is reported due to the use of this antibiotic as a standard protocol together with the results of the pivotal European study carried out by the ESCRS in more than 16,000 patients using a well-designed methodology. A search of PubMed was performed and all the articles published until December 2010 including cefuroxime and specific issues such as pharmacodynamics/pharmacokinetics/clinical trials carried out in the proposed indication/side effects in the title and abstract, were selected then analysed.

VI.2.3 Unknowns relating to treatment benefits

Overall, the patients enrolled in the pivotal clinical trial (ESCRS study) represent the population that would expect to receive cefuroxime, with the exception of children, pregnant women, patients allergic to penicillins and cephalosporins and special patient groups (patients with severe risk of infection, patients with complicated cataracts, patients having combined operations with cataract surgery, patients with severe thyroid disease, patients with less 2,000 corneal endothelial cells).

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Allergic reactions (Hypersensitivity)	Serious allergic reactions to cefuroxime are rare but higher in patients with a known allergy to penicillin.	Yes, by avoiding use of cefuroxime in patients with hypersensitivity to cefuroxime or to the cephalosporins group of antibiotics, or with a tendency to develop allergies and asthma. Special care is indicated in patients who have experienced an allergic reaction to penicillins or any other beta-lactam antibiotics as cross-reactions may occur. Also by monitoring for early symptoms.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Risk of retinal toxicity (macular oedema)	Risks of retinal and corneal toxicity can occur during cataract surgery and can be due to medication errors and off label use: • dilution error: overdose – use of inappropriate solvent – injection of visible particles, • injection via unapproved route, • use in unapproved population and surgery.
Risk of corneal toxicity (corneal endothelial cell loss)	
Risk of medication error (inappropriate dilution of medication)	
Risk of off label use	

Missing information

Risk	What is known
Use in children	Reports of use of cefuroxime in children undergoing cataract surgery for congenital or developmental cataract were published. Fibrinous uveitis is a common complication during the post early postoperative period in pediatric eyes undergoing cataract surgery due to increased reactivity in children. In Sweden, Cefuroxime is being routinely used in children but there is no available data on this population.
Use in special patient groups (patients with severe risk of infection, patients with complicated cataracts, patients having combined	Absence of data. APROKAM should only be used after careful risk/benefit assessment.

Risk	What is known
operations with cataract surgery, patients with severe thyroid disease, patients with less 2,000 corneal endothelial cells)	

VI.2.5 Summary of risk minimisation measures by safety concern

This medicine has a Summary of Product Characteristics (SmPC) which provides physicians (ophthalmologists), pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

An update of section 6.6 of the SmPC has been approved on 10 April 2014 for a clear communication on the reconstitution protocol to prevent incidents (dilution error : overdose – injection of visible particles – use of inappropriate solvent, use via unapproved route or in unapproved surgery or unapproved population). This measure is known as routine risk minimisation measure.

VI.2.6 Planned post authorisation development plan

Not applicable : none was planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
01	14 May 2012	• Allergic reaction (Hypersensitivity) • Risk of retinal toxicity (macular oedema) • Risk of corneal toxicity (Corneal endothelial cell loss) • Risk of medication error (Inappropriate dilution of medication) • Risk of off label use • Use in paediatrics • Use in special patient groups (patients with severe risk of infection, patients with complicated cataracts, patients having combined operations with cataract surgery, patients with severe thyroid disease, patients with less 2,000 corneal endothelial cells)	First version of the RMP
02	30 July 2015	*No new safety concern* • Allergic reaction (Hypersensitivity) • Risk of retinal toxicity (Macular oedema)	Update of section 6.6 of the SmPC in order to

Version	Date	Safety Concerns	Comment
		• Risk of corneal toxicity (Corneal endothelial cell loss) • Risk of medication error (Inappropriate dilution of medication) • Risk of off label use • Use in paediatrics • Use in special patient groups (Patients with severe risk of infection, patients with complicated cataracts, patients having combined operations with cataract surgery, patients with severe thyroid disease, patients with less 2,000 corneal endothelial cells)	harmonise the administration instructions for Aprokam across relevant guidelines and treatment recommendations as well as clinical practice and harmonisation of the RMP with legislation (new format of the RMP)
02.1	30 December 2015	*No new safety concern*	Answer to question raised by Health Authorities on 10 December 2015