Part VI: Summary of the risk management plan by product - VERKAZIA

VI.1 Summary of risk management plan for VERKAZIA

This summary of the RMP for VERKAZIA should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. The medicine and what is it used for

VERKAZIA® 1mg/ml, eye drops, emulsion is authorised for Treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents (see SmPC for the full indication). It contains ciclosporin as the active substance and it is given by ocular route.

Further information about the evaluation of VERKAZIA®'s benefits can be found in VERKAZIA®'s EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage (https://www.ema.europa.eu/medicines/human/EPAR/verkazia).

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

II.A List of important risks and missing information

Important risks of VERKAZIA® 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 VERKAZIA®. 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	Peri-ocular skin cancer, conjunctival or corneal neoplasia
Missing information	None

II.B Summary of important risks

PERI-OCULAR SKIN CANCER, CONJUNCTIVAL OR CORNEAL NEOPLASIA	
Evidence for linking the risk to the medicine	The reason to consider peri-ocular skin cancer, conjunctival or corneal neoplasia as a potential risk for ophthalmic ciclosporin is based on scarce information available in literature and general knowledge about the characteristics of immunosuppressive medicines, like ciclosporin. Ciclosporin has already been used for decades as a systemic immunosuppressant for the prevention of graft rejection following organ/tissue transplantation. Ophthalmic formulations of

	ciclosporin (including IKERVIS and hospital formulations in Europe; and a commercial product in the US) have also been widely used without generating evidence to this potential risk in clinical studies or post-marketing use. Additionally, the information available in literature is limited and conflicting and widely related to the systemic use of ciclosporin with significantly higher doses. Thus, there is no evidence that peri-ocular skin cancer, conjunctival or corneal neoplasia would occur in relation to the use of VERKAZIA.
Risk factors and risk groups	Patients with local malignant/pre-malignant conditions in or around the eye.
Risk minimisation measures	VERKAZIA: - Proposed text in section 4.2 with corresponding information in PIL. - Proposed text in section 4.3 with corresponding information in PIL. - Proposed text in section 4.4 with corresponding information in PIL. - Specific follow up form for serious ADRs reported to VERKAZIA
Additional pharmacovigilance activities	FEASIBILITY STUDY FOR VERKAZIA PASS: - A feasibility study for a case-control study linked to existing cancer registries - completed - A PASS study was assessed not to be feasible due to limited number of available patients in databases and only two data sources could identify specifically VKC.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

Not applicable

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

Study **Status**	**Summary of objectives**	**Safety concerns addressed**	**Milestones**
Category 3 Required additional pharmacovigilance activities (by the competent authority)			
FEASIBILITY STUDY FOR VERKAZIA PASS: A feasibility study for a case-control study linked to existing	To understand the data sources and analytic methods available to quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children	Risk of local malignancies: Peri-ocular skin cancer, conjunctival or corneal neoplasia	16 Nov 2018: Submission of PAM protocol 20 Jan 2020: Approval of PAM protocol by EMA 30 Mar 2021: Submission of the study report to EMA 24 Jun 2021: Assessment

cancer registries Completed	treated with Verkazia for VKC.		Report for the PAM by EMA
VERKAZIA PASS: A Phase IV case control study linked to existing cancer registries. Cancelled	To quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia for VKC.		The conduct of this study is conditional, depending on the outcome of the feasibility study: the study was concluded not to be feasible.