Summary of risk management plan for Rhokiinsa (netarsudil)

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

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

This summary of the RMP for Rhokiinsa 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 Rhokiinsa's RMP.

I. The medicine and what it is used for

Rhokiinsa is authorised for the reduction of elevated intraocular pressure in adult patients with primary open-angle glaucoma or ocular hypertension (see SmPC for the full indication). It contains netarsudil as the active substance and it is given via eye drops.

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

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

Important risks of Rhokiinsa together with measures to minimise such risks and the proposed studies for learning more about Rhokiinsa'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;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so as 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 Rhokiinsa is not yet available, it is listed under "missing information" below.

II.A List of important risks and missing information

Important risks of Rhokiinsa 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 Rhokiinsa. 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	• Damage to the corneal and conjunctival epithelium due to use of eye drops containing preservatives
Missing information	• Use in Pregnancy and lactating//breastfeeding women • Long term safety of netarsudil (beyond 12 months) • Use in patients with compromised corneal epithelium

II.B Summary of important risks

Important potential Risk: Damage to the corneal and conjunctival epithelium due to use of eye drops containing preservatives	
Evidence for linking the risk to the medicine	The formulation is packaged as a multi-dose product and preserved with benzalkonium chloride (BAK) as the preservative of choice. BAK has demonstrated toxic effects in laboratory, experimental, and clinical studies.
Risk factors and risk groups	Any substance instilled into the eye, whether it is an active agent, preservative, or inactive ingredient, has the potential for inducing at least some cellular toxicity and ocular surface changes in the patient population. With long-term use, eye drops containing preservatives may result in corneal or conjunctival damage depending on the duration and frequency of use.

Risk minimisation measures	Care should therefore be taken to avoid the long-term use of preservatives. SmPC section 4.4 Special warnings and precautions for use (guidance with respect to the potential effects of benzalkonium chloride) Patient Information Leaflet Section 2 What you need to know before you use Rhokiinsa (guidance with respect to the potential effects of benzalkonium chloride) Legal status: Restricted medical prescription. There are no additional risk minimisation measures planned.

Missing information: Use in Pregnancy, lactating and breastfeeding women	
Risk minimisation measures	Routine risk minimisation measures • SmPC section 4.6 Fertility, Pregnancy and Lactation (guidance with respect to the lack of data in pregnancy and breastfeeding). • Patient Information Leaflet Section 2 What you need to know before you use Rhokiinsa (guidance with respect to the lack of data in pregnancy and breastfeeding). Legal status: Restricted medical prescription. There are no additional risk minimisation measures.

Missing information: Long-term safety of netarsudil (beyond 12 months)	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.4 Special warnings and precautions for use (guidance with respect to lack of data beyond 12 months) Legal status: Restricted medical prescription. There are no additional risk minimisation measures.
Additional pharmacovigilance activities	Post-authorisation safety study: observational cohort study.

Missing information: Use in patients with compromised corneal epithelium	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 5.1 Pharmacodynamic properties (guidance with respect to lack of data in patients with compromised corneal epithelium*)* Legal status: Restricted medical prescription. There are no additional risk minimisation measures.
Additional pharmacovigilance activities	Post-authorisation safety study: observational cohort study.

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.

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

Non-interventional (Observational cohort) study

Purpose of the study:

This non-interventional (observational cohort) study aims to collect additional ocular safety of Rhokiinsa in adult patients under routine prescribed conditions over a 2-year period. Primary evaluation will focus on ocular safety at each time point (approximately 6 monthly intervals), recording the number, percentage and severity of each category of event.