Part VI: Summary of the risk management plan

Summary of risk management plan for NAKAFRI. This is a summary of the risk management plan (RMP) for NAKAFRI. The RMP details important risks of NAKAFRI how these risks can be minimised, and how more information will be obtained about NAKAFRI's risks and uncertainties (missing information). NAKAFRI's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how NAKAFRI should be used.

I. The medicine and what it is used for

NAKAFRI is authorised for the regular treatment of nasal polyps and associated symptoms of nasal obstruction.

It contains Fluticasone propionate as the active substance and it is given by intranasal route of administration (nasal drops suspension).

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

Important risks of NAKAFRI, together with measures to minimise such risks and the proposed studies for learning more about NAKAFRI'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 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*.

If important information that may affect the safe use of NAKAFRI is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of NAKAFRI are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 NAKAFRI. 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);

Summary of safety concerns	
Important identified risks	- Drug-interaction with CYP3A4 inhibitors - Eye disorders (Cataract, glaucoma and chorioretinopathy)
Important potential risks	- Systemic effects (Cushing´s syndrome, adrenal suppression)
Missing information	- Pregnancy and lactation - Paediatric population (children less than 16 years)

II.B Summary of important risks

Important identified risk: Drug-interaction with CYP3A4 inhibitors	
Evidence for linking the risk to the medicine	Is a known adverse reaction of corticosteroids
Risk factors and risk groups	Patients who took drugs CYP3A4 inhibitors
Risk minimisation measures	**Routine risk minimisation measures** SmPC *section 4.4 and 4.5* PIL *section 2* **Additional risk minimisation measures** No risk minimisation measures

Important identified risk: Eye disorders (Cataract, glaucoma and chorioretinopathy)	
Evidence for linking the risk to the medicine	Severe adverse reactions occurring with high frequency in the targeted population that could have a severe impact on the patient.
Risk factors and risk groups	The population can be divided into two general groups: a minority called 'steroid responders' who exhibit this response in a mild or severe form, and a majority in whom treatment with corticosteroids does not result in elevation of IOP. In general, the ability of a particular corticosteroid to induce elevation of IOP is proportional to several factors:

	its anti-inflammatory potency, the dosage of the drug, and duration of treatment. Interestingly, the formulation may also influence the ocular hypertensive property of the agent. Most evidence suggests that the cause of corticosteroid-induced hypertension is a reduction in outflow of aqueous fluid through the trabecular meshwork in the anterior chamber of the eye in susceptible individuals.
Risk minimisation measures	**Routine risk minimisation measures** SmPC *section 4.4 and 4.8* PIL *section 4* **Additional risk minimisation measures** No risk minimisation measures

Important potential risk: Systemic effects (Cushing´s syndrome, adrenal suppression)	
Evidence for linking the risk to the medicine	Is a known adverse reaction of corticosteroids
Risk factors and risk groups	Prolonged treatment of patients with high doses of corticosteroids may result systemic effect: adrenal suppression and Cushing's syndrome. The frequency of their occurrence is not well known although it is said that suppression of hypothalamic–pituitary–adrenal function by chronic administration of corticosteroids is the most common cause of adrenal insufficiency.
Risk minimisation measures	**Routine risk minimisation measures** SmPC *section 4.4* PIL *section 4* **Additional risk minimisation measures** No risk minimisation measures

Missing Information: Pregnancy and lactation	
Risk minimisation measures	**Routine risk minimisation measures** None **Additional risk minimisation measures** No risk minimisation measures

Missing Information: Paediatric population (children less than 16 years)	
Risk minimisation measures	**Routine risk minimisation measures** None **Additional risk minimisation measures** No risk minimisation measures

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 NAKAFRI

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

There are no studies required for NAKAFRI.