PART VI: Summary of the risk management plan

Summary of risk management plan for Tolak 40mg/g (5-FU 4% cream) (5-Fluorouracil)

This is a summary of the risk management plan (RMP) for Tolak 40mg/g (5-FU 4% cream). The RMP details important risks of Tolak 40mg/g (5-FU 4% cream), how these risks can be minimised, and how more information will be obtained about Tolak 40mg/g (5-FU 4% cream)'s risks and uncertainties (missing information).

Tolak 40mg/g (5-FU 4% cream)'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tolak 40mg/g (5-FU 4% cream) should be used.

Important new concerns or changes to the current ones will be included in updates of Tolak 40mg/g (5-FU 4% cream)'s RMP.

I. The medicine and what it is used for

Tolak 40mg/g (5-FU 4% cream) is indicated for the topical treatment of actinic keratosis lesions of the face, ears, and/or scalp. Tolak is indicated in adults only (see SmPC for the full indication).

It contains 5-fluorouracil as the active substance and it is given topically (40.0 mg of fluorouracil per gram (4%))

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

Important risks of Tolak 40mg/g (5-FU 4% cream), together with measures to minimise such risks and the proposed studies for learning more about Tolak 40mg/g (5-FU 4% cream)'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.

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 Tolak 40mg/g (5-FU 4% cream) is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Tolak 40mg/g (5-FU 4% cream) 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 Tolak 40mg/g (5-FU 4% cream). 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	• None
Important potential risks	• Toxicity in patients with severe dihydropyrimidine dehydrogenase (DPD) deficiency •
Missing information	• None

II.B Summary of important risks

Important potential risk 1- Toxicity in patients with severe dihydropyrimidine dehydrogenase (DPD) deficiency	
Evidence for linking the risk to the medicine	This potential risk is based on the known role of DPD in catabolism of fluorouracil and potential consequences for patients (partially) lacking this enzyme. The exaggerated fluorouracil toxicities may include mucositis, hair loss, diarrhoea, neutropenia, skin rash, and neurologic toxicities based on the experience with systemic fluorouracil. Evidence is supported by the data published in the scientific literature.
Risk factors and risk groups	Beside DPD deficiency itself, the risk factors include increased absorption of fluorouracil because of severe widespread erosion and ulceration of the skin surface, thinner skin than usual, low body mass, and prolonged exposure to the drug.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PL section 4.2
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

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 Tolak 40mg/g (5-FU 4% cream).

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

There are no studies required for Tolak 40mg/g (5-FU 4% cream).