Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for Tacforius (tacrolimus) 0.5 mg, 1 mg, 3 mg and 5 mg prolonged-release hard capsules

This is a summary of the risk management plan (RMP) for Tacforius (tacrolimus) 0.5 mg, 1 mg, 3 mg and 5 mg prolonged-release hard capsules (hereinafter referred to as Tacrolimus). The RMP details important risks of Tacrolimus, how these risks can be minimised, and how more information will be obtained about Tacrolimus's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Tacforius (tacrolimus) 0.5 mg, 1 mg, 3 mg and 5 mg prolonged-release hard capsules are authorised for:

- Prophylaxis of transplant rejection in adult kidney or liver allograft recipients;
- Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients (see SmPC for the full indication).

They contain Tacrolimus as the active substance and they are taken orally.

Further information about the evaluation of Tacrolimus's benefits can be found in Tacrolimus'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/tacforius.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Tacrolimus, together with measures to minimise such risks and the proposed studies for learning more about Tacrolimus'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, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of Important Risks and Missing Information

Important risks of Tacrolimus 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 Tacrolimus. 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).

Table 1: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Malignant neoplasms • Serious infections and reactivation of pre-existing infections • Medication errors resulting in under or over exposure to tacrolimus-containing medicinal products with potentially serious consequences • Interaction with other medication and herbal drugs • Ventricular hypertrophy • Cardiomyopathies • Use during pregnancy • Use during lactation
Important potential risks	• None
Missing information	• None

II.B Summary of Important Risks

Table 2: Summary of Pharmacovigilance Activities and Additional Risk Minimisation Activities by Safety Concern

Important identified risk: Malignant neoplasms	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL sections 2 and 4. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.
Important identified risk: Serious infections and reactivation of pre-existing infections	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL section 4. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.
Important identified risk: Medication errors resulting in under or over exposure to tacrolimus-containing medicinal products with potentially serious consequences	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2, 4.4 and 4.8. PL sections 2 and 3. Medicinal product subject to restricted medical prescription. Labelling measures: The terms ‘prolonged-release’ and ‘once daily’ are prominent on the blister, aluminium wrap and outer carton. Additional risk minimisation measures None.
Important identified risk: Interaction with other medication and herbal drugs	
Risk minimisation measures	Routine risk minimisation measures Risk is addressed in SmPC sections 4.2, 4.4 and 4.5. Addressed in PL section 2. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.
Important identified risk: Ventricular hypertrophy	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL section 4. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.

Important identified risk: Cardiomyopathies	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL section 4. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.
Important identified risk: Use during pregnancy	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.6 and 5.3. PL section 2. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures None.
Important identified risk: Use during lactation	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.6 and 5.3. PL section 2. Medicinal product subject to restricted medical prescription. Additional risk minimisation measures 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 Tacrolimus.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Tacrolimus.