Part VI: Summary of the risk management plan (RMP) – Tacrolimus, 0.5 mg, 0.75 mg, 1 mg, 2 mg and 5 mg, hard capsule and 0.5 mg, 1 mg, 2 mg, 3 mg and 5 mg, Prolonged-release hard capsule

This is a summary of the RMP for tacrolimus, 0.5 mg, 0.75 mg, 1 mg, 2 mg and 5 mg, hard capsule and 0.5 mg, 1 mg, 2 mg, 3 mg and 5 mg, prolonged-release hard capsule. The RMP details important risks of tacrolimus hard capsule and prolonged-release hard capsule, how these risks can be minimized, and how more information will be obtained about tacrolimus's risks and uncertainties (missing information).

Tacrolimus hard capsule and prolonged-release hard capsule's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals (HCPs) and patients on how tacrolimus hard capsule and prolonged-release hard capsule should be used.

Important new concerns or changes to the current ones will be included in updates of the tacrolimus hard capsule and prolonged-release hard capsule's RMP.

9.1 Part VI: I. The medicine and what it is used for

Tacrolimus hard capsule and prolonged-release hard capsule are immunosuppressants (drugs or medicines that lower the body's ability to reject a transplanted organ) and are used to control
body's immune response which tries to reject the new organ, enabling the body to accept the transplanted organ. Also, these can be used for an ongoing rejection of transplanted liver, kidney, heart or other organ when any previous treatment was unable to control this immune response after the transplantation.
It contains tacrolimus as active substances and is given orally as hard capsule (0.5 mg, 0.75 mg, 1 mg, 2 mg and 5 mg) and prolonged-release hard capsule (0.5 mg, 1 mg, 2 mg, 3 mg and 5 mg).

Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of tacrolimus hard capsule and prolonged-release hard capsule, together with measures to minimize such risks are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and HCPs;
- Important advice on the medicine's packaging;
- The authorized 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 minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Reports (PSURs) assessment (if applicable) 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 tacrolimus hard capsule and prolonged-release hard capsule is not yet available, it is listed under 'missing information' below.

9.2.1 Part VI – II.A: List of important risks and missing information

Important risks of tacrolimus hard capsule and prolonged-release hard capsule are risks that need special risk management activities to further investigate or minimize 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 hard capsule and prolonged-release hard capsule. 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 9-1 List of important risks and missing information

Important identified risks	Medication errors
	Hypertension
	Torsade de Pointes
	Cardiac arrhythmias
	Prolonged QT interval
	Ventricular hypertrophy
	Cardiomyopathies
	Neurological and visual disorders
	Diabetogenicity
	Electrolyte changes
	Galactose intolerance
	Hepatic dysfunction
	Renal dysfunction
	Blood cell count changes
	Coagulopathies
	Use during pregnancy and lactation
	Gastrointestinal (GI) perforation
	Diarrhea
	Neoplasms
	Serious infections and reactivation of pre-existing infections
	Pure red cell aplasia (PRCA)
Important potential risks	Interaction with Mycophenolate mofetil (MMF)
Missing information	None

9.2.2 Part VI – II.B: Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

9.2.3 Part VI – II.C: Post-authorization development plan

9.2.3.1 II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of tacrolimus hard capsule and prolonged-release hard capsule.

9.2.3.2 II.C.2. Other studies in post-authorization development plan

There are no studies required for tacrolimus hard capsule and prolonged-release hard capsule.