Summary of risk management plan for Rapamune (sirolimus)

This is a summary of the Risk Management Plan (RMP) for Rapamune. The RMP details the important identified risk of Rapamune, how this risk can be minimised and how more information will be obtained about Rapamune uncertainties (missing information).

The Rapamune summary of product characteristics (SmPC) and its patient information leaflet give essential information to healthcare professionals and patients on how Rapamune should be used.

This summary of the RMP for Rapamune 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 the RMP for Rapamune.

I. The medicine and what it is used for

Rapamune is currently authorised for the prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving a renal transplant. The MAH is seeking an indication for the treatment of patients with sporadic LAM with moderate lung disease or declining lung function. The medicine contains sirolimus as the active substance and it is given orally.

Further information about the evaluation of the benefits of sirolimus can be found in the EPAR for SRL, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

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

The important risk of Rapamune together with measures to minimise this risk and the proposed studies for learning more about Rapamune's risks, are outlined below.

Measures to minimise 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 public (eg, 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 events is collected continuously and regularly analysed, including Periodic Safety Update Report (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 SRL is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Rapamune 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 Rapamune. 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 risk	Malignancy
Important potential risk	None
Missing information	Long term safety in patients with sporadic LAM

LAM - lymphangioleiomyomatosis

II.B. Summary of Important Risks

Important identified risk: Malignancy

Evidence for linking the risk to the medicine	Malignancy has been reported with the use of immunosuppressant medications such as sirolimus.
Risk factors and risk groups	All patients on immunosuppressant agents may be at an increased risk of malignancy. The risk of malignancy also depends on the immunosuppressant used. Patients on CNIs may have an increased incidence of malignancy compared to those on sirolimus. Unintended transmission of malignant cells from a donor, although rare, may also result in cancer in the immunosuppressed transplant recipient.
Risk minimisation measures	Routine risk minimisation measures None Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Missing Information

Risk minimisation measures	Routine risk minimisation measures SmPC section 4.2 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	A population-based cohort study to monitor the safety and effectiveness of sirolimus use among patients with sporadic lymphangioleiomyomatosis (LAM).

UK – United Kingdom; US – United States

II.C. Post-authorisation development plan

II.C.1. Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorisation:

- Category 1 (imposed mandatory additional pharmacovigilance activities which are conditions of the marketing authorisation): None
- Category 2 (imposed mandatory additional pharmacovigilance activities which are Specific Obligations in the context of a conditional marketing authorisation or a marketing authorisation under exceptional circumstances): None

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

Category 3 (required additional pharmacovigilance activities): 1 (pending)

Study short name: A population-based cohort study to monitor the safety and effectiveness of sirolimus use among patients with sporadic lymphangioleiomyomatosis (LAM).

Purpose of the study: To further understand and characterise the safety profile of long term sirolimus use in the sporadic LAM population within the clinical practice setting.