6.1 Part V.1. Routine risk minimization measures

N/A

6.2 Part V.2. Additional Risk minimization measures

Routine risk minimization activities as described in Part V.1 are sufficient to manage the safety concerns of the medicinal product.

6.3 Part V.3. Summary of risk minimization measures

N/A

7 Part VI: Summary of the risk management plan (Everolimus, 0.25 mg, 0.5 mg, 0.75 mg and 1.0 mg, Tablets)

This is a summary of the risk management plan (RMP) for everolimus. The RMP details important risks of everolimus, how these risks can be minimized, and how more information will be obtained about everolimus' risks and uncertainties (missing information).

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

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

Everolimus is authorized for prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic renal or cardiac transplant (should be used in combination with ciclosporin and corticosteroids) or in adult patients receiving a hepatic transplant (should be used in combination with tacroliums and corticosteroids). It contains everolimus as the active substance and it is given orally, in the form of 0.25 mg, 0.5 mg, 0.75 mg and 1.0 mg, tablets.

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

Important risks of everolimus, 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 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 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 analysed, including Periodic Safety Update Report 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 everolimus is not yet available, it is listed under 'missing information' below.

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

Important risks of everolimus 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 everolimus. 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 7-1 List of important risks and missing information

Important identified risks	Everolimus and calcineurin inhibitor (CNI) induced renal dysfunction
	Proteinuria
	Wound-healing complications
	Hyperlipidemia
	Renal graft thrombosis
	New onset diabetes mellitus (NODM)
	Thrombotic microangiopathies (TMA)
	Interstitial lung disease (ILD)
	Infections
	Malignancies
	Angioedema
	Edema (including peripheral edema)
	Venous thrombosis
	Interaction with inhibitors/ inducers of CYP3A4 and P-gP (e.g. ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin, ritonavir,rifampicin, rifabutin, carbamazepine, phenytoin, pimozide, astemizole, cisapride, quinidine and ergot alkaloid derivatives)
Important potential risks	Impaired male fertility
	Teratogenicity
Missing information	Exposure during pregnancy and lactation
	Use in pediatric population
	Severe liver function impairment
	Patients at high immunological risk
	Use of everolimus with immunosuppressive agents other than ciclosporin, basiliximab, tacrolimus and corticosteroids

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

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

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

7.2.3.1 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 everolimus.

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

There are no studies required for everolimus.