Part VI: Summary of the risk management plan

Summary of risk management plan for Fingolimod SDZ 0,5 mg, harde capsules and Inzolfi 0,5 mg, harde capsules (Fingolimod hydrochloride)

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

Fingolimod SDZ and Inzolfi summary of product characteristics (SmPCs) and its Package Leaflets (PLs) give essential information to Healthcare Professionals (HCP) and patients on how Fingolimod SDZ and Inzolfi should be used.

Important new concerns or changes to the current ones will be included in updates of the Fingolimod SDZ and Inzolfi RMP.

I. The medicine and what it is used for

Fingolimod SDZ and Inzolfi are authorised for:

Fingolimod SDZ and Inzolfi is indicated as single disease modifying therapy in highly active relapsing-remitting Multiple Sclerosis (MS) for the following groups of adult patients and paediatric patients aged 10 years and older:

- Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy.

or

- Patients with rapidly evolving severe relapsing-remitting MS defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain Magnetic Resonance Imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI.

It contains fingolimod hydrochloride as an active substance and it is given orally.

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

Important risks of Fingolimod SDZ and Inzolfi, together with measures to minimise such risks and the proposed studies for learning more about Fingolimod SDZ and Inzolfi 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 PLs and SmPCs addressed to patients and HCPs;

- 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 the case of the Fingolimod SDZ and Inzolfi, these measures are supplemented with *additional risk minimisation measure* mentioned under relevant important risks, below.

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*.

If important information that may affect the safe use of Fingolimod SDZ and Inzolfi is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Fingolimod SDZ and Inzolfi 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 Fingolimod SDZ and Inzolfi. 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 risks	Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose
	Liver transaminase elevation
	Macular edema
	Opportunistic infections, including progressive multifocal leukoencephalopathy (PML), varicella zoster virus (VZV), herpes viral infections other than VZV, fungal infection
	Reproductive toxicity
	Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma)
	Lymphoma
Important potential risks	Other malignant neoplasms

List of important risks and missing information	
Missing information	Long-term use in paediatric patients, including impact on growth and development (including cognitive development)

II.B Summary of important risks

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

Important identified risk: Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.3, 4.4, 4.5 and 4.8. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

Important identified risk: Liver transaminase elevation	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.2, 4.3, 4.4, 4.8 and 5.2. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

Important identified risk: Macular edema	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.4 and 4.8. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients:

	-Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

Important identified risk: Opportunistic infections including PML, VZV, herpes viral infections other than VZV, fungal infection	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.3, 4.4 and 4.8. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

Important identified risk: Reproductive toxicity	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.3, 4.4 and 4.6. PL section 2. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide. -Pregnancy-specific patient reminder card.

Important identified risk: Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.4 and 4.8. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

Important identified risk: Lymphoma	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.3, 4.4, 4.5 and 4.8. PL sections 2 and 4. Legal status: Prescription only. **Additional risk minimisation measures:** None.

Important potential risk: Other malignant neoplasms	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section 4.4. PL section 2. Legal status: Prescription only. **Additional risk minimisation measures:** None.

Missing information: Long-term use in paediatric patients, including impact on growth and development (including cognitive development)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections 4.2 and 5.2. Legal status: Prescription only. **Additional risk minimisation measures:** Educational materials for physicians and patients: -Physician's checklist for adult and paediatric population. -Patient/Parent/Caregiver guide.

II. 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 Fingolimod SDZ and Inzolfi.

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

There are no studies required for Fingolimod SDZ and Inzolfi.