Part VI: Summary of the risk management plan

Summary of risk management plan for Fingolimod 0.5 mg hard capsules

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

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

I. The medicine and what it is used for

Fingolimod 0.5 mg hard capsules are authorised for:

as single disease modifying therapy in highly active relapsing remitting multiple sclerosis 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 multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.

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

Important risks of Fingolimod, together with measures to minimise such risks, are outlined below.

In the case of Fingolimod, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

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

II.A List of important risks and missing information

Table 1

Summary of safety concerns	
Important identified risks	• Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose • Hypertension • Liver transaminase elevation • Posterior reversible encephalopathy syndrome (PRES) • Macular oedema • Infections, including opportunistic infections (PML, VZV, herpes viral infections other than VZV, fungal infection • Reproductive toxicity • Bronchoconstriction • Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma) • Convulsions
Important potential risks	• Acute disseminated encephalomyelitis- like (ADEM-like) events • Lymphoma • Other malignant neoplasm • Thrombo-embolic events • QT interval prolongation
Missing information	• Long-term use in paediatric patients, including impact on growth and development (including cognitive development) • Elderly patients (≥65 years) • Lactating women • Patients with diabetes mellitus • Patients with cardiovascular conditions including myocardial infarction, angina pectoris, Raynaud's phenomenon, cardiac failure or severe cardiac disease, increased QTc interval, uncontrolled hypertension, patients at risk for bradyarrhythmia and who may not tolerate bradycardia, patients with second degree Mobitz type 2 or higher AV block, sick-sinus syndrome, sino-artrial heart block, history

Summary of safety concerns	
	of cardiac arrest, cerebrovascular disease and severe sleep apnea • Long term risk of cardiovascular morbidity/mortality • Long term risk of malignant neoplasms • Unexplained death • Switch from other disease modifying therapy

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

II.B Summary of important risks

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 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide
Important Identified Risk: Hypertension	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8 Additional risk minimisation measures: None
Important Identified Risk: Liver transaminase elevation	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3, 4.4, 4.8, and 5.2 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide
Important Identified Risk: Posterior reversible encephalopathy syndrome (PRES)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8

	Additional risk minimisation measures: None
Important Identified Risk: Macular oedema	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide
Important Identified Risk: Infections, including opportunistic infections (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 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide
Important Identified Risk: Reproductive toxicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Pregnancy specific patient reminder card
Important Identified Risk: Bronchoconstriction	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8 and 5.1 Additional risk minimisation measures: None
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 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide
Important Identified Risk: Convulsions	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 Additional risk minimisation measures: educational material for physicians and patients: • Physician's checklist • Patient/Parent/Caregiver guide

Important potential Risk: Acute disseminated encephalomyelitis- like (ADEM-like) events	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8 Additional risk minimisation measures: None
Important potential Risk: Other malignant neoplasm	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 Additional risk minimisation measures: None
Important potential Risk: Thrombo-embolic event	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8 Additional risk minimisation measures: None
Important potential Risk: QT interval prolongation	

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.9 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 Fingolimod.

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

There are no studies required for Fingolimod.