Part VI: Summary of the risk management plan

RMP Part VI is valid for all products in this RMP, Fingolimod Devatis 0.25 mg harde capsules / Fingolimod Devatis 0.25 mg Hartkapseln and Fingolimod Devatis 0.5 mg harde capsules / Fingolimod Devatis 0.5 mg Hartkapseln.

Summary of risk management plan for Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln (fingolimod)

This is a summary of the risk management plan (RMP) for Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln. The RMP details important risks of Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln, how these risks can be minimised, and how more information will be obtained about Fingolimod Devatis's risks and uncertainties (missing information).

Fingolimod Devatis' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln should be used.

Important new concerns or changes to the current ones will be included in updates of Fingolimod Devatis' RMP.

I. The medicine and what it is used for

Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln is authorised for the following groups of adult patients and paediatric patients aged 10 years and older in the EEA (see SmPC for the full indication): 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. It contains fingolimod (a sphingosine-1-phosphate (S1P) receptor modulator) as the active substance and it is given by oral hard capsule (see SmPC for the full indication).

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

Important risks of Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln, together with measures to minimise such risks and the proposed studies for learning more about Fingolimod Devatis' 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 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 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 Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln, these measures are supplemented with *additional risk minimisation measures* 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*.

Information about birth outcome in patients who have become pregnant will be collected continuously and regularly analysed so that immediate action can be taken as necessary.

Event-specific follow-up questionnaires are included for the important identified risks: Bradyarrhythmia, Liver transaminase elevation, Macular oedema, Opportunistic infections including PML, VZV, herpes viral infections other than VZV, fungal infection, Skin cancer, Reproductive toxicity, Convulsions, Lymphoma and Other malignant neoplasms. These questionnaires and risks are in line with the reference medicinal product.

If important information that may affect the safe use of Fingolimod Devatis 0.25 mg / 0.5 mg hard capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Fingolimod Devatis 0.25 mg / 0.5 mg hard capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln 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 Devatis 0.25 mg / 0.5 mg hard capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln. 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 (long term use in paediatric patients, elderly patients, lactating women, patients with diabetes mellitus, patients with cardiovascular conditions, long-term risk of cardiovascular morbidity/mortality, long-term risk of malignant neoplasms, unexplained death, and switch from other disease modifying therapy).

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 oedema; • Opportunistic infections including PML, 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);

List of important risks and missing information	
	• Convulsions; • Lymphoma.
Important potential risks	• Other malignant neoplasms.
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 reference medicinal 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 section 2* Additional risk minimisation measures *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder 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* Additional risk minimisation measures: *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder guide*
Important identified risk: Macular oedema	
Risk minimisation measures	Routine risk minimisation measures *SmPC sections 4.4 and 4.8* *PL sections 2 and 4* Additional risk minimisation measures *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population*

	- *Patient/Parent/Caregiver reminder 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* Additional risk minimisation measures *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder 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* Additional risk minimisation measures *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder 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* Additional risk minimisation measures: *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder guide*
Important identified risk: Convulsions	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.4 (paediatric patients) and 4.8* *PL section 2* Additional risk minimisation measures:

	Educational materials for physicians and patients: - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder guide*
Important identified risk: Lymphoma	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.8 and 5.3* *PL section 4* Additional risk minimisation measures: No additional risk minimisation measures
Important potential risk: Other malignant neoplasms	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4* Additional risk minimisation measures: No additional risk minimisation measures
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* Additional risk minimisation measures: *Educational materials for physicians and patients:* - *Physician's checklist for adult and paediatric population* - *Patient/Parent/Caregiver reminder guide*

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 Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln.

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

There are no studies required for Fingolimod Devatis 0.25 mg / 0.5 mg harde capsules / Fingolimod Devatis 0.25 mg / 0.5 mg Hartkapseln.