Part VI: Summary of the risk management plan

Summary of risk management plan for Fingolimod Orion (fingolimod)

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

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

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

I. The medicine and what it is used for

Fingolimod Orion is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis for certain groups of adult patients and paediatric patients aged 10 years and older (see SmPC for the full indication). It contains fingolimod as the active substance and it is given by mouth.

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

Important risks of Fingolimod Orion, together with measures to minimise such risks and the proposed studies for learning more about Fingolimod Orion's 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 Orion, 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*.

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

II.A List of important risks and missing information

Important risks of Fingolimod Orion 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 Orion. 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 • Infections, including opportunistic infections (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) • Convulsions • Lymphoma
Important potential risks	• Other malignant neoplasms
Missing information	• Long-term use in pediatric 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: Information in SmPC sections 4.3, 4.4, 4.5 and 4.8. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

Important identified risk: Liver transaminase elevation	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC sections 4.2, 4.3, 4.4, 4.8 and 5.2. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

Important identified risk: Macular edema	
Risk minimisation measures	Routine risk minimisation measures:

Important identified risk: Macular edema	
	Information in SmPC sections 4.4 and 4.8. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • 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: Information in SmPC sections 4.3, 4.4 and 4.8. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

Important identified risk: Reproductive toxicity	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC section 4.3, 4.4, 4.6. Additional risk minimisation measures: • Physician's checklist for adult and pediatric 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: Information in SmPC sections 4.4 and 4.8. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

Important identified risk: Convulsions	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC sections 4.4 and 4.8. Additional risk minimisation measures:

Important identified risk: Convulsions	
	• Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

Important identified risk: Lymphoma	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC sections 4.8 and 5.3 Additional risk minimisation measures: none

Important potential risk: Other malignant neoplasms	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC section 4.4 Additional risk minimisation measures: none

Missing information: Long-term use in pediatric patients, including impact on growth and development (including cognitive development)	
Risk minimisation measures	Routine risk minimisation measures: Information in SmPC sections 4.2, 4.4, 4.8 and 5.2. Additional risk minimisation measures: • Physician's checklist for adult and pediatric population • Patient/Parent/Caregiver guide

II.C Post-authorisation development plan

There are no studies required for Fingolimod Orion.