Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Fingolimod Glenmark (Fingolimod Hydrochloride)

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

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

I. The medicine and what it is used for

Fingolimod Glenmark is authorised 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 with body weight above 40 kg:

- 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 Magnetic resonance imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI.

It contains fingolimod (as hydrochloride) as the active substance and it is given by oral route.

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

Important risks of Fingolimod Glenmark, together with measures to minimise such risks and the proposed studies for learning more about Fingolimod Glenmark 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 Glenmark, 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, including PSUR assessment (the Marketing Authorisation Holder will perform a review of all the

pregnancy cases received in the PSUR submissions).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 Glenmark is not yet available, it is listed under ‘missing information’ below.

II.A. List of important risks and missing information

Important risks of Fingolimod Glenmark 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 Glenmark. 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 risk(s)	• Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose • Hypertension • Liver transaminase elevation • Posterior Reversible Encephalopathy Syndrome (PRES) • Macular edema • Infections, including opportunistic infections (Progressive Multifocal Leukoencephalopathy [PML], Varicella-zoster Virus [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 risk(s)	• Acute disseminated encephalomyelitis-like (ADEM-like) events • Lymphoma • Other malignant neoplasms • Thrombo-embolic events • QT interval prolongation
Missing information	• Long-term use in paediatric patients, including impact on growth and development (including cognitive development)

List of Important Risks and Missing Information	
	• 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 Atrioventricular [AV] block, sick-sinus syndrome, sino-atrial heart block, history of cardiac arrest, cerebrovascular disease and severe sleep apnoea • Long-term risk of cardiovascular morbidity/mortality • Long-term risk of malignant neoplasms • Unexplained death • Switch from other disease modifying therapy

II.B. Summary of important risk

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	**<u>Routine risk minimisation measures:</u>** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.4: Special warnings and precautions for use • Section 4.5: Interaction with other medicinal products and other forms of interaction • Section 4.8: Undesirable effects **Patient Information Leaflet (PIL)** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **<u>Additional risk minimisation measures:</u>** 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	**<u>Routine risk minimisation measures:</u>** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.2: Posology and method of administration • Section 4.3: Contraindications • Section 4.4: Special warnings and precautions for use • Section 4.8: Undesirable effects • Section 5.2: Pharmacokinetic properties **PIL** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **<u>Additional risk minimisation measures:</u>** Educational materials for physicians and patients: • Physician's checklist for adult and paediatric population • Patient/Parent/Caregiver guide

Important Identified Risk – Macular oedema	
Risk minimisation measures	**<u>Routine risk minimisation measures:</u>** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.4: Special warnings and precautions for use • Section 4.8: Undesirable effects **PIL** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **<u>Additional risk minimisation measures:</u>** Educational materials for physicians and patients: • Physician's checklist for adult and paediatric 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:** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.3: Contraindications • Section 4.4: Special warnings and precautions for use • Section 4.8: Undesirable effects **PIL** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **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:** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.3: Contraindications • Section 4.4: Special warnings and precautions for use • Section 4.6: Fertility, pregnancy and lactation **PIL** • Section 2: What you need to know before you take fingolimod **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	**<u>Routine risk minimisation measures:</u>** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.4: Special warnings and precautions for use • Section 4.8: Undesirable effects **PIL** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **<u>Additional risk minimisation measures:</u>** 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	**<u>Routine risk minimisation measures:</u>** The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.4: Special warnings and precautions for use • Section 4.8: Undesirable effects **PIL** • Section 2: What you need to know before you take fingolimod • Section 4: Possible side effects **<u>Additional risk minimisation measures:</u>** Educational materials for physicians and patients: • Physician's checklist for adult and paediatric population • Patient/Parent/Caregiver guide

Missing Information – Long-term use in paediatric patients, including impact on growth and development (including cognitive development)	
Risk minimisation measures	**<u>Routine risk minimisation measures:</u>**

Missing Information – Long-term use in paediatric patients, including impact on growth and development (including cognitive development)	
	The information regarding this safety concern is mentioned in the following section(s): **SmPC** • Section 4.2: Posology and method of administration • Section 4.4: Special warnings and precautions for use • Section 5.2: Pharmacokinetic properties **PIL** No information is provided in PIL. **<u>Additional risk minimisation measures:</u>** Educational materials for physicians and patients: • Physician's checklist for adult and paediatric population • Patient/Parent/Caregiver 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 Glenmark.

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

There are no studies required for Fingolimod Glenmark