

## VI.1 Summary of risk management plan for Gaxenim hard capsules (fingolimod)

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

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

Important new concerns or changes to the current ones will be included in updates of Gaxenim hard capsules' RMP.

### 1.1.1. I. The medicine and what it is used for

Gaxenim hard capsules is authorised for the treatment of as single disease modifying therapy in highly active relapsing remitting multiple sclerosis of adult 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 (for exceptions and information about washout periods see sections 4.4 and 5.1 of the SmPC).

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.

See SmPC for the full indication. It contains fingolimod as the active substance and it is given orally.

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

Important risks of Gaxenim hard capsules together with measures to minimise such risks and the proposed studies for learning more about Gaxenim hard capsules' 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 Gaxenim hard capsules, 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 Gaxenim hard capsules is not yet available, it is listed under missing information below.

### *II.A List of important risks and missing information*

Important risks of Gaxenim hard capsules 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 Gaxenim hard capsules. 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                      | <ul style="list-style-type: none"> <li>• Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose;</li> <li>• Liver transaminase elevation;</li> <li>• Macular edema;</li> <li>• Opportunistic infections including PML, VZV, herpes viral infections other than VZV, fungal infection;</li> <li>• Reproductive toxicity;</li> <li>• Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma);</li> <li>• Lymphoma.</li> </ul> |
| Important potential risks                       | <ul style="list-style-type: none"> <li>• Other malignant neoplasms.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Missing information                             | <ul style="list-style-type: none"> <li>• Long-term use in paediatric patients, including impact on growth and development (including cognitive development).</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                   |

### 1.1.3. II.B Summary of important risks

#### Important identified risks

| Important identified risk: Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| Risk minimisation measures                                                                                                                     | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.3, 4.4, 4.5 and 4.8</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities                                                                                                        | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

| Important identified risk Liver transaminase elevation |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|--------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Risk minimisation measures                             | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.2, 4.3, 4.4, 4.8 and 5.2</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities                | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

| Important identified risk: Macular edema |                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| Risk minimisation measures               | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.4 and 4.8</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> </ul> </li> </ul> |

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|-----------------------------------------|--------------------------------------------|
|                                         | – Patient/Parent/Caregiver guide           |
| Additional pharmacovigilance activities | No additional pharmacovigilance activities |

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| Important identified risk: Opportunistic infections including PML, VZV, herpes viral infections other than VZV, fungal infection |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Risk minimisation measures                                                                                                       | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.3, 4.4 and 4.8</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities                                                                                          | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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| Important identified risk: Reproductive toxicity |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Risk minimisation measures                       | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC section 4.3, 4.4 and 4.6</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Pregnancy prevention</li> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> <li>– Pregnancy-specific patient reminder card</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities          | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

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| 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: |

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|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                         | <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.4 and 4.8</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                    |

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| Important identified risk: Lymphoma     |                                                                                                                                                                                                                                                                                                                                        |
| Risk minimisation measures              | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.8 and 5.3</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• No additional risk minimization measures</li> </ul> |
| Additional pharmacovigilance activities | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                             |

#### Important potential risks

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|-----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Important potential risk: Other malignant neoplasms |                                                                                                                                                                                                                                                                                                                               |
| Risk minimisation measures                          | <p>Routine risk minimisation measures:</p> <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC section 4.4</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• No additional risk minimization measures</li> </ul> |
| Additional pharmacovigilance activities             | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                    |

#### Missing information

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| Missing information: Long-term use in paediatric patients, including impact on growth and development (including cognitive development) |                                     |
| Risk minimisation measures                                                                                                              | Routine risk minimisation measures: |

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|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                         | <ul style="list-style-type: none"> <li>• Routine risk communication in SmPC sections 4.2 and 5.2</li> <li>• Prescription medicine only</li> </ul> <p>Additional risk minimisation measures</p> <ul style="list-style-type: none"> <li>• Educational materials in form of: <ul style="list-style-type: none"> <li>– Physician's checklist for adult and paediatric population</li> <li>– Patient/Parent/Caregiver guide</li> </ul> </li> </ul> |
| Additional pharmacovigilance activities | No additional pharmacovigilance activities                                                                                                                                                                                                                                                                                                                                                                                                    |

## 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 Gaxenim hard capsules.

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

There are no studies required for Gaxenim hard capsules.