Summary of Risk Management Plan (RMP)

Plegridy™ (peginterferon beta-1a)

Biogen Switzerland AG

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Summary of the Risk Management Plan (RMP) for Plegridy™ (peginterferon beta-1a)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of Plegridy™ is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Plegridy™ in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Biogen Switzerland AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Plegridy™.

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SUMMARY OF THE RISK MANAGEMENT PLAN FOR PLEGRIDY (PEGINTERFERON BETA-1A)

The European (EU) Risk Management Plan (RMP) details important risks of Plegridy™ (peginterferon beta-1a), and how more information will be obtained about the uncertainties (missing information) of administration of Plegridy to specific populations.

The Plegridy Summary of Product Characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how Plegridy should be used.

This summary of the EU RMP for Plegridy should be read in the context of all available relevant information, including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new safety concerns or changes to the current described safety concerns will be included in updates of the EU RMP for Plegridy.

1 The medicine and what it is used for

Plegridy is authorised for use in adult patients for the treatment of Relapsing Remitting Multiple Sclerosis (RRMS). It contains peginterferon beta-1a as the active substance, and it is given by either subcutaneous or intramuscular injection every 2 weeks.

Further information about the evaluation of the benefits of Plegridy can be found in the EPAR for Plegridy, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002827/human_med_001782.jsp&mid=WC0b01ac058001d124

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

Important risks of Plegridy, together with measures to minimise such risks and the proposed studies for learning more about the risks of Plegridy, 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, respectively.
- Important advice on the medicine's packaging.
- The authorised pack size — the amount of medicine in a pack is chosen to ensure that the medicine is used correctly; and
- 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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, 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 Plegridy is not yet available, it is listed under 'missing information' in Section VI: 2.1.

2.1 List of important risks and missing information

Important risks of Plegridy are risks that need special risk management activities to further investigate or minimise the risk so that the medicinal product can be safely administered. Important risks can be categorised as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Plegridy. 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 needs to be collected (e.g. on the long- term use of the medicine).

The list of important risks and missing information is presented below.

List of important risks and areas of missing information	
Important identified risks	None
Important potential risks	None
Areas of missing information	• Use during second and third trimester of pregnancy

2.2 Summary of important risks

There are no important identified risks or important potential risks associated with Plegridy treatment.

A summary of relevant areas of missing information is presented below.

Areas of Missing Information	
Use during second and third trimester of pregnancy	
Risk minimisation measures	***Routine risk minimisation measures:*** • Information in Section 4.6 of the SmPC describing the paucity of data in relation to drug exposure during the second and third trimester of pregnancy ***Other routine risk minimisation measures beyond the Product Information:*** Legal status: Prescription only medicine. Use restricted to physicians experienced in the treatment of MS. ***Additional risk minimisation measures:*** • None

Areas of Missing Information	
Additional pharmacovigilance activities	***Additional pharmacovigilance activities***: • Drug utilization study in pregnancy (exposure in second and third trimester) *See Section VI:2.3 of this summary for an* overview of the post-authorisation development plan.

2.3 Post-authorisation development plan

2.3.1 Studies that are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation for Plegridy.

2.3.2 Other studies in post-authorisation development plan

Other studies in the post authorisation development plan are as follows:

- **Drug utilization study in pregnancy (exposure in second and third trimester)**
  - *Purpose of the study*: Analysis of 948 pregnancy outcomes from the EPID MS Pregnancy Study (EUPAS13054) and the European Interferon-beta Pregnancy Registry indicated that the prevalence of major congenital anomalies in live births and spontaneous abortions were within the background rate of both the untreated MS population and the general population. However, most of the available data corresponded to exposure during first trimester of pregnancy, the period of most vulnerability due to organogenesis.

    To further address the remaining uncertainty pertaining to exposure during second and third trimesters of pregnancy, a first-stage study is planned to evaluate interferon-beta use amongst pregnant women in Sweden and Finland using a staggered approach, which will comprise:

    - Evaluation of interferon-beta utilization among pregnant women with MS in Sweden and Finland at 3 years and, if needed, 5 years following label implementation using aggregate level data; and
    - Evaluation of trends in drug utilisation patterns in the target population before and after label implementation.

    Aggregate data analysis at 3 and 5 years (if needed) will inform an overall assessment of whether it is appropriate and feasible to proceed with a second stage - a full study on the effect on pregnancy outcomes of interferon exposure during second and third trimester of pregnancy using individual level data, based on the observed pattern of interferon-beta use among pregnant women.