PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

ELREXFIO (ELRANATAMAB)

MARKETING AUTHORIZATION NUMBER 68646

Solution for injection, 40 mg/ml

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

BICR	Blinded Independent Central Review
CRS	Cytokine Release Syndrome
DLT	Dose-Limiting Toxicity
EPAR	European Public Assessment Report
EU	European Union
ICANS	Immune effector Cell-Associated Neurotoxicity Syndrome
IMiD	Immunomodulatory Drug
MM	Multiple Myeloma
ORR	Objective Response Rate
PFS	Progression Free Survival
PI	Proteasome Inhibitor
PL	Patient Leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
RP3D	Recommended Phase 3 Dose
RRMM	Relapsed/Refractory Multiple Myeloma
SmPC	Summary of Product Characteristics (Europe)

OVERVIEW

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 for elranatamab 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 elranatamab in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of elranatamab.

SUMMARY OF RISK MANAGEMENT PLAN FOR ELRANATAMAB

Summary of the risk management plan for Elrexfio

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

Elrexfio's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how elranatamab should be used.

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

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

I. The Medicine and What it is Used for

Elrexfio is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy. It contains elranatamab as the active substance and is given by subcutaneous injection.

Further information about the evaluation of Elrexfio's benefits can be found in Elrexfio's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage link to the EPAR summary landing page.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Elrexfio, together with measures to minimise such risks and the proposed studies for learning more about Elrexfio'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 Elrexfio, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse events 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 Elrexfio is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Elrexfio 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 regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Elrexfio. 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 safety of the medicine).

Table 1. List of Important Risks and Missing Information

Important Identified Risks	Cytokine Release Syndrome (CRS)
	Neurologic Toxicity including Immune effector cell-associated neurotoxicity syndrome (ICANS)
	Serious infections
Important Potential Risks	Virus reactivation*
	Cytopenias*
Missing Information	Long term safety

* Important potential risk as requested by Swissmedic. Applies to Switzerland only.

II.B. Summary of Important Risks

Table 2. Important Identified Risk: Cytokine Release Syndrome (CRS)

Evidence for linking the risk to the medicine:	The relationship between elranatamab administration and CRS has been clearly demonstrated in clinical studies. Risk factors important for the management of CRS were identified in Phase 1 study 1001 and measures to mitigate them were implemented in following studies.
Risk factors and risk groups:	The risk for CRS is greatest following the first 2-3 doses of elranatamab and occurs infrequently following later doses. The risk for CRS is dose related. There are no known risk groups for CRS.
Risk minimisation measures:	Routine risk minimisation measures: SmPC Sections 4.2, 4.4, 4.5 and 4.8: PL Sections 2, 3 and 4. Additional risk minimisation measures: Patient Card
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

Table 3. Important Identified Risk: Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Evidence for linking the risk to the medicine:	The relationship between elranatamab administration and Neurologic toxicity including ICANS has been clearly demonstrated in clinical studies. Risk factors important for the management of ICANS were identified in Phase 1 study 1001 and measures to mitigate them were implemented in following studies.
Risk factors and risk groups:	The risk for ICANS is greatest following the first 2-3 doses of elranatamab; ICANS occurs infrequently following later doses. ICANS occurs commonly in association with CRS but can occur without CRS. The risk for ICANS is dose related. There are no known risk groups for ICANS.
Risk minimisation measures:	Routine risk minimisation measures: SmPC Sections 4.2, 4.4, 4.7 and 4.8: PL Sections 2, 3 and 4. Additional risk minimisation measures: Patient Card
Additional pharmacovigilance activities	Additional pharmacovigilance activities:

Table 3. Important Identified Risk: Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

	Study C1071003 - An open-label, multicenter, non-randomized Phase 2 study of elranatamab monotherapy in participants with MM who are refractory to at least one PI, one IMiD and one anti-CD38 antibody. See section II.C of this summary for an overview of the post-authorisation development plan.

Table 4. Important Identified Risk: Serious Infections

Evidence for linking the risk to the medicine:	The relationship between elranatamab administration and serious infections has been demonstrated in clinical studies.
Risk factors and risk groups:	Patients with RRMM are at increased risk for serious infection due to well documented disease related immunosuppression (neutropenia, lymphopenia and hypogammaglobulinemia), which can be worsened with elranatamab treatment and lead to an increased risk for the development of serious infections.
Risk minimisation measures:	Routine risk minimisation measures: SmPC Sections 4.2, 4.4 and 4.8: PL Sections 2 and 4. Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study C1071003 - An open-label, multicenter, non-randomized Phase 2 study of elranatamab monotherapy in participants with MM who are refractory to at least one PI, one IMiD and one anti-CD38 antibody. See section II.C of this summary for an overview of the post-authorisation development plan.

Table 5. Summary of Important Potential Risks

Cytopenias*	
Evidence for linking the risk to the medicine:	The potential relationship between elranatamab administration and cytopenias has been observed in clinical studies.
Risk factors and risk groups:	Patients with RRMM are at increased risk for cytopenias due to known disease-related bone marrow suppression; cytopenias may be worsened by elranatamab treatment.
Risk minimisation measures:	Routine risk minimisation measures: Swiss information for professionals sections “Warnings and precautions” and “Undesirable Effects”. Additional risk minimisation measures: None
Virus reactivation*	
Evidence for linking the risk to the medicine:	The potential relationship between elranatamab administration and virus reactivation has been observed in clinical studies.

Table 5. Summary of Important Potential Risks

Risk factors and risk groups:	Patients with RRMM are at increased risk for infection, including virus reactivation, due to well documented disease-related immunosuppression (neutropenia, lymphopenia and hypogammaglobulinemia), which may be worsened during elranatamab treatment and may lead to an increased risk for the development of new and reactivated infections.
Risk minimisation measures:	Routine risk minimisation measures: Swiss information for professionals sections “Warnings and precautions” and “Undesirable Effects”. Additional risk minimisation measures: None

* Important potential risk as requested by Swissmedic. Applies to Switzerland only.

Table 6. Missing Information: Long Term Safety

Risk minimisation measures:	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study C1071003 - An open-label, multicenter, non-randomized Phase 2 study of elranatamab monotherapy in participants with MM who are refractory to at least one PI, one IMiD and one anti-CD38 antibody. See section II.C of this summary for an overview of the post-authorisation development plan.

II.C. Post-Authorisation Development Plan

II.C.1. Studies Which are Conditions of the Marketing Authorisation

The following studies are conditions of the marketing authorization:

Study name

Study C1071005 - An Open-Label, 3-Arm, Multicenter, Randomized Phase 3 Study to Evaluate the Efficacy and Safety of Elranatamab (PF-06863135) Monotherapy and Elranatamab + Daratumumab Versus Daratumumab + Pomalidomide + Dexamethasone in Participants with Relapsed/Refractory Multiple Myeloma

Purpose of the study: Part 1: To assess DLTs, safety and tolerability of elranatamab + daratumumab in order to select a RP3D for the combination to be used in Part 2 of this study.

Part 2:

- To compare the efficacy of elranatamab (Arm A) vs daratumumab + pomalidomide + dexamethasone (Arm C) as measured by PFS
- To compare the efficacy of elranatamab + daratumumab (Arm B) vs. Arm C as measured by PFS.

II.C.2. Other Studies in Post-Authorisation Development Plan

Study name

Study C1071003 - An open-label, multicenter, non-randomized Phase 2 study of elranatamab monotherapy in participants with MM who are refractory to at least one PI, one IMiD and one anti-CD38 antibody.

Purpose of the study: Primary: To determine the efficacy of elranatamab in Cohort A and Cohort B, ORR by BICR. Secondary Safety: To determine the safety and tolerability of elranatamab.