Swiss Summary of the Risk Management Plan for Vyvgart® (efgartigimod alfa)

Version 1.0 (dated 14 November 2024)

Based on the EU-RMP Version 1.0 (dated 21 June 2022)

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 Vyvgart® 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 Vyvgart® in Switzerland, is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedicinfo.ch), approved and authorized by Swissmedic.

Argenx Switzerland SA is fully responsible for the accuracy and correctness of the content of the published summary RMP of Vyvgart®.

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PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for VYVGART (efgartigimod)

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

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

This summary of the RMP for VYVGART 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 VYVGART's RMP.

I THE MEDICINE AND WHAT IT IS USED FOR

VYVGART is used together with standard therapy to treat adults with generalized myasthenia gravis (gMG), an autoimmune disease that causes muscle weakness. It contains efgartigimod alfa as the active substance and it is given by intravenous infusion (see SmPC).

Further information about the evaluation of VYVGART's benefits can be found in VYVGART's EPAR, including in its plain-language summary, available on the EMA website: https://www.ema.europa.eu/en/medicines/human/EPAR/vyvgart.

II RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of VYVGART, together with measures to minimize such risks and the proposed studies for learning more about VYVGART's risks, are outlined below.

Measures to minimize 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 authorized 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 (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse events is collected continuously and regularly analyzed, including periodic safety update reports (PSUR) assessments 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 VYVGART is not yet available, it is listed under “missing information” below.

II.A List of Important Risks and Missing Information

Important risks of VYVGART are risks that need special risk management activities to further investigate or minimize 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 VYVGART. 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 (eg, on the long-term use of the medicine).

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	Serious infections Malignancies
Missing information	Use in pregnant women Effect on vaccination efficacy and the use of live/attenuated vaccines Use with monoclonal antibodies Use in patients with moderate and severe renal impairment Long-term safety of efgartigimod treatment Use in immunocompromised patients

II.B Summary of Important Risks

Important Potential Risk: Serious Infections	
Evidence for linking the risk to the medicine	No evidence for an increased risk of serious infections (defined as any infection meeting the seriousness criteria for an individual case safety report) with the use of efgartigimod was seen in the clinical development program. The majority of infections observed in patients treated with efgartigimod were mild or moderate and, transient. The type and severity of infections observed in patients treated with efgartigimod was comparable to that observed in patients receiving placebo and their frequency did not increase with repeated cycles of treatment. None of the patients who received efgartigimod treatment had opportunistic infections. VYVGART (efgartigimod) binds to a specific protein in the body called neonatal Fc Receptor (FcRn). Efgartigimod binds to and blocks FcRn which results in a transient lowering of a type of antibody called immunoglobulin G (IgG). In patients testing positive for acetylcholine receptor (AChR) antibodies, the maximum mean percentage decrease in total IgG levels compared to baseline reached 61% one week after the last infusion of the initial treatment cycle and returned to baseline levels 9 weeks after the last infusion. Similar effects were also observed for all subtypes of IgG. This lowering of IgG levels could increase the risk of infections. The observed reductions in total antibodies were specific to IgG as no relevant decrease in all the other types of antibodies (IgA, IgD, IgE, IgM), nor albumin levels were observed. Additionally, due to the mode

	of action of efgartigimod of blocking FcRn, no impact on IgG production is expected. Therefore, given the potential mechanism of action of VYVGART, serious infections are considered an important potential risk.
Risk factors and risk groups	Underlying immunodeficiency conditions, either acquired or due to immunosuppressive drugs, represent a general risk factor for serious infections. The risk increases with more pronounced impairment of the immune system.
Risk minimization measures	Routine risk minimization measures: • SmPC section 4.4 and 4.8 • PL section 2 and 4 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • ARGX-113-1705 • Post-authorization safety study
Important Potential Risk: Malignancies	
Evidence for linking the risk to the medicine	During the clinical development program, an imbalance was seen between neoplasms in patients treated with efgartigimod and patients receiving placebo, with 11 events of neoplasms observed in 8 patients treated with efgartigimod (1 in study ARGX-113-1704 and 10 in 7 patients in study ARGX-113-1705) and only 1 event observed in the placebo group. All malignant neoplasms were assessed as not related to efgartigimod by the investigator. Available data on other IgG-reducing agents or treatments do not suggest a correlation between IgG reduction and an increased risk of developing any type of cancer. No literature could be found associating chronic use of plasma exchange, immunoadsorption, and plasmapheresis therapies reducing IgGs with the development of malignancies. Immunosuppressants, which patients with MG take concomitantly with efgartigimod, can impair the immune response to cancer. Therefore, malignancies are considered an important potential risk.
Risk factors and risk groups	Risk factors for malignancy include traditional risk factors such as advancing age, smoking, drinking alcohol, obesity, sun exposure, radiation and chemicals exposure, hormonal disturbance, and family history.
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study

Missing Information: Use in Pregnant Women	
Risk minimization measures	Routine risk minimization measures: • SmPC section 4.6 • PL section 2 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study
Missing Information: Effect on Vaccination Efficacy and the Use of Live/attenuated Vaccines	
Risk minimization measures	Routine risk minimization measures: • SmPC section 4.4 and 4.5 • PL section 2 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study
Missing Information: Use With Monoclonal Antibodies	
Risk minimization measures	Routine risk minimization measures: • SmPC section 4.5 • PL section 2 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study
Missing Information: Use in Patients With Moderate and Severe Renal Impairment	
Risk minimization measures	Routine risk minimization measures: • SmPC section 4.2 and 5.2 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study

Missing Information: Long-term Safety of Efgartigimod Treatment	
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • ARGX-113-1705 • Post-authorization safety study
Missing Information: Use in immunocompromised patients	
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Post-authorization safety study

PL=package leaflet, SmPC=summary of product characteristics

II.C Post-authorization Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligations of VYVGART.

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

ARGX-113-1705 - A long-term, single-arm, open-label, multicenter, phase 3 follow-on study of ARGX-113-1704 to evaluate the safety and tolerability of ARGX-113 in patients with myasthenia gravis having generalized muscle weakness.

Purpose of the study: to evaluate the long-term safety and tolerability of efgartigimod administered to patients with gMG. This extension study was designed to collect additional safety data to supplement that from the randomized placebo-controlled study ARGX-113-1704 and to offer efgartigimod treatment for patients who were randomized to receive placebo in the study ARGX-113-1704.

Post-authorization Safety Study

Purpose of the study: to investigate the safety profile of efgartigimod in a larger patient population for a longer duration than in clinical studies and under conditions of normal clinical practice. The focus is to further characterize potential risks and areas of missing information. In addition, given that long-term safety data is limited, the post-authorization safety study will evaluate whether there are specific and/or unexpected patterns of adverse events.