Swiss Summary of the Risk Management Plan

Invented name / Brand name:	VYEPTI®
Active substance(s) (INN or common name):	Eptinezumab
Version number of the RMP Summary:	1.0, Summary of Core RMP version 2.0
Date of report:	25 November 2021
Marketing Authorisation Holder:	Lundbeck (Schweiz) AG Balz-Zimmermann-Strasse 7 8152 Glattbrugg

Disclaimer:

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

Summary of risk management plan for VYEPTI® (eptinezumab)

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

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

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

I. The medicine and what it is used for

VYEPTI is authorised for the prophylactic treatment of migraine in adults (see SmPC for the full indication). It contains eptinezumab as the active substance and it is given by intravenous (IV) administration.

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

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

II.A List of important risks and missing information

Important risks of VYEPTI 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 VYEPTI. 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	None
Important potential risks	None
Missing information	Use in pregnant women (including those at risk of pre-eclampsia) Cardiovascular outcomes in patients with pre-existing myocardial infarction, cerebrovascular accident, transient ischemic attack, angina unstable and poorly controlled hypertension Long-term safety

II.B Summary of important risks

Missing information: Use in pregnant women (including those at risk of pre-eclampsia)	
Risk minimisation measures	Routine risk minimisation measures The SmPC section *Pregnancy, Lactation* describes the (limited) data available on use in pregnancy and includes advice that VYEPTI should not be used by pregnant women unless absolutely necessary. No additional risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Eptinezumab Post-marketing Pregnancy Program

Missing information: Cardiovascular Outcomes in patients with pre-existing myocardial infarction, cerebrovascular accident, transient ischemic attack, angina unstable and poorly controlled hypertension	
Risk minimisation measures	Routine risk minimisation measures The SmPC section *Warnings and Precautions* includes information that patients with a history of cardiovascular disease were excluded from the clinical trials and no safety data are available for these patients. No additional risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Eptinezumab Real-World Use and Long-term Cardiovascular Safety Study

Missing information: Long-term safety	
Risk minimisation measures	No routine risk minimisation measures No additional risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Eptinezumab Real-World Use and Long-term Cardiovascular Safety Study

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 VYEPTI.

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

Eptinezumab Real-World Use and Long-term Cardiovascular Safety Study

Purpose of the study:

Migraine is a chronic condition. Therefore, long-term eptinezumab use is expected in routine clinical practice. Adverse effects which are infrequent or have a longer latency period, such as cardiovascular disease, could appear after longer and larger patient exposure. However, data on exposures beyond 1 year is limited and the safety of eptinezumab beyond 2 years has not been investigated in the clinical trial program. Additionally, patients with recent acute cardiovascular events and/or serious cardiovascular risk were excluded from the clinical trial population and use in this group of patients may also occur in everyday clinical practice. Therefore, the use patterns in real life and long-term cardiovascular safety, including the safety of patients with a known history of cardiovascular disease, requires further characterisation.

The objective of this study is to characterise the utilisation of eptinezumab in routine clinical practice and to estimate rates of cardiovascular events over the long-term in patients exposed to eptinezumab, including the subgroup of exposed patients with a known history of cardiovascular disease.

Eptinezumab Post-marketing Pregnancy Program

Purpose of the study:

Migraine is common among women of child-bearing age, with an estimated prevalence of 25% (1,2). Pregnant women were not included in the clinical development program; however, the indicated population is predominantly women, many of whom are of childbearing age. The population of pregnant women treated with eptinezumab is therefore one which warrants further characterization, as effects on the woman and the fetus after exposure in utero are unknown.

The objective of the Post-marketing Pregnancy Program is to collect information and assess the potential risk of use of eptinezumab during pregnancy. The potential increase in the risks of adverse maternal, fetal, and infant outcomes will be evaluated, including risks of birth defects, other adverse pregnancy outcomes and postnatal health of liveborn children up to one year of age among the offspring of women exposed to eptinezumab. Data will be collected on women exposed to eptinezumab during pregnancy and their offspring, as well as data on two comparative groups of eptinezumab-unexposed pregnant women with migraine and their offspring.

References:

1 Myint A.A., et al. Special Issues in Managing Migraine in Women: A Review Article. International Journal of Collaborative Research on Internal Medicine & Public Health. Vol. 5 No. 6 (2013), 478 – 491

2 Lipton R.B., et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68(5); 343-349