VIMPAT®

SUMMARY OF RISK MANAGEMENT PLAN

Version 1.0

Active substance(s) (INN or common name):	Lacosamide
Product(s) concerned (brand name(s)):	Vimpat®
Marketing authorization holder:	UCB-Pharma AG
Version number :	1.0 (summary of EU RMP v17.0 , dated 17-May-2023)
Date of final sign off :	15-May-2024

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

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PART I: THE MEDICINE AND WHAT IT IS USED FOR

Pharmaceutical form(s) and strength(s)	Current: 50mg, 100mg, and 150mg, 200mg film-coated tablets, 10mg/mL syrup 10mg/mL solution for infusion
	Proposed: Not Applicable
Is/will the product be subject to additional monitoring in the EU?	No
Is/will the product be subject to additional monitoring in Switzerland ?	No

Lacosamide is authorized as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in patients aged 2 years and above with epilepsy (see SmPC for the full indication). Lacosamide is also indicated as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in adults, adolescents, and children from 4 years of age with idiopathic generalized epilepsy. It contains Lacosamide as the active substance and it is given by oral tablet in the following strengths: 50mg, 100mg, 150mg, and 200mg film- coated tablets; by 10mg/mL syrup; or by injection of 10mg/mL solution for infusion.

Further information about the evaluation of Lacosamide benefits can be found in the LCM EPAR, including its plain-language summary, available on the European Medicines Agency website, under the medicine's webpage:
https://www.ema.europa.eu/en/medicines/human/EPAR/vimpat

For UCB Lacosamide EPAR, the link is :
https://www.ema.europa.eu/en/medicines/human/EPAR/lacosamide-ucb

PART II: RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERISE THE RISKS

Important risks of Lacosamide (LCM), together with measures to minimize such risks and the proposed studies for learning more about LCM risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be as follows:

- 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 reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report assessment so that prompt action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of LCM is not yet available, it is listed under "missing information" in Table 2–1 below.

2.1 List of important risks and missing information

Important risks of LCM are risks that need special risk management activities to further investigate or minimize 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 LCM. 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).

Table 2–1: List of important risks and missing information

Important identified risks	Cardiac adverse events that may be potentially associated with PR interval prolongation or sodium channel modulation
Important potential risks	None
Missing information	Pregnant or lactating women Impact on long-term growth, long-term neurodevelopment, and puberty in pediatric population

2.2 Summary of important risks

Table 2–2: Summary of important risks

Important identified risk: Cardiac adverse events (AEs) that may be potentially associated with PR interval prolongation or sodium channel modulation	
Evidence for linking the risk to the medicine	Prolongations in PR interval with lacosamide (LCM) have been observed in clinical studies. A phase 1 study revealed a small dose-related increase in the mean PR interval with LCM-treated subjects. Nonclinical studies revealed an interaction with LCM and cardiac sodium channels which could potentially affect normal cardiac electrophysiology. This risk was upgraded by UCB from important potential risk to important identified risk based on a cumulative analysis of postmarketing data which indicated a causal relationship with LCM.
Risk factors and risk groups	The risk factors for developing AEs related to PR prolongation include a presence of pre-existing heart failure or a recent myocardial infarction or known conduction abnormalities (Ryvlin et al, 2013; Strzelczyk et al, 2008; Rocamora et al, 2003). Studies on the risk factors for AEs related to PR prolongation have been done in the general population. The incidence of atrial fibrillation increases with age (Friberg et al, 2010). Other risk factors for atrial fibrillation include a history of hypertension and cardiac diseases including valvular, ischemic, and congestive heart failure (Krahn et al, 1995).The frequency of cardiac syncope also increases with age from approximately 1.1% in people less than 40 years to 16% in individuals more than 75 years of age (Rvylin et al, 2013; Olde et al, 2009; Ungar et al, 2006). Ictal bradycardia is most prevalent in individuals with temporal lobe epilepsy (Monté et al, 2007; Reeves et al, 1996). There is no data available on the risk factors specific to antiepileptic drugs (AEDs). Lacosamide should be used with caution in patients with underlying proarrhythmic conditions such as patients with known cardiac conduction problems or severe cardiac disease (eg, myocardial ischemia/infarction, heart failure, structural heart disease, or cardiac sodium channelopathies) or patients treated with medicinal products affecting cardiac conduction, including antiarrhythmics and sodium channel blockers. Older age (>65 years) and/or intravenous therapy were not identified as independent risk factors.
Risk minimization measures	Routine risk minimization measures: Summary of Product Characteristics (SmPC) Section 4.2 (Posology and method of administration - intravenous formulation), Section 4.3 (Contraindications), SmPC Section 4.4 (Special warnings and precautions for use), SmPC Section 4.5 (Interaction with other medicinal products and other forms of interaction), SmPC Section 4.8 (Undesirable effects), SmPC Section 5.3 (Preclinical

	safety data) Available by prescription only Additional risk minimization measures: None
Missing information: Pregnant or lactating women	
Risk minimization measures	Routine risk minimization measures: SmPC Section 4.6 (Fertility, pregnancy and lactation), SmPC Section 5.3 (Preclinical safety data) Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: participation in and sponsorship of pregnancy registries (European and International Registry of AEDs in Pregnancy and North American AED Pregnancy Registry) See Section 2.3.2 of this summary for an overview of the postauthorization development plan.
Missing information: Impact on long-term growth, long-term neurodevelopment, and puberty in pediatric population	
Risk minimization measures	Routine risk minimization measures: No additional wording in SmPC Available by prescription only. Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: ongoing pediatric study with a follow-up of up to 5 years in EP0012 (according to the actual study protocol). See Section 2.3.2 of this summary for an overview of the postauthorization development plan.

AE=adverse event; AED=antiepileptic drug; LCM=lacosamide; SmPC=summary of product characteristics

2.3 Postauthorization development plan

2.3.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of LCM.

2.3.2 Other studies in postauthorization development plan

Additional pharmacovigilance activities include the following:

- Registry studies to monitor pregnancy outcomes: participation in and sponsorship of European and International Registry of Antiepileptic Drugs (AEDs) in Pregnancy (EURAP) and in the North American AED Pregnancy Registry (NAAPR).

Activities include provision of requested data from UCB to the registries and regular review of interim outputs from the registries. The protocols for EURAP and NAAPR include possible activities to follow-up on the children.

Prescribers and reporters of pregnancy cases are encouraged to register pregnant women exposed to AEDs into the EURAP and NAAPR. References to registries are included on the pregnancy follow-up letter, US Call Center script, and information for Medical Science Liaisons.

- Study EP0012 is an ongoing clinical trial including pediatric patients who are followed for up to 5 years (according to the actual study protocol):
  - Endocrinology, body weight, height, and calculated body mass index will be measured in the studies per protocol.
  - Neurodevelopmental maturation will be assessed in the pediatric studies as per protocol by the investigator using physical examination and neurodevelopmental validated scales including the Achenbach Child Behavior Checklist, Behavior Rating Inventory of Executive Function®/Behavior Rating Inventory of Executive Function®-preschool version, and Tanner staging.

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