Summary of risk management plan for Lacosamide Adroiq (Lacosamide)

This is a summary of the risk management plan (RMP) for Lacosamide Adroiq. The RMP details important risks of Lacosamide Adroiq, risk minimisation measures needed to minimise these risks and routine pharmacovigilance activities needed to obtain more information about Lacosamide Adroiq's risks and uncertainties (missing information).

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

This summary of the RMP for Lacosamide Adroiq 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 Lacosamide Adroiq's RMP.

I. The medicine and what it is used for

Lacosamide Adroiq is authorized for monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adults, adolescents and children from 2 years of age with epilepsy (see Summary of Product Characteristics [SmPC] for the full indication). Lacosamide Adroiq 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 injection of 10mg/mL solution for infusion.

Further information about the evaluation of Lacosamide Adroiq's benefits can be found in Lacosamide Adroiq's EPAR. Including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/lacosamide-adroiq.

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

Important risks of Lacosamide Adroiq, together with measures to minimise such risks and learning more about Lacosamide 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 leaflets 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, including periodic safety update report 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 LCM is not yet available, it is listed under 'missing information' in Table 2-1 below

II.A List of Important Risks and Missing Information

Important risks of Lacosamide Adroiq 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 Lacosamide Adroiq. 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.

List of important risks and missing information	
Important identified risks	Cardiac AEs 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

AE=adverse event

II.B Summary of Important Risks

The safety information in the proposed product information is aligned to the reference medicinal product.

Summary of important risks

Important identified risk: Cardiac 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, 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 iv 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 - iv formulation), SmPC 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	None

II.C Post-authorisation Development Plan

No post authorisation study is planned for this product.

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 Lacosamide Adroiq.

II.C.2 Other Studies in post-authorisation Development Plan

There are no studies required for Lacosamide Adroiq.