PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets (lacosamide)

This is a summary of the risk management plan (RMP) for lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets. The RMP details important risks of lacosamide, how these risks can be minimised, and how more information will be obtained about lacosamide's risks and uncertainties (missing information).

Lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablet's summary of product characteristics (SmPC) give essential information to healthcare professionals and patients on how it should be used.

I. The medicine and what it is used for

Lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy. It contains lacosamide as the active substance and it is given by oral route.

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

Important risks of lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets, together with measures to minimise such 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute routine risk minimisation measures.

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

II.A List of important risks and missing information

Important risks of lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken by patients. 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 Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets. 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/use in special patient populations etc.);

Table 6 Part VI: Summary of safety concerns

List of important risks and missing information	
Important identified risks	• Cardiac AEs that may be potentially associated with PR interval prolongation and sodium channel modulation
Important potential risks	None
Missing information	• Pregnant or lactating women • Impact on long-term growth, long-term neurodevelopment, and on puberty in pediatric population aged 4 to < 16 years

II.B Summary of important risks

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

Cardiac AEs that may be potentially associated with PR interval prolongation and sodium channel modulation	
Evidence for linking the risk to the medicine	In line with the reference RMP, this safety concern has been classified as an important identified risk.
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 minimisation measures	Routine risk minimization measures: SmPC sections 4.2, 4.3, 4.4, 4.5, 4.8 and 5.3

Cardiac AEs that may be potentially associated with PR interval prolongation and sodium channel modulation	
	Other risk minimisation measures beyond the Product Information: Medicine's legal status: POM Additional risk minimisation measures Not applicable as there are no additional risk minimisation measures for this safety concern

Pregnant or lactating women	
Risk minimisation measures	Routine risk minimization measures: SmPC sections 4.6 and 5.3 Additional risk minimisation measures Not applicable as there are no additional risk minimisation measures for this safety concern
Additional pharmacovigilance activities	Additional pharmacovigilance activities: In order to support the collection of additional data on pregnancy under therapy with lacosamide and for comparison of different anti-epileptics regarding teratogenicity, the marketing authorisation holder encourages reporters to register and to report pregnant women with epilepsy in the European Registry of Antiepileptic Drugs and Pregnancy (EURAP). See section II.C of this summary for an overview of the post-authorisation development plan.

Impact on long-term growth, long-term neurodevelopment, and on puberty in pediatric population aged 4 to < 16 years	
Risk minimisation measures	Routine risk minimisation measures No additional wording in SmPC Additional risk minimisation measures None

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 lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg Film-coated tablets.

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

There are no studies required for lacosamide Mylan 50 mg, 100 mg, 150 mg, 200 mg film-coated tablets.