III.2 Additional pharmacovigilance activities

Not applicable.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

Not applicable.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

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

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2. Additional Risk Minimisation Measures

Routine risk minimization activities as described in Part V.1 are sufficient to manage the safety concerns of the medicinal product.

V.3 Summary of risk minimisation measures

Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for Levetiracetam 100 mg / mL Concentrate for solution for infusion

This is a summary of the risk management plan (RMP) for Levetiracetam 100 mg / mL Concentrate for solution for infusion (hereinafter referred to as LEVETIRACETAM). The RMP details important risks of LEVETIRACETAM, how these risks can be minimised, and how more information will be obtained about LEVETIRACETAM 's risks and uncertainties (missing information).

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

I. The medicine and what it is used for

LEVETIRACETAM is authorised as monotherapy in the treatment of partial onset seizures with or without secondary generalization in adults and adolescents from 16 years of age with newly diagnosed

epilepsy, as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalization in adults, adolescents and children from 4 years of age with epilepsy, in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy, in the treatment of primary generalized tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalized Epilepsy (see SmPC for the full indication). It contains levetiracetam as the active substance and it is given by intravenous infusion.

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

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

II.A List of important risks and missing information

Important risks of LEVETIRACETAM 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 LEVETIRACETAM. 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).

Summary of safety concerns	
Important identified risks	Suicidality and abnormal behaviour Blood dyscrasias Acute kidney injury Encephalopathy
Important potential risks	Increased methotrexate toxicity on concomitant use Use during breastfeeding Seizures during pregnancy

Summary of safety concerns	
Missing information	Long-term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children

II.B Summary of important risks

Important identified risk: Acute kidney injury	
Evidence for linking the risk to the medicine	Acute kidney injury previously classified as important potential risk is to be reclassified as important identified risk as there is sufficient scientific evidence that it is caused by levetiracetam. According to the SmPC, it is a known adverse reaction occurring rarely, with a time onset ranging from a few days to several months.
Risk factors and risk groups	Not applicable
Risk minimization measures	No risk minimization measures

Important identified risk: Encephalopathy	
Evidence for linking the risk to the medicine	Encephalopathy, previously classified as important potential risk is to be reclassified as important identified risk as there is sufficient scientific evidence that it is caused by levetiracetam. According to the SmPC, it is a known adverse reaction occurring rarely, generally at the beginning of the treatment (few days to a few months) and reversible after treatment discontinuation.
Risk factors and risk groups	Not applicable
Risk minimization measures	No risk minimization measures

Important potential risk: Seizures during pregnancy	
Evidence for linking the risk to the medicine	Seizure worsening, previously classified as important potential risk is to be rephrased to "seizures during pregnancy" remaining as important potential risk. The reason for this change is to better reflect the risk of breakthrough seizures, due to sudden discontinuation of levetiracetam, which could have serious consequences for the woman and the unborn child. Moreover, physiological changes during pregnancy may affect levetiracetam concentration. Decrease in levetiracetam plasma concentrations has been observed during pregnancy, more pronounced during the third trimester, prompting appropriate clinical management of pregnant women treated with levetiracetam.
Risk factors and risk groups	Not applicable
Risk minimization measures	No risk minimization measures

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 LEVETIRACETAM.

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

There are no studies required for LEVETIRACETAM.