Summary of risk management plan for Inovelon (rufinamide)

This is a summary of the risk management plan (RMP) for Inovelon®. The RMP details important risks of Inovelon®, how these risks can be minimised and how more information will be obtained about Inovelon®'s risks and uncertainties (missing information).

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

This summary of the RMP for Inovelon® 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 Inovelon®'s RMP.

I The Medicine and What it is Used for

Inovelon® is authorised for the indication of as adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients four years of age and older. It contains rufinamide as the active substance and it is given orally as a suspension or as film-coated tablet(s).

Further information about the evaluation of Inovelon®'s benefits can be found in Inovelon®'s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: Inovelon EPAR summary

II Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

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

II.A List of Important Risks and Missing Information

Important risks of Inovelon® are risks that need special risk management activities to further investigate or minimise 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 Inovelon®. 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).

List of Important Risks and Missing Information	
Important identified risks	• Rash and Hypersensitivity including DRESS and SJS • Decreased Appetite and Weight Loss • Coordination Abnormal (Ataxia) • Somnolence • Dizziness
Important potential risks	• Status Epilepticus • Shortened QT interval on ECG • Suicidality
Missing information	• Pregnancy • Hepatic Impairment • Children Younger than 1 Year of Age

DRESS = Drug Reaction with Eosinophilia and Systemic Symptoms, ECG = electrocardiogram, SJS = Stevens-Johnson syndrome.

II.B Summary of Important Risks

Important Identified Risks	
Rash and Hypersensitivity including DRESS and SJS (Rash and allergies or over reactions of the immune system including drug reaction with eosinophilia [increased eosinophils in the body] and systemic symptoms [DRESS] and Stevens-Johnson syndrome [SJS])	
Evidence for linking the risk to the medicine	Evidence from placebo-controlled (comparing Inovelon® with placebo) and open-label extension (treatment is known to both participants and the investigators) studies.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.8 • PL Sections 2 and 4
Decreased Appetite and Weight Loss	

Evidence for linking the risk to the medicine	Evidence from placebo-controlled and open-label extension studies.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.8 • PL Section 4
Coordination Abnormal (Ataxia)	
Evidence for linking the risk to the medicine	Evidence from placebo-controlled and open-label extension studies and postmarketed AE reporting.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • SmPC Section 4.8 • PL Sections 2 and 4
Important Identified Risks (continued)	
Somnolence (Sleepiness)	
Evidence for linking the risk to the medicine	Evidence from placebo-controlled and open-label extension studies.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • SmPC Section 4.7 • SmPC Section 4.8 • PL Sections 2 and 4
Dizziness	
Evidence for linking the risk to the medicine	Evidence from placebo-controlled and open-label extension studies.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • SmPC Section 4.7 • SmPC Section 4.8 • PL Sections 2 and 4
Important Potential Risks	
Status Epilepticus (A single epileptic seizure lasting a long time or 2 or more seizures that lasts a longer time without recovery between 2 seizures)	
Evidence for linking the risk to the medicine	Current evidence from completed clinical studies.
Risk groups and risk factors	In patients with known epilepsy, status epilepticus is frequently triggered from a discontinuation or change in AED therapy or the

	presence of a concurrent febrile illness. During the development of rufinamide a standardised definition of status epilepticus was not provided to the investigators and the events were reported according to local definitions. There is currently no evidence to suggest a sub-population, or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • SmPC Section 4.8 • PL Sections 2 and 4
Important Potential Risks (continued)	
Shortened QT interval on ECG	
Evidence for linking the risk to the medicine	Evidence from the QT_c study (Study E2080-A001-002).
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • PL Section 2
Suicidality (Tendency to commit suicide)	
Evidence for linking the risk to the medicine	Evidence from placebo-controlled and open-label extension studies.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4 • PL Sections 2 and 4
Missing information	
Hepatic Impairment (Liver Impairment)	
Evidence for linking the risk to the medicine	No studies have been performed in patients with hepatic impairment.
Risk groups and risk factors	The risks of rufinamide in patients with liver damage are not known.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.2 • SmPC Section 5.2 • PL Section 2, Section 4
Pregnancy	
Evidence for linking the risk to the medicine	No events associated with drug exposure during pregnancy have been reported; this is a potential risk in humans.
Risk groups and risk factors	There is currently no evidence to suggest a subpopulation or risk factor, that some individuals are more susceptible than others.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4

	• SmPC Section 4.5 • SmPC Section 4.6 • PL Section 2
Children Younger than 1 Year of Age	
Evidence for linking the risk to the medicine	No studies have been performed in children younger than 1 year of age.
Risk groups and risk factors	The risks of rufinamide in children younger than 1 year of age are not known.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.2 • SmPC Section 5.2 • PL Section 2

AE = adverse event, AED = antiepileptic drug, DRESS = drug reaction with eosinophilia and systemic symptoms, ECG = electrocardiogram, PL = Package Leaflet, QT interval = time interval from the onset of the QRS complex to the end of the T wave on an ECG tracing, QT_c = corrected QT interval, SJS = Stevens-Johnson syndrome, SmPC = Summary of Product Characteristics.

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 obligations for Inovelon®.

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

There are no studies required for Inovelon®.