Summary of risk management plan for Nitisinone MDK (Nitisinone)

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

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

This summary of the RMP for Nitisinone MDK 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 Nitisinone MDK's RMP.

I. The medicine and what it is used for

Nitisinone MDK is authorised Nitisinone MDK is authorized for the treatment of adult and paediatric (in any age range) patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT 1) in combination with dietary restriction of tyrosine and phenylalanine (see SmPC for the full indication). It contains nitisinone as the active substance and it is given orally.

Further information about the evaluation of Nitisinone MDK's benefits can be found in Nitisinone MDK's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage <link to the EPAR summary landing page>.

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

Important risks of Nitisinone MDK, together with measures to minimise such risks and the proposed studies for learning more about Nitisinone MDK'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.

If important information that may affect the safe use of Nitisinone MDK is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Nitisinone MDK 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 Nitisinone MDK. 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);

List of important risks and missing information	
Important identified risks	None
Important potential risks	Developmental and cognitive disorders Embryo-fetal toxicity
Missing information	Use in elderly Use in pregnant women

II.B Summary of important risks

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

Important potential risk: Developmental and cognitive disorders	
Evidence for linking the risk to the medicine	Literature review, post-marketing surveillance
Risk factors and risk groups	All HT-1 patients treated with Nitisinone MDK. Most likely patients with poor compliance with diet restrictions
Risk minimisation measures	No risk minimization measures identified.
Additional pharmacovigilance activities	Questionnaire for follow-up for developmental and cognitive disorders

Important potential risk: Embryo-fetal toxicity	
Evidence for linking the risk to the medicine	Literature review, post-marketing surveillance
Risk factors and risk groups	All HT-1 patients treated with Nitisinone MDK and with high levels of tyrosine. Potentially, HT-1 patients with poor compliance with diet restrictions and ensuing high levels of tyrosine most likely have an increased potential risk.
Risk minimisation measures	Routine risk minimization measures SmPC section 4.6

Additional pharmacovigilance activities	Questionnaire for follow-up of drug exposure during pregnancy

Missing information: Use in elderly	
Risk minimisation measures	No risk minimization measures identified

Missing information: Use in pregnant women	
Risk minimisation measures	Routine risk minimization measures SmPC section 4.6
Additional pharmacovigilance activities	Questionnaire for follow-up of drug exposure during pregnancy

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 Nitisinone MDK.

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

There are no studies required for Nitisinone MDK.