Part VI: Summary of the risk management plan

Summary of risk management plan for NITYR (Nitisinone)

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

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

This summary of the RMP for Nityr 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 Nityr's RMP.

I. The medicine and what it is used for

Nityr is authorised for treatment of adult and paediatric patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Nityr is authorised for the treatment of adult patients with alkaptonuria (AKU).

It contains nitisinone as the active substance and it is administered orally.

Further information about the evaluation of Nityr ’s benefits can be found in Nityr ’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/nityr*

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

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

II.A List of important risks and missing information

Important risks of Nityr 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 Nityr. 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	None
Important potential risks	Developmental and cognitive disorders (for the indication hereditary tyrosinemia type 1)
	Embryo-fetal toxicity
Missing information	Use in elderly
	Use in pregnant women

II.B Summary of important risks

Important potential risk: Developmental and cognitive disorders (for the indication hereditary tyrosinemia type 1)	
Evidence for linking the risk to the medicine	Completed clinical studies, literature review, and post marketing surveillance.
Risk factors and risk groups	All HT-1 patients treated with Nityr. Most likely patients with poor compliance with diet restrictions.
Risk minimization measures	No risk minimization measures identified
Additional pharmacovigilance activities	None

Important potential risk: Embryo-fetal toxicity	
Evidence for linking the risk to the medicine	Completed clinical studies, literature review, and post marketing surveillance.
Risk factors and risk groups	All HT-1 and AKU patients treated with Nityr 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 minimization measures	Routine risk minimization measures SmPC section 4.6
Additional pharmacovigilance activities	None

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

Missing information: Use in pregnant women.	
Risk minimization measures	Routine risk minimization measures SmPC section 4.6

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 authorization or specific obligation of Nityr.

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

There are no studies in post-authorisation development plan for Nityr.