Summary of risk management plan for Orfadin

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

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

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

I. The medicine and what it is used for

Orfadin is authorized for treatment of adults and children with hereditary tyrosinemia type I (HT-1) in combination with dietary restriction of tyrosine and phenylalanine. Orfadin is also indicated for treatment of adults with alkaptonuria (AKU). (see SmPC for the full indications). It contains nitisinone as the active substance and it is given by mouth as capsules or suspension.

Further information about the evaluation of Orfadin's benefits can be found in Orfadin's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Orfadin, together with measures to minimize such risks and the proposed studies for learning more about Orfadin's risks, are outlined below.

Measures to minimize 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 authorized 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including yearly PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of Orfadin are risks that need special risk management activities to further investigate or minimize 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 Orfadin. 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 postmarketing surveillance.
Risk factors and risk groups	All HT-1 patients treated with Orfadin. 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 postmarketing surveillance.
Risk factors and risk groups	All HT-1 and AKU patients treated with Orfadin 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 Postauthorization development plan

II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Orfadin.

II.C.2 Other studies in postauthorization development plan

There are no studies in the postauthorization development plan.