Risk Management Plan on	Date of the RMP
Nitisinone Dipharma 2 mg hard capsules Nitisinone Dipharma 5 mg hard capsules Nitisinone Dipharma 10 mg hard capsules Nitisinone Dipharma 20 mg hard capsules	27-Mar-2019

Part VI – Summary of the risk management plan by product

Summary of risk management plan for:
Nitisinone Dipharma 2 mg hard capsules
Nitisinone Dipharma 5 mg hard capsules
Nitisinone Dipharma 10 mg hard capsules
Nitisinone Dipharma 20 mg hard capsules

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

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

I. The medicine and what it is used for

Nitisinone Dipharma is authorised 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. This product contains Nitisinone and is taken orally.

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

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

Risk Management Plan on	Date of the RMP
Nitisinone Dipharma 2 mg hard capsules Nitisinone Dipharma 5 mg hard capsules Nitisinone Dipharma 10 mg hard capsules Nitisinone Dipharma 20 mg hard capsules	27-Mar-2019

II.A List of important risks and missing information

Important risks of Nitisinone Dipharma 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 Dipharma. 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);

Important identified risks	Increased tyrosine levels
	Hypertyrosinemia related eye disorders
	Leukopenia/Granulocytopenia
Important potential risks	Lack of efficacy
	Development and cognitive disorders
	Embryo-fetal toxicity
	Exposure to nitisinone during breast-feeding
Missing information	Interactions with substances known to induce or inhibit CYP3A4
	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.

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 Dipharma.

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

There are no studies required for Nitisinone Dipharma.