Part VI: Summary of the risk management plan

Summary of risk management plan for Cufence (trientine)

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

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

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

I. The medicine and what it is used for

Cufence is authorised for the treatment of Wilson's disease in patients intolerant of D-Penicillamine therapy (see SmPC for the full indication). It contains trientine as the active substance and it is given orally.

Further information about the evaluation of Cufence's benefits can be found in Cufence'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/cufence.

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

Important risks of Cufence, together with measures to minimise such risks and the proposed studies for learning more about Cufence'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;
- 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 Periodic Safety Update Report (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 Cufence is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Cufence 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 Cufence. 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	None
Missing information	Drug exposure during pregnancy Use of drug in lactation and in neonates

II.B Summary of important risks

Missing information: Drug exposure during pregnancy	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.6.* *PL section 2.* Routine risk minimisation activities recommending specific clinical measures to address the risk: Additionally, the pregnancy should be monitored in order to detect possible foetal abnormality and to assess maternal serum copper levels throughout the pregnancy. The dose of trientine used should be adjusted in order to maintain serum copper levels within the normal range. Babies born to mothers being treated with trientine should be monitored for serum copper and ceruloplasmin levels where appropriate. Additional risk minimisation measures: None

Missing information: Use of drug in lactation and in neonates	
Risk minimisation measures	Routine risk minimisation measures:

	SmPC section 4.6. *PL section 2.* Additionally, babies born to mothers being treated with trientine should be monitored for serum copper and ceruloplasmin levels where appropriate. It is unknown definitively whether trientine is excreted in human breast milk during breastfeeding. Additional risk minimisation measures: None

II.C Post-authorisation development plan

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

The following studies are conditions of the marketing authorisation:

Study Short name: *Efficacy and safety of trientine dihydrochloride in Wilson's disease patients (UNV-TR-004)*

Purpose of the study:
- To assess the efficacy of treatment with trientine dihydrochloride by analyses of the course of hepatic, neurological and psychiatric disease.
- To evaluate the pharmacokinetic (PK) – pharmacodynamic (PD) relationship of a single dose of Cufence by analysis of trientine exposure and the direct pharmacodynamic (PD) effect on Cu storage and metabolism parameters.
- To evaluate dosing and titration practices based on a response-guided approach vs conventional treatment.

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

There are no studies required for Cufence.