Part VI: Summary of the Risk Management Plan

Summary of risk management plan for RAVICTI (glycerol phenylbutyrate)

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

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

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

I. The medicine and what it is used for

RAVICTI is authorized for use as adjunctive therapy for chronic management of patients with urea cycle disorders (UCDs) (see SmPC for the full indication). It contains glycerol phenylbutyrate as the active substance and it is given by oral administration.

Further information about the evaluation of RAVICTI's benefits can be found in RAVICTI'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/ravicti.

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

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

II. A List of important risks and missing information

Important risks of RAVICTI 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 RAVICTI. 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	• Use in patients with renal impairment • Safety in pregnancy and lactation • Long-term safety

II. B Summary of important risks

Missing information: Use in patients with renal impairment	
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.2 including recommendation to maintain lowest necessary dose • SmPC Section 5.2 • PL Section 2 and 3 Additional risk minimisation measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • None

Missing information: Safety in pregnancy and lactation	
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4, and PL Section 2 where advice to use effective contraceptive measures by women of child-bearing potential • SmPC Section 4.6and 5.3 Additional risk minimisation measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • None

Missing information: Long-term safety	
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.8 Additional risk minimisation measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • None

II. C Post-authorisation development plan

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

None

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

None