Part VI: Summary of the risk management plan

Summary of risk management plan for Raxone

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

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

This summary of the RMP for Raxone® 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 Raxone®'s RMP.

I. The medicine and what it is used for

Raxone® is authorised for the treatment of LHON (see SmPC for the full indication). It contains idebenone as the active substance and it is given by oral route.

Further information about the evaluation of Raxone®'s benefits can be found in Raxone®'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/raxone*.

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

Important risks of Raxone®, together with measures to minimise such risks and the proposed studies for learning more about Raxone®'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.

If important information that may affect the safe use of Raxone® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Raxone® 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 Raxone®. 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	Abnormal liver function test and hepatitis Blood count abnormalities
Missing information	Use in children under 14 years of age with LHON Use in patients with hepatic impairment Use in patients with renal impairment Use in elderly patients Use in pregnancy and in breastfeeding patients Potential for inhibition of P-gp.

II.B Summary of important risks

Potential risk: Abnormal liver function test and hepatitis	
Evidence for linking the risk to the medicine	Clinical trial data and post-marketing experience
Risk factors and risk groups	LHON patients, as a result of their debilitating disease, often suffer from reactive depression and may present behavioural traits of alcohol abuse and dependence which will predispose them to liver toxicity.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Potential risk: Blood count abnormalities	
Evidence for linking the risk to the medicine	Clinical trial data and post-marketing experience.
Risk groups or risk factors	No risk groups or risk factors could be identified.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 1: Use in children under 14 years of age with LHON	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 2: Use in patients with hepatic impairment	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 3: Use in patients with renal impairment	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:**

	None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 4: Use in elderly patients with LHON	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 5: Use in pregnancy and in breastfeeding patients with LHON	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

Missing information 6: Potential for inhibition of P-gp.	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None*

*The PASS study (PAROS) was completed on 09-Jul-2021 (Database locked) and the CSR was released on 20 Dec 2021. Currently no additional PV activities are active.

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:	**Purpose of the study:**
None	

Imposed mandatory additional pharmacovigilance activity (key to benefit risk)

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

Imposed mandatory additional pharmacovigilance activity (key to benefit risk)

Description of activity (or study title if known)	**Milestone(s)**	**Due Date(s)**
None	Not applicable	Not applicable