SEPHIENCE™

Oral powder, 250 mg and 1,000 mg

Summary of the Risk Management Plan (RMP) for SEPHIENCE (sepiapterin)

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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of SEPHIENCE™ is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of SEPHIENCE™ in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. PTC Therapeutics Switzerland GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of SEPHIENCE™.

I THE MEDICINE AND WHAT IT IS USED FOR

Sepiapterin is a manmade version of a naturally occurring substance required to produce co-factor BH4. This is needed by certain enzymes (proteins) in the body to break down the amino acid phenylalanine into tyrosine.

Sepiapterin is used to treat hyperphenylalaninemia (high blood levels of phenylalanine) in patients of all ages with phenylketonuria (PKU). Our bodies break down the protein in foods into amino acids. PKU is an inherited disease where people cannot break down the amino acid phenylalanine, causing it to build up in the blood and brain, which can be harmful. Sepiapterin helps the body break down phenylalanine, which allows it to reduce the harmful excess of phenylalanine in the blood. Sephience is taken by mouth.

II RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

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

II.A List of Important Risks and Missing Information

Important risks of sepiapterin 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 sepiapterin. 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 administration of the medicine).

Table 1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	None
Missing information	Long-term safety
	Use during pregnancy and lactation

II.B Summary of Important Risks

Missing Information: Long-Term Safety	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections "Warnings and Precautions" and "Undesirable effects"* *PL Section "What you need to know before you take Sephience" and "Possible side effects"* Other routine risk minimisation measures beyond the Product Information: *SmPC section "Dosage/Administration"* *PL section "How to take Sephience"* Additional risk minimisation measures: *None*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: *Study PTC923-MD-004-PKU* See section II.C of this summary for an overview of the post- authorisation development plan.
Missing information: Use during pregnancy and lactation	
Risk minimisation measures	Routine risk minimisation measures *SmPC sections "Pregnancy/lactation" and "Preclinical data"* *PL section "What you need to know before you take Sephience"* Other routine risk minimisation measures beyond the Product Information: *SmPC section "Dosage/Administration"* *PL section "How to take Sephience"*

Additional pharmacovigilance activities	Additional pharmacovigilance activities: *None* See section II.C of this summary for an overview of the post- authorisation development plan.

Abbreviations: SmPC, summary of product characteristics.

II.C Post-Authorisation Development Plan

II.C.1 Studies That Are Conditions of the Marketing Authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of sepiapterin.

II.C.2 Other Studies in Post-Authorisation Development Plan

Study short name: PTC923-MD-004-PKU

A Phase 3 Open-label Study of PTC923 (Sepiapterin) in Phenylketonuria

Purpose of the study:

PTC923-MD-004-PKU is an ongoing, long-term efficacy and safety study to evaluate the long-term safety of sepiapterin in subjects with PKU and to evaluate changes from baseline in dietary Phe/protein consumption.