Part VI: Summary of the risk management plan

Summary of risk management plan for Sapropterin Day Zero 100 mg soluble tablets

This is a summary of the risk management plan (RMP) for Sapropterin Day Zero. The RMP details important risks of Sapropterin Day Zero and how more information will be obtained about Sapropterin Day Zero's risks and uncertainties (missing information).

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

Important new concerns or changes to the current ones will be included in updates of Sapropterin Day Zero's RMP.

I. The medicine and what it is used for

Sapropterin Day Zero is indicated:
- For the treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of all ages with phenylketonuria (PKU) who have been shown to be responsive to such treatment.
- For the treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of all ages with tetrahydrobiopterin (BH4) deficiency who have been shown to be responsive to such treatment.

It contains sapropterin as the active substance and it is given orally.

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

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

II.A List of important risks and missing information

Important risks of Sapropterin Day Zero 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 Sapropterin Day Zero. 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);

Summary of safety concerns	
Important identified risks	Hypersensitivity Hypophenylalaninaemia Interaction with vasodilators using NO metabolism, DHFR Inhibitors, or levodopa
Important potential risks	Behavioral change Convulsion, including worsening Epigastric ulcer Gastroesophageal reflux disease Nephrotoxicity Nephrolithiasis New-onset anxiety disorder Worsening psychiatric disorder
Missing information	Long-term use Limited BH4 deficiency data Subgroup experience: - Use in the elderly - Use in breast-feeding - Use in patients with hepatic failure - Use in patients with renal failure - Use in patients with moderate to severe neurocognitive disability

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 Sapropterin Day Zero.

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

There are no studies required for Sapropterin Day Zero.