Summary of risk management plan for Sapropterin Dipharma

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

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

This summary of the RMP for Sapropterin Dipharma 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 Sapropterin Dipharma's RMP.

I. The medicine and what it is used for

Sapropterin Dipharma is authorised to treat high blood levels of phenylalanine in adults and children of all ages with the genetic disorders phenylketonuria (PKU) or tetrahydrobiopterin (BH4) deficiency. It contains sapropterin dihydrochloride as the active substance and it is given orally as a soluble tablet (100 mg) or as powder for oral solution (100 or 500 mg).

Further information about the evaluation of Sapropterin Dipharma's benefits can be found in Sapropterin Dipharma's EPAR, including its plain-language summary, available on the EMA website, under the medicine's webpage:

https://www.ema.europa.eu/en/medicines/human/EPAR/sapropterin-dipharma

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

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

II.A List of important risks and missing information

Important risks of Sapropterin Dipharma 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 Dipharma. 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	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	Size of safety database
	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, Kuvan.

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 Dipharma.

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

There are no studies required for Sapropterin Dipharma.