Part VI: Summary of the risk management plan for Sapropterin dihydrochloride, 100 mg, Soluble tablets

This is a summary of the risk management plan (RMP) for sapropoterin dihydrochloride 100 mg, soluble tablets. The RMP details important risks of sapropoterin dihydrochloride, how these risks can be minimized, and how more information will be obtained about sapropoterin dihydrochloride's risks and uncertainties (missing information).

Sapropoterin dihydrochloride soluble tablets ' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how sapropoterin dihydrochloride100 mg soluble tablets should be used.

Important new concerns or changes to the current ones will be included in updates of sapropoterin dihydrochloride's RMP.

Part VI: I. The medicine and what it is used for

Sapropoterin dihydrochloride, soluble tablets] are authorized for the treatment of hyperphenylalaninaemia (HPA) in adults and pediatric patients of all ages with:

- phenylketonuria (PKU) or
- tetrahydrobiopterin (BH4) deficiency

who have been shown to be responsive to such treatment (see SmPC for the full indication).

It contains sapropoterin dihydrochloride as the active substance and it is given by oral application as soluble tablet of 100 mg dose strength.

Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of sapropoterin dihydrochloride, soluble tablets, together with measures to minimize such 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 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 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 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 sapropoterin dihydrochloride, soluble tablets is not yet available, it is listed under ‘missing information’ below.

Part VI: II.A: List of important risks and missing information

Important risks of sapropoterin dihydrochloride, soluble tablets 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 sapropoterin dihydrochloride, soluble tablets. 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).

Table 0-1 List of important risks and missing information

List of important risks and missing information	
Important identified risks	Hypersensitivity
	Hypophenylalaninaemia
	Interaction with vasodilators using nitric oxide (NO) metabolism, dihydrofolate reductase (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

Part VI: II.B: Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Part VI: II.C: Post-authorization development plan

II.C.1. Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of sapropoterin dihydrochloride 100 mg soluble tablets.

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

There are no studies required for sapropoterin dihydrochloride 100 mg soluble tablets.