Part VI: Summary of the risk management plan

Summary of risk management plan for Quinine Sulphate 200 mg film-coated tablets (Quinine Sulphate)

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

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

Important new concerns or changes to the current ones will be included in updates of Quinine Sulphate RMP.

I. The medicine and what it is used for

Quinine Sulphate is authorised for the treatment and prophylaxis of nocturnal leg cramps in adults when these are very frequent or particularly painful and treatable causes of the cramps have been ruled out and non-pharmacological measures cannot sufficiently relieve the symptoms. (see SmPC for the full indication). It contains quinine sulphate as the active substance and it is given by mouth.

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

Important risks of Quinine Sulphate together with measures to minimise such risks and the proposed studies for learning more about Quinine Sulphate 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*.

II.A List of important risks and missing information

Important risks of Quinine Sulphate 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 Quinine Sulphate. 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	• Thrombocytopenia, Thrombotic Thrombocytopenic syndrome (TTP), Haemolytic uraemic syndrome (HUS)
Important potential risks	• Off-label use (e.g., use for mild to moderate nocturnal leg cramps, use in children and adolescents under the age of 18 years, use for malaria)
Missing information	• None

II.B Summary of important risks

As the RMP of the reference medicinal product is not available for the applicant, the safety concerns and their risk minimisation measures were specified in accordance with the guidance provided in GVP V Rev 2.

Important identified risk 1: Thrombocytopenia, Thrombotic Thrombocytopenic syndrome (TTP), Haemolytic uraemic syndrome (HUS)	
Evidence for linking the risk to the medicine	German Procedure of the graduate scheme (“Stufenplanverfahren”) from 30.03.2015 Literature (Aster et al. 2007[1], Kojouri et al., 2001[3] and Deirdra et al., 2010[2])
Risk factors and risk groups	Genetic predisposition for thrombocytopenia in different patient populations (e.g., age-, sex- and origin) Hypersensitivity for quinine sulphate
Risk minimisation measures	Routine risk minimisation measures: SmPC section: 4.4 & 4.8 *PL section:* 2. & 4. Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities None

Important potential risk 2: Off-label use (e.g., use for mild to moderate nocturnal leg cramps, use in children and adolescents under the age of 18 years, use for malaria)	
Evidence for linking the risk to the medicine	SmPC for Quinine Sulphate 300mg Coated Tablets, Teva B.V. Netherland, last revision date August 2022[4], which is authorised for the treatment of malignant tertian malaria including treatment of chloroquine resistant malaria.
Risk factors and risk groups	Patients with mild to moderate nocturnal leg cramps Children and adolescents under the age of 18 years Patients suffering from malaria
Risk minimisation measures	Routine risk minimisation measures: *SmPC section:* 4,2 *PL section:* 2. Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities None

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 Quinine Sulphate.

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

There are no studies required for Quinine Sulphate.