Part VI: Summary of the risk management plan

Summary of risk management plan for PYRAMAX (Pyronaridine tetraphosphate/Artesunate)

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

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

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

I. The medicine and what it is used for

PYRAMAX Tablets are authorised for the treatment of acute, uncomplicated malaria infection caused by *Plasmodium falciparum* or by *Plasmodium vivax* in adults and children weighing 20 kg or more.

PYRAMAX granules for oral suspension are authorised for the treatment of acute, uncomplicated malaria infection caused by *Plasmodium falciparum* or by *Plasmodium vivax* in children and infants weighing 5 kg to under 20 kg (see SmPC for the full indication). It contains Pyronaridine Tetraphosphate Artesunate as the active substance and it is given by mouth.

Further information about the evaluation of PYRAMAX's benefits can be found in PYRAMAX's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/pyramax-h-w-2319.

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

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

II.A List of important risks and missing information

Important risks of PYRAMAX 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 PYRAMAX. 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 types of patients who might receive the medicine).

Summary of safety concerns	
Important potential risks	Use in pregnancy and lactation • Embryotoxicity/teratogenicity

II.B Summary of important risks

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

Important Potential Risk 1 **Use in pregnancy and lactation:- embryotoxicity/teratogenicity**	
Evidence for linking the risk to the medicine	ISS (Module 5.3.5.3.1), CSRs for SP-C-002-05, SP-C-005-06 and SP-C-006-06, Module 2.4 (Nonclinical Overview); SP-C-013-11, SP-C-021-15; SP-C-026-18; Post authorisation pregnancy registry
Risk factors and risk groups	There is a potential risk of embryonic death particularly in the first trimester of pregnancy if PYRAMAX is taken during this time.
Risk minimisation measures	Information in sections 4.4, 4.6, 4.6.1 and 5.3 of the SmPC
Additional pharmacovigilance activities	PYRAMAX pregnancy registry (SP-PV-001-12) and utilise currently available registries

II.C Post-authorisation development plan

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

There are no further studies which are conditions of the marketing authorisation or specific obligation of PYRAMAX.

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

SP-PV-001-12 Pregnancy Registry

Monitor all pregnancies and their outcomes. Monitor use in pregnant and lactating women – including risk of embryotoxicity/ teratogenicity

Ongoing

3 year reporting cycle