PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR MACITENTAN 10 mg FILM-COATED TABLETS (macitentan)

This is a summary of the risk management plan (RMP) for MACITENTAN 10 mg FILM-COATED TABLETS (hereafter referred to as 'Macitentan). The RMP details important risks of Macitentan, how these risks can be minimised, and how more information will be obtained about Macitentan risks and uncertainties (missing information).

Macitentan Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how Macitentan should be used.

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

I. The medicine and what it is used for

Macitentan is authorised for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of World Health Organisation Functional Class II to III (see SmPC for the full indication).

It contains macitentan as the active substance and it is given orally once daily.

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

Important risks of Macitentan, together with measures to minimise such risks and the proposed studies for learning more about Macitentan 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 the case of macitentan, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report assessment 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 Macitentan 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 Macitentan. 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	Hepatotoxicity Teratogenicity
Important potential risks	None
Missing information	None

II.B Summary of important risks

Important Identified Risk: Hepatotoxicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3 contraindication SmPC sections 4.4 Special warnings, and precautions for use SmPC sections 4.8. Undesirable effects PL section 2 and 4. Instructions for liver function monitoring and actions to be taken in case of elevated hepatic enzymes are provided in SmPC section 4.4 Legal status: Prescription only medicine Additional risk minimisation measures: Patient alert card

Important Identified Risk: Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3 contraindication SmPC sections 4.4 Special warnings, and precautions for use SmPC sections 4.6 Fertility, Pregnancy, and lactation PL section 2. Instructions for the use of macitentan in women of childbearing potential and recommendation for monthly pregnancy tests during treatment are provided in SmPC section 4.4 Legal status: Prescription only medicine Additional risk minimisation measures: Patient alert card

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 Macitentan.

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

There are no studies required for Macitentan.