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. The RMP details important risks of Macitentan, 10 mg film-coated tablets, how these risks can be minimized, and how more information will be obtained about Macitentan, 10 mgfilm-coated tablets risks and uncertainties (missing information).

Macitentan, 10 mg film-coated tablets SmPC and Package Leaflet give essential information to healthcare professionals and patients on how Macitentan, 10 mg film-coated tablets. should be used.

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

I. The medicine and what it is used for

Macitentan, 10 mg film-coated tablets are authorized for: as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

It contains macitentan as the active substance and it is given by oral route of administration as 10 mg film-coated tablets.

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

Important risks of Macitentan, 10 mg film-coated tablets, together with measures to minimize such risks and the proposed studies for learning more about Macitentan, 10 mg film-coated tablets' 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 packaging;
- The authorized pack size – the amount of medicine in a pack is chosen as 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 minimize risks.

Together, these measures constitute *routine risk minimization* measures.

In the case of Macitentan, 10 mg film-coated tablets, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed 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 Macitentan, 10 mg film-coated tablets is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Macitentan, 10 mg film-coated tablets are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered or 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, film-coated 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);

List of important risks and missing information	
Important identified risks	Anaemia, decrease in haemoglobin concentration Hepatotoxicity Teratogenicity Symptomatic hypotension
Important potential risks	Menstrual disorders (primarily bleeding) Ovarian cysts Pulmonary edema associated with pulmonary veno-occlusive disease (PVOD) Testicular disorders and male infertility
Missing information	Pediatric patients

II.B Summary of important risks

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

Important identified risk: Hepatotoxicity	
Risk minimization measures	**Routine risk communication:** SmPC Section 4.3, 4.4, and 4.8. PL Section 4 and 2. **Routine risk minimization activities recommending specific clinical measures to address the risk:** Liver enzyme tests must be obtained prior to initiation of macitentan and monthly monitoring of aminotransferases during treatment with macitentan is

	recommended. Patients must be monitored for signs of hepatic injury and monthly monitoring of ALT and AST is recommended are included in SmPC Section 4.4. **Other routine risk minimization measures beyond the Product Information:** Pack size: Limited pack sizes. Legal status: Prescription-only medicine. **Additional risk minimization measures:** • Patient card.
Important identified risk: Teratogenicity	
Risk minimization measures	**Routine risk communication:** SmPC Section 4.3, 4.4, and 4.6. PL Section 2. **Routine risk minimization activities recommending specific clinical measures to address the risk:** Monthly pregnancy tests during treatment with macitentan are recommended to allow early detection of pregnancy as included in SmPC Sections 4.4, and 4.6. **Other routine risk minimization measures beyond the Product Information:** Pack size: Limited pack sizes. Legal status: Prescription-only medicine. **Additional risk minimization measures:** • Patient card.

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 macitentan, 10 mg film-coated tablets.

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

There are no studies required for macitentan, 10 mg film-coated tablets.