PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for ambrisentan

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

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

This summary of the RMP for ambrisentan should be read in the context of all this information, including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. The medicine and what it is used for

Ambrisentan is authorised for the treatment of pulmonary arterial hypertension (PAH) in adult patients (see SmPC for the full indication). It contains ambrisentan as the active substance and it is given by oral route.

Further information about the evaluation of ambrisentan ’s benefits can be found in ambrisentan’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/ambrisentan-mylan.

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

Important risks of ambrisentan, together with measures to minimise such 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 public (e.g. with or without prescription) can help to minimise its risks.

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

In the case of Ambrisentan Mylan, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse events is collected continuously and is regularly analysed, including in 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 ambrisentan is not yet available, it is listed under "Missing information" below.

II.A List of important risks and missing information

Important risks of ambrisentan 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 ambrisentan. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but the definite causal 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 1 Part VI: Summary of safety concerns

List of important risks and missing information	
Important identified risks	• Teratogenicity • Decreased haemoglobin, haematocrit, anaemia including anaemia requiring transfusion • Hepatotoxicity
Important potential risks	• Testicular tubular atrophy/male infertility
Missing information	None

II.B Summary of important risks

Important Identified Risk Teratogenicity	
Evidence for linking the risk to the medicine	In line with the reference RMP, this safety concern has been classified as an important identified risk.
Risk factors and risk groups	Pregnant women and women of childbearing potential
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.2, 4.3, 4.4, 4.6 and 5.3 PL section 2 Restricted medical prescription Additional risk minimisation measures Educational materials (Patient Reminder Card)

Important Identified Risk Decreased haemoglobin, haematocrit, anaemia including anaemia requiring transfusion	
Evidence for linking the risk to the medicine	In line with the reference RMP, this safety concern has been classified as an important identified risk.
Risk factors and risk groups	Patients treated with ambrisentan
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4, 4.8, 5.1 PL sections 2 and 4 Restricted medical prescription Additional risk minimisation measures Not applicable as there are no additional risk minimisation measures for this safety concern

Important Identified Risk Hepatotoxicity	
Evidence for linking the risk to the medicine	In line with the reference RMP, this safety concern has been classified as an important identified risk.
Risk factors and risk groups	Patients treated with ambrisentan

Important Identified Risk Hepatotoxicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 PL sections 2 and 4 Restricted medical prescription Additional risk minimisation measures Educational materials (Patient Reminder Card)

Important Potential Risk Testicular tubular atrophy/male infertility	
Evidence for linking the risk to the medicine	In line with the reference RMP, this safety concern has been classified as an important potential risk.
Risk factors and risk groups	Male patients treated with ambrisentan
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6 and 5.3 PL section 2 Restricted medical prescription Additional risk minimisation measures Not applicable as there are no additional risk minimisation measures for this safety concern

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 ambrisentan.

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

There are no studies required for ambrisentan.