Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for AMBRISENTAN 5mg and 10mg film-coated tables

This is a summary of the risk management plan (RMP) for AMBRISENTAN 5 mg and 10 mg film-coated tables, (hereinafter referred to as 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 Ambrisentan should be used.

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 pulmonary arterial hypertension (see SmPC for the full indication). It contains ambrisentan as the active substance and it is given orally.

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 and the proposed studies for learning more about Ambrisentan'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 the case of Ambrisentan, 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, 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 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 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).

Table 8: 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

Table 9: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures Contraindication for use in pregnant women and women of child-bearing potential who are not using reliable contraception in SmPC section 4.3. Use in women of child-bearing potential is discussed in SmPC section 4.4. Detailed information on fertility and pregnancy are presented in SmPC section 4.6. Monthly pregnancy tests during treatment with ambrisentan are recommended in SmPC sections 4.4 and 4.6. Prescription only medicine. Additional risk minimisation measures Patient Reminder Card
Important identified risk: Hepatotoxicity	
Risk minimisation measures	Routine risk minimisation measures Recommendation for liver function monitoring is included in SmPC sections 4.4. Information on patients with hepatic impairment is presented in SmPC section 4.2.

	Contraindications stated in section 4.3 of the SmPC. Liver function abnormalities are discussed in SmPC section 4.4. Risk is listed in SmPC section 4.8. Prescription only medicine. Additional risk minimisation measures Patient Reminder 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 Ambrisentan.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Ambrisentan.