Part VI: Summary of the risk management plan

Summary of risk management plan for Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets (Ambrisentan)

This is a summary of the risk management plan (RMP) for Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets. The RMP details important risks of Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets, how these risks can be minimised, and how more information will be obtained about Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets' risks and uncertainties (missing information).

Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Ambrisentan 2.5 mg, 5 mg & 10 mg Film-coated tablet's RMP.

I. The medicine and what it is used for

Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets are indicated for treatment of pulmonary arterial hypertension (PAH) in adult and paediatric (aged 8 to less than 18 years) patients of WHO Functional Class (FC) II to III, including use in combination treatment (See SmPC for the full indication).

It contains Ambrisentan as the active substance and it is given by oral route.

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

Important risks of Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablet'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;

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- 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 2.5 mg, 5 mg & 10 mg film-coated tablets, 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 2.5 mg, 5 mg & 10 mg film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 2.5 mg, 5 mg & 10 mg 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	• Teratogenicity • Hepatotoxicity
Important potential risks	• None
Missing information	• None

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II.B Summary of important risks

Important Identified Risk - Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures: • SmPC Sections: 4.3, 4.4, 4.6 and 5.3 • PIL Section: 2 • Recommendation for monthly pregnancy tests during treatment with ambrisentan in section 4.4 and 4.6 of the SmPC • Need for exclusion of pregnancy and practice reliable contraception before initiating ambrisentan in section 4.4 of the SmPC • Prescription only status of the product Additional risk minimisation measures: • Patient reminder card
Important Identified Risk - Hepatotoxicity	
Risk minimisation measures	Routine risk minimisation measures: • SmPC Sections: 4.2, 4.3, 4.4, 4.8 and 5.3 • PIL Section: 2 • Need for hepatic aminotransferases evaluation prior to initiation of ambrisentan in section 4.4 of the SmPC • Need for exclusion of patients with severe hepatic impairment and with baseline values of ALT and/or AST >3xULN in sections 4.2, 4.3, and 4.4 of the SmPC • Recommendations to monitor patients for signs of hepatic injury and monthly monitoring of ALT and AST in section 4.4 of the SmPC

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	• Need to discontinue ambrisentan therapy if patients develop sustained, unexplained, clinically significant ALT and/or AST elevation, or if ALT and/or AST elevation is accompanied by signs or symptoms of hepatic injury (e.g., jaundice) in section 4.4 of the SmPC • Recommendation on re-initiation of ambrisentan therapy in patients without clinical symptoms of hepatic injury or jaundice, following resolution of hepatic enzyme abnormalities with the advice of a hepatologist in section 4.4 of the SmPC • Prescription only status of the product 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 2.5 mg, 5 mg & 10 mg film-coated tablets.

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

There are no studies required for Ambrisentan 2.5 mg, 5 mg & 10 mg film-coated tablets.

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