Summary of risk management plan for Bosentan 62.5 mg and 125 mg film-coated tablets (Bosentan) Orion Corporation

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This is a summary of the risk management plan (RMP) for Bosentan 62.5 mg and 125 mg film-coated tablets (hereinafter referred to as bosentan). The RMP details important risks of bosentan, how these risks can be minimised, and how more information will be obtained about bosentan risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Bosentan is used to treat the Pulmonary arterial hypertension (PAH): PAH is a disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels (the pulmonary arteries) that carry blood from the heart to the lungs. This pressure reduces the amount of oxygen that can get into the blood in the lungs, making physical activity more difficult. Bosentan widens the pulmonary arteries, making it easier for the heart to pump blood through them. This lowers the blood pressure and relieves the symptoms.

Bosentan is used to treat patients with class III pulmonary arterial hypertension (PAH) to improve exercise capacity (the ability to carry out physical activity) and symptoms. The 'class' reflects the seriousness of the disease: 'class III' involves marked limitation of physical activity. Some improvements have also been shown in patients with class II PAH. 'Class II' involves slight limitation of physical activity. The PAH for which bosentan is indicated can be:

• primary (with no identified cause or familial);

• caused by scleroderma (also called systemic sclerosis, a disease where there is abnormal growth of the connective tissue that supports the skin and other organs);

• caused by congenital (inborn) heart defects with shunts (abnormal passageways) causing abnormal flow of blood through the heart and lungs.

• Digital ulcers: (sores on the fingers and toes) in adult patients with a condition called scleroderma. Bosentan reduces the number of new finger and toe ulcers that appear. (SmPC for full indication). It contains bosentan as an active substances and is given by orally.

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

Important risks of bosentan, together with measures to minimise such risks and the proposed studies for learning more about bosentan'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 minimises its risks.

Together, these measures constitute routine risk minimisation measures.

In the case of bosentan, these measures are supplemented with additional risk minimisation measures mentioned under relevant risks, below.

☐ Hepatotoxicity
☐ Teratogenicity

Additional Risk Minimisation measures:

- Patient Alert card

In addition to these measures, information about the adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) 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 bosentan 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 bosentan. 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

List of important risks and missing information	
	Teratogenicity
Important potential risks	None
Missing information	None

II.B Summary of important risks

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

Important identified risk information : Hepatotoxicity	
Evidence for linking the risk to the medicine	Inline with the PRAC recommendation
Risk factors and risk groups	Patients with known history of hepatic impairment.
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.5 Interaction with other medicinal products and other forms of interaction, 4.8 Undesirable effects, 5.2 Pharmacokinetic properties and 5.3 Preclinical safety data Listings in PIL section 2. What you need to know before you take bosentan and 4. Possible side effects <u>Routine risk minimisation activities recommending specific clinical measures to address the risk:</u> Recommendation on patients monitoring for aminotransferase levels (ALT/AST) and liver function are included in SmPC 4.4 Special warnings and precautions for use and 4.8 Undesirable effects. Recommendation on patients monitoring for liver and blood values are included in PIL section 4.4 Possible side effects **Additional risk minimisation measures** ➢ Patient Alert card

Important identified risk information: Teratogenicity	
Evidence for linking the risk to the medicine	Inline with the PRAC recommendation
Risk factors and risk groups	Not applicable
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.5 Interaction with other medicinal products and other forms of interaction, 4.6 fertility, pregnancy and lactation and 5.3 Preclinical safety data Listings in PIL section 2. What you need to know before you take bosentan.

Important identified risk information: Teratogenicity	
	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 bosentan.

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

There are no studies required for bosentan.