Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for SELEXIPAG 200 µg, 400 µg, 600 µg, 800 µg, 1000 µg, 1200 µg, 1400 µg and 1600 µg film-coated tablets

This is a summary of the risk management plan (RMP) for SELEXIPAG 200 µg, 400 µg, 600 µg, 800 µg, 1000 µg, 1200 µg, 1400 µg and 1600 µg film-coated tablets (hereinafter referred to as Selexipag). The RMP details important risks of Selexipag, how these risks can be minimised, and how more information will be obtained about Selexipag's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Selexipag is authorised for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies. 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 (see SmPC for the full indication). It contains Selexipag 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 Selexipag, together with measures to minimise such risks and the proposed studies for learning more about Selexipag'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 Selexipag, 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*.

If important information that may affect the safe use of Selexipag is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Selexipag 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 Selexipag. 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).

Summary of safety concerns	
Important identified risks	• Hypotension • Anaemia • Hyperthyroidism • Concomitant use with strong inhibitors of CYP2C8
Important potential risks	• Pulmonary oedema associated with PVOD • MACE • Renal functional impairment / acute renal failure • Bleeding events • Light-dependent non-melanoma skin malignancies • Ophthalmological effects associated with retinal vascular system • GI disturbances denoting intestinal intussusception (manifested as ileus or obstruction) • Medication error
Missing information	• Use in paediatric patients • Use in elderly over 75 years old • Use during pregnancy and lactation • Concomitant use with strong inhibitors of UGT1A3 and UGT2B7

II.B Summary of Important Risks

Important potential risk: Medication error	
Risk minimisation measures	Routine risk minimisation measures Risk is listed in SmPC section 4.2. Described in PL section 3. Prescription only medicine. Additional risk minimisation measures Controlled Access System Educational material in a Prescriber Kit containing: • Cover Letter to the HCP • SmPC • HCP A4 laminated titration guide for the physician specifically describing treatment initiation and titration with a selexipag starting dose of 200 µg) • Patient Titration Guide included in the titration pack of the 200 µg tablets • Package leaflet

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 Selexipag.

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

There are no studies required for Selexipag.