Part VI: Summary of the risk management plan

Summary of risk management plan for Busulfan Koanaa 6 mg/ml concentrate for solution for infusion.

This is a summary of the risk management plan (RMP) for Busulfan Koanaa 6 mg/ml concentrate for solution for infusion The RMP details important risks of Busulfan Koanaa 6 mg/ml concentrate for solution for infusion, how these risks can be minimised, and how more information will be obtained about Busulfan Koanaa 6 mg/ml concentrate for solution for infusion 's risks and uncertainties (missing information).

Busulfan Koanaa 6 mg/ml concentrate for solution for infusion summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Busulfan Koanaa 6 mg/ml concentrate for solution for infusion should be used.

I. The medicine and what it is used for

Busulfan Koanaa 6 mg/ml concentrate for solution for infusion is authorised for the treatment of following indications.

- Busulfan followed by cyclophosphamide (BuCy2) is indicated as conditioning treatment prior to conventional haematopoietic progenitor cell transplantation (HPCT) in adult patients when the combination is considered the best available option.
- Busulfan following fludarabine (FB) is indicated as conditioning treatment prior to haematopoietic progenitor cell transplantation (HPCT) in adult patients who are candidates for a reduced-intensity conditioning (RIC) regimen.
- Busulfan followed by cyclophosphamide (BuCy4) or melphalan (BuMel) is indicated as conditioning treatment prior to conventional haematopoietic progenitor cell transplantation in paediatric patients.

It contains busulfan as the active substance and it is administered by intravenous infusion via central venous catheter. It is available as 6mg/ml Concentrate for solution for infusion.

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

Important risks of Busulfan Koanaa 6 mg/ml concentrate for solution for infusion, together with measures to minimise such risks and the proposed studies for learning more about 6 mg/ml concentrate for solution for infusion 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.

II.A List of important risks and missing information

Important risks of Busulfan Koanaa 6 mg/ml concentrate for solution for infusion 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 Busulfan Koanaa. 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.

List of important risks and missing information	
Important identified risks	• Hepatic venoocclusive disease • Seizure • Myelosuppression • Drug interaction with paracetamol • Reproductive toxicity • Impaired fertility • Secondary Malignancies • Interstitial pulmonary fibrosis • Lens disorders/cataracts
Important potential risks	• Cardiac tamponade • Drug interaction with itraconazole
Missing information	• Use in patients with hepatic impairment • Use in patients with renal impairment • Use in obese children and adolescents • Use in elderly patients (> 65 years)

The above stated safety concerns are obtained from list of safety concerns as per approved Risk Management Plan (RMP) of Busulfan Version 2.0 dated 28 October 2015 (Accord Healthcare Limited), published by CMDh.

II.B Summary of important risks

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

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 Busulfan Koanaa 6 mg/ml concentrate for solution for infusion.

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

There are no studies required for Busulfan Koanaa 6 mg/ml concentrate for solution for infusion.