Part VI: Summary of the risk management plan

Summary of risk management plan for Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection (Bupivacaine Heavy)

This is a summary of the risk management plan (RMP) for Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection. The RMP details important risks of Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection, how these risks can be minimised and how more information will be obtained about Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection's risks and uncertainties (missing information).

Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection should be used.

I. The medicine and what it is used for

Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection is authorised in adults and children of all ages for intrathecal (subarachnoid) spinal anaesthesia for (obstetric) surgery; for urological or lower limbs surgery, including hip surgery lasting 1.5 to 3 hours; and for lower abdominal surgery (including caesarean section) lasting 1.5 to 3 hours (see SmPC for the full indication). It contains bupivacaine heavy as the active substance and it is given by intrathecal injection.

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

Important risks of Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection, together with measures to minimise such risks and the proposed studies for learning more about Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection'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.

II.A List of important risks and missing information

Important risks of Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection 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 Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection. 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	- Systemic toxicity - CNS and cardiovascular toxicity - Consequences of accidental intravascular injection - Neurological damage, such as paralysis and motor weakness
Important potential risks	- None
Missing information	- None

II.B Summary of important risks

Systemic toxicity	
Evidence for linking the risk to the medicine	According to international literature and SmPC, systemic toxicity is rarely associated with spinal anaesthesia but might occur after accidental intravascular injection.
Risk factors and risk groups	- Concomitant administration of other local anaesthetics. In these cases, toxic effects are additive and may cause systemic toxic reactions. - Accidental intravascular injection, and especially in patients with following conditions: o Comorbidities which can increase the risk of local anaesthetic overdose, such as hepatic dysfunction, cardiac disease, pregnancy, and metabolic syndromes (Mahajan A et al; 2018). o Patients at extremes of age due to reduced clearance of the anaesthetics (Mahajan A et al; 2018). o Patients with renal dysfunction and uremic patients, due to reduced clearance (Dillane D et al; 2010).
Risk minimisation measures	**Routine risk minimisation measures:** - SmPC Section 4.4 Special warning and precautions of use; - SmPC Section 4.9 Overdose; - PIL Section 3 and 4.

	Additional risk minimisation measures: Not applicable.

CNS and cardiovascular toxicity	
Evidence for linking the risk to the medicine	According to international literature and SmPC, CNS and cardiovascular toxicity are important consequences of local anaesthetic systemic toxicity.
Risk factors and risk groups	- Concomitant administration of other local anaesthetics. In these cases, toxic effects are additive. - Concomitant administration of anti-arrhythmic drugs class III (e.g. amiodarone). These patients should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive. - Accidental intravascular injection, and especially in patients with following conditions: o Comorbidities which can increase the risk of local anaesthetic overdose, such as hepatic dysfunction, cardiac disease, pregnancy, and metabolic syndromes (Mahajan A et al; 2018). o Patients at extremes of age due to reduced clearance of the anaesthetics (Mahajan A et al; 2018). o Patients with renal dysfunction and uremic patients, due to reduced clearance (Dillane D et al; 2010).
Risk minimisation measures	**Routine risk minimisation measures:** - SmPC Section 4.4 Special warning and precautions of use; - SmPC Section 4.9 Overdose; - PIL Section 3 and 4. **Additional risk minimisation measures:** Not applicable.

Consequences of accidental intravascular injection	
Evidence for linking the risk to the medicine	According to international literature and SmPC, accidental intravascular injection might induce systemic toxicity.
Risk factors and risk groups	- Concomitant administration of other local anaesthetics.

	- Concomitant administration of anti-arrhythmic drugs class III (e.g. amiodarone). - Comorbidities which can increase the risk of local anaesthetic overdose, such as hepatic dysfunction, cardiac disease, pregnancy, and metabolic syndromes (Mahajan A et al; 2018). - Patients at extremes of age due to reduced clearance of the anaesthetics (Mahajan A et al; 2018). Patients with renal dysfunction and uremic patients, due to reduced clearance (Dillane D et al; 2010).
Risk minimisation measures	**Routine risk minimisation measures:** - SmPC Section 4.4 Special warning and precautions of use; - SmPC Section 4.9 Overdose; - PIL Section 3 and 4. **Additional risk minimisation measures:** Not applicable.

Neurological damage, such as paralysis and motor weakness	
Evidence for linking the risk to the medicine	According to international literature and SmPC, neurological injury is a rare consequence of intrathecal anaesthesia and may result in paraesthesia, anaesthesia, motor weakness and paralysis. Occasionally these are permanent. Neurological disorders, such as multiple sclerosis, hemiplegia, paraplegia and neuromuscular disturbances are not thought to be adversely affected by intrathecal anaesthesia, but caution should be exercised.
Risk factors and risk groups	Unknown
Risk minimisation measures	**Routine risk minimisation measures:** - SmPC Section 4.4 Special warning and precautions of use; - SmPC Section 4.8 Undesirable effects; - PIL Section 4. **Additional risk minimisation measures:** Not applicable.

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 Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection.

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

There are no studies required for Bupivacaine Heavy Panpharma 5 mg/ml, solution for injection.