Annex IV

Conditions to the marketing authorisations

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National competent authorities of Member State(s) or reference Member State(s) if applicable, shall ensure that the following conditions are fulfilled by the MAH(s):

Conditions	Date
The MAH(s) should perform two phase IV randomised clinical trials (RCTs) with an appropriate control and clinically meaningful endpoints to demonstrate the efficacy and safety in the perioperative setting and trauma. The primary composite endpoint is 90-day mortality and 90-days renal failure. The secondary endpoints are: - major peri-operative complications (e.g. infections, bleedings, anastomosis insufficiency, reoperation rate, diagnosis of pulmonary oedema). - Haemodynamic stabilisation in relation to dose (e.g. Heart rate, mean arterial pressure, central venous pressure, central venous oxygen saturation, serum lactate level, base excess and urine output) - length of stay, morbidity, coagulation, inflammation, hospital mortality - measurement of creatinine (GFR) 1/ The protocol of the studies should be submitted to the NCAs 2/ Final study reports by:	1/ Within 6 months after EC decision 2/ End of 2016
The MAH(s) should conduct a drug utilisation study in several Member States to evaluate the effectiveness of the risk minimisation measures taken. Study protocol by: Final study report by:	Within 6 months after EC decision Within 24 months after protocol agreement
The MAH(s) should submit the core elements (including protocol of DUS, protocol of the RCTs) of a risk management plan in EU format.	Within 6 months after EC decision
DHPC Communication circulation according to the PRAC agreed communication plan and conditions.	Within 1 week from CMDh adopted position