



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

29 November 2012
EMA/757392/2012
EMA/H/A-31/1348

Review of hydroxyethyl-starch-containing solutions for infusion started

The European Medicines Agency has started a review of solutions containing hydroxyethyl starch (HES) used for the management of hypovolaemia (low blood volume caused by dehydration or blood loss) and hypovolaemic shock (a steep fall in blood pressure caused by drop in blood volume) in critically ill patients and, in particular, patients with sepsis (damage to organs caused by bacteria and their toxins in the blood following an infection).

HES-containing solutions are given by infusion (drip) into a vein and are used as volume expanders to replace lost fluids in patients with hypovolaemia to prevent shock.

Safety concerns have been raised following the publication of recent studies comparing HES with other volume expanders in critically ill patients. A study¹ comparing HES with Ringer's acetate (another volume expander) in patients with severe sepsis showed that patients treated with HES had a higher risk of death and were more likely to receive renal replacement therapy (treatment for kidney failure such as dialysis). These results were similar to those of an earlier study² in patients with severe sepsis. In addition, a more recent study³ carried out in 7,000 intensive care patients comparing HES with saline solution also showed a higher need for renal replacement therapy but no increased risk of death in patients treated with HES.

The European Medicines Agency will evaluate the benefit-risk balance of HES-containing solutions for infusion and issue an opinion on whether their marketing authorisations should be maintained, varied, suspended or withdrawn across the EU.

¹ Perner, A. *et al.* Hydroxyethyl Starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med* 2012; 367(2): 124-134.

² Brunkhorst, F.M. *et al.* Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med*, 2008; 358(2): 125-39.

³ Myburgh, J.A. *et al.* Hydroxyethyl starch or saline for fluid resuscitation in intensive care; *N Engl J Med* 2012; 367(20): 1901-11.



More about the medicine

Infusion solutions containing HES are frequently used volume expanders and belong to the class of colloids. There are two main types of volume expanders: crystalloids and colloids. Colloids contain large molecules such as starch whereas crystalloids such as saline solutions contain smaller molecules. In the EU, HES-containing solutions for infusion have been approved via national procedures.

More about the procedure

The review of HES solutions for infusion has been initiated at the request of the German medicines agency under Article 31 of Directive 2001/83/EC.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As HES-containing medicines are all authorised nationally, the PRAC recommendation will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which is a regulatory body that represents national medicines regulatory authorities of the EU Member States. This will result in harmonised measures to be implemented in all Member States.