
Review of hydroxyethyl-starch containing solutions for infusion started

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Information on Medicinal Product

Hydroxyethyl starch (HES)-containing solutions are given by infusion (drip) into a vein and are used as volume expanders to replace lost fluids in critically ill patients with hypovolaemia (low blood volume caused by dehydration or blood loss) to prevent hypovolaemic shock (a steep fall in blood pressure caused by drop in blood volume). 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. HES colloid volume expanders authorised nationally and marketed in Malta are Volulyte 6% Solution for Infusion (Fresenius Kabi) and Plasma Volume Redibag 6% Solution for Infusion (Baxter Healthcare). In the European Union (EU), HES-containing solutions for infusion have been approved via national procedures.

Information from European Medicines Agency about the safety concern

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

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.

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.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on volume expander solutions. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at <http://www.medicinesauthority.gov.mt/pub/adr.doc> or to the marketing authorisation holder or their local representatives.>

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.