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Hydroxyethyl-starch solutions (HES) no longer to be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

On 23 October 2013, the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)*, endorsed by majority the recommendations of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that HES solutions must no longer be used to treat patients with sepsis (bacterial infection in the blood) or burn injuries or critically ill patients because of an increased risk of kidney injury and mortality.

HES solutions may continue to be used in patients to treat hypovolaemia (low blood volume) caused by acute (sudden) blood loss, where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient. In order to minimise potential risks in these patients, HES solutions should not be used for more than 24 hours and patients' kidney function should be monitored after HES administration. In addition to updating the product information, further studies should be carried out on the use of these medicines in elective surgery and trauma patients.

The review of HES solutions was carried out by the PRAC following the publication of studies showing an increased risk of mortality in patients with sepsis^{1,2} and an increased risk of kidney injury requiring dialysis in critically ill patients^{1,2,3} following treatment with HES solutions.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and, on 19 December 2013, adopted a final legally binding decision valid throughout the European Union (EU).

Information for patients

- Because of the risk of kidney injury and mortality, HES solutions must no longer be used in patients with sepsis (bacterial infection in the blood) or burn injuries or critically ill patients.
- HES solutions may continue to be used to treat hypovolaemia (low blood volume) caused by acute (sudden) blood loss. However, the doctor should monitor the patient's kidney function after HES administration.

* The CMDh is a medicines regulatory body representing the European Union (EU) Member States



- Patients who have any questions or concerns should speak to the treating doctor, pharmacist or nurse.

Information for healthcare professionals

- Because of the risk of kidney injury and mortality, HES solutions must no longer be used in patients with sepsis, burn injuries or critically ill patients.
- HES solutions should only be used for the treatment of hypovolaemia due to acute blood loss when crystalloids alone are not considered sufficient.
- There is a lack of robust long-term safety data in patients undergoing surgical procedures and in patients with trauma. The expected benefit of treatment should be carefully weighed against the uncertainties with regard to long-term safety, and other available treatment options should be considered. Additional studies will be performed with HES solutions in patients with trauma and in elective surgery.
- HES solutions should be used at the lowest effective dose for the shortest period of time. Treatment should be guided by continuous haemodynamic monitoring so that the infusion is stopped as soon as appropriate haemodynamic goals have been achieved.
- HES solutions are now contraindicated in patients with renal impairment or renal replacement therapy. The use of HES must be discontinued at the first sign of renal injury. An increased need for renal replacement therapy has been reported up to 90 days after HES administration. Patients' kidney function should be monitored after HES administration.
- HES solutions are contraindicated in severe coagulopathy. HES solutions should be discontinued at the first sign of coagulopathy. Blood coagulation parameters should be monitored carefully in case of repeated administration.

These recommendations are based on a review of all available safety and efficacy data, including recent data^{4,5,6}, from clinical studies, meta-analyses and post-marketing experience.

Healthcare professionals have been informed in writing of the outcome of the review and the changes to the use of HES solutions.

References:

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6. Rational Fluid Therapy in Germany (RaFTinG). Available on ClinicalTrials.gov (NCT01122277) last updated on 07 July 2011:
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More about the medicine

Infusion solutions containing HES are frequently used for volume replacement and belong to the class known as colloids. There are two main types of medicines used for volume replacement: crystalloids and colloids. Colloids contain large molecules such as starch, whereas crystalloids, such as saline (salt) solutions or Ringer's acetate, contain smaller molecules.

In the EU, HES-containing solutions for infusion have been approved via national procedures and are available in all Member States under various trade names.

More about the procedures

A review of HES solutions for infusion was initiated on 29 November 2012 at the request of the German medicines agency, under Article 31 of Directive 2001/83/EC. This review, which had been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), concluded on 13 June 2013, but some of the marketing authorisation holders requested a re-examination.

While the re-examination was ongoing, some Member States decided to suspend or limit the marketing or use of these medicines in their territories. In accordance with EU legislation, this type of action required that an EU review procedure be carried out. Consequently, on 27 June 2013, the UK triggered an EU review of HES solutions under Article 107i of Directive 2001/83/EC. This review procedure ran in parallel with the re-examination of the PRAC's June 2013 recommendation and both procedures were finalised on 10 October 2013. For the re-examination procedure the PRAC confirmed its previous position. However, new evidence was considered in the parallel Article 107i procedure and this was the basis for the PRAC's final recommendation on the use of HES solutions.

As HES-containing solutions for infusion are all authorised nationally, the PRAC recommendations were forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which adopted a final position. The CMDh, a body representing EU Member States, is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and adopted an EU-wide legally binding decision on 19 December 2013.

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