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PRAC confirms that hydroxyethyl-starch solutions (HES) should no longer be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed its review of HES solutions following an assessment of new information and commitments from companies for additional studies and risk minimisation activities. The Committee confirmed 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, however, continue to be used in patients to treat hypovolaemia (low blood volume) caused by acute blood loss, provided that appropriate measures are taken to reduce potential risks and that additional studies are carried out.

The review of HES solutions was initially triggered by the German medicines agency, the Federal Institute for Drugs and Medical Devices (BfArM), following studies showing an increased risk of mortality in patients with sepsis and an increased risk of kidney injury requiring dialysis in critically ill patients following treatment with HES solutions.

The PRAC had initially concluded on 13 June 2013 that HES solutions should be suspended in all patient populations. Since then, the PRAC has analysed and considered new evidence that was not available at the time of the initial recommendation, including new studies. The Committee has also looked at new proposals for additional risk minimisation measures, including restrictions on use and a commitment from the companies to conduct additional studies.

The PRAC, on the basis of all data available to date, considered whether a group of patients could be identified for whom HES treatment remains beneficial. The Committee concluded that there was clear evidence for an increased risk of kidney injury and mortality in critically ill and septic patients, and that therefore HES should no longer be used in these patients. However the PRAC agreed that HES could continue to be used in patients with hypovolaemia caused by acute blood loss where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient. The PRAC acknowledged the need for measures to minimise potential risks in these patients and recommended that HES solutions should not be used for more than 24 hours and that patients' kidney

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function should be monitored for at least 90 days. In addition, the PRAC requested that further studies be carried out on the use of these medicines in elective surgery and trauma patients.

The PRAC recommendation will now be sent to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), for consideration at its meeting on 21-23 October 2013.

More about the medicine

Infusion solutions containing HES are frequently used for volume replacement and belong to the classknown 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 European Union (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 recommendation will now be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt 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.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

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