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Hydroxyethyl-starch solutions for infusion to be suspended – CMDh endorses PRAC recommendation

Suspension due to serious risks of kidney injury and death in certain patient populations

The CMDh[1] has endorsed the recommendation to suspend the marketing authorisations of hydroxyethyl-starch (HES) solutions for infusion across the European Union. These products are used as plasma volume replacement following acute (sudden) blood loss, where treatment with alternative products known as 'crystalloids' alone is not considered to be sufficient.

The review of HES solutions for infusion has been carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC). The CMDh endorsed the suspension recommended by the PRAC due to the fact that these medicines have continued to be used in critically ill patients and patients with sepsis despite restrictions on use in these patient populations introduced in 2013 to reduce the risk of kidney injury and death. The final decision, however, will be taken by the European Commission.[2]

The PRAC reviewed results of drug utilisation studies, together with the currently available data on benefits and risks from clinical trials and observational studies and feedback received from stakeholders and experts. Based on this review, the PRAC concluded that the restrictions introduced in 2013 have not been sufficiently effective.

The PRAC also explored the possibility of introducing additional measures to protect patients at risk but concluded that such measures would be ineffective or insufficient.

The CMDh has now agreed with the PRAC recommendation that, in view of the serious risks that certain patients are exposed to, HES solutions for infusion should be suspended. Alternative treatment options are available.

As the CMDh position was adopted by majority vote, the CMDh position will now be sent to the European Commission, which will take an EU-wide legally binding decision.

Information for patients

- HES solutions for infusion are replacement fluids given to patients who have lost blood following injury or surgery.

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.
[2] Text modified to clarify next procedural steps. Changes made on 2 February 2018.

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- These products are being suspended in the EU in view of the serious risks that certain patients (for example those who are very ill or have blood poisoning) are exposed to.
- Other treatment options are available for treating blood loss in the EU.
- This suspension does not apply to the use of HES in clinical trials, where patient selection is tightly controlled. Member States where trials with HES solutions for infusion are ongoing may review the way these trials are conducted in light of the outcome of this review.
- If you are in a clinical trial with HES solutions for infusion and have any questions or concerns about these products speak to the doctor who is giving it to you.

Information for healthcare professionals

- The marketing authorisations of HES solutions for infusion are being suspended in the EU because of the risk of kidney injury and death in certain patient populations, including critically ill patients or patients with sepsis. Despite contraindications introduced in 2013, drug utilisation studies show that HES solutions for infusion have continued to be used in these patients.
- Experience in clinical practice suggests that it is difficult to clearly distinguish patients who can be administered HES solutions for infusion from those who should not. In addition, some patients may become critically ill or septic while receiving the product.
- As further measures to minimise the risks are unlikely to be sufficiently effective, HES solutions for infusion are being suspended to protect patient health.
- Alternative therapeutic options are available for routine clinical practice (including albumin, gelatins and dextrans) and should be selected according to relevant clinical guidelines.
- The suspension concerns use of HES solutions for infusion in routine clinical practice, where it was found that the medicine was used in contraindicated populations; it does not apply to their use in clinical trials, where patient selection is tightly controlled. Member States where trials with HES solutions for infusion are ongoing may review the way these trials are conducted in light of the outcome of this review.
- Several clinical trials with HES solutions for infusion are ongoing; these include two studies previously requested by the PRAC in patients with trauma and in elective surgery, which is the population for which the products are currently indicated.
- For the suspension to be lifted, the marketing authorisation holders should provide reliable and convincing evidence on a favourable benefit-risk balance in a well-defined population, with feasible and effective measures to adequately minimise exposure of patients at an increased risk of serious harm.
- Healthcare professionals will be informed in writing of the outcome of the review and the suspension of the marketing authorisations of HES solutions for infusion.

More about the medicine

HES solutions for infusion are used for the management of hypovolaemia (low blood volume) caused by acute blood loss, where treatment with alternative infusion solutions known as ‘crystalloids’ alone is

not considered to be sufficient. They are given by infusion (drip) into a vein and are used as blood volume expanders to prevent shock following acute bleeding. They belong to the class of medicines known as colloids. Besides blood products, there are two types of medicines used for plasma volume replacement: crystalloids and colloids. Colloids contain large molecules such as starch, whereas crystalloids, such as saline or Ringer's solutions, are pure electrolyte solutions.

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

More about the procedure

The review of HES solutions for infusion was initiated on 17 October 2017 at the request of the Swedish Medical Products Agency, under Article 107i of Directive 2001/83/EC.

The review was first conducted by the Pharmacovigilance Risk Assessment Committee (PRAC). The PRAC recommendation was sent to 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, the CMDh position will now be sent to the European Commission, which will take an EU-wide legally binding decision.

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