EUROPEAN MEDICINES AGENCY
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Hydroxyethyl-starch solutions for infusion recommended for suspension from the market

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Update as of 25 May 2022:

On 24 May 2022, the European Commission issued a legal decision confirming the suspension of the marketing authorisations of HES solutions for infusion.

If necessary for public health reasons, individual EU Member States may delay the suspension for no longer than 18 months and keep HES solutions on the market, subject to agreed risk minimisation measures.

On 11 February 2022, EMA's safety committee, PRAC, recommended that the marketing authorisations for hydroxyethyl-starch (HES) solutions for infusion should be suspended across the European Union. These products were authorised as an addition to other treatments for plasma volume replacement following acute (sudden) blood loss.

The safety of HES solutions for infusion was reviewed in two separate procedures in 2013, and a number of restrictions and measures to minimise the risk of kidney injury and death in certain patients (those critically ill, with burn injuries or with sepsis, a bacterial infection in the blood) were put in place at the time.

As a result of a third review conducted in 2018, the use of HES solutions for infusion was further restricted to accredited hospitals, and healthcare professionals prescribing or administering the medicines had to be trained in their appropriate use. Additionally, further warnings were introduced in the product information to remind healthcare professionals that these medicines must not be used in patients with sepsis or kidney impairment or in other vulnerable patients such as the critically ill. These measures were put in place to ensure that HES solutions for infusion were not used in patients who were at increased risk of harm. Companies marketing HES solutions for infusion were also requested to conduct a drug utilisation study to check whether these restrictions were adhered to in clinical practice, and to submit the results of this study to EMA.

The PRAC reviewed the results from this study, which show that HES solutions for infusion are still being used outside the recommendations included in the product information. The

Committee concluded that the further restrictions introduced in 2018 have not sufficiently ensured that the medicines are used safely, and that HES solutions continue to be used in certain groups of patients in whom serious harm has been demonstrated.

Since adherence to the set of measures agreed in 2018 was a condition for the safe use of HES solutions for infusion, and the study has shown this has not happened, the benefits of these medicines are no longer considered to outweigh their risks. The PRAC explored the possibility of introducing additional measures to ensure HES solutions are used according to the product information but concluded that there were no other measures, or combination of measures, that would be feasible and sufficient to protect patients.

In view of the serious risks that certain patient populations are still exposed to, the PRAC therefore recommended the suspension of the marketing authorisations for HES solutions for infusion in the EU.

The PRAC recommendation was sent to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which adopted its position on 23 February 2022. As the CMDh position was adopted by majority vote, it will now be sent to the European Commission, which will take an EU-wide legally binding decision in due course.

Information for patients

- HES solutions for infusion are replacement fluids given to patients who have lost blood following injury or surgery.
- EMA is recommending these medicines be removed from the EU market in view of the serious risks (kidney injury and death) in certain patients (for example those who are very ill or have blood poisoning).
- Other treatment options are available.

Information for healthcare professionals

- The marketing authorisations of HES solutions for infusion are being recommended for suspension because of the risk of kidney injury and death in certain patient populations, including critically ill patients and patients with sepsis.
- Despite the introduction of contraindications and warnings in 2013 and further measures in 2018, the latest drug utilisation study shows that HES solutions for infusion continue to be used outside the recommendations included in the product information, which still exposes certain patient populations to serious risks.
- As no other feasible and effective measures to minimise the risks could be identified, EMA is recommending HES solutions for infusion be suspended from the EU market to protect patient health.
- Treatment alternatives are available and should be selected according to relevant clinical guidelines.

If the suspension is confirmed by the European Commission, a direct healthcare professional communication (DHPC) will be sent to relevant healthcare professionals in due course, and

published on a dedicated page on the EMA website.

More about the medicine

HES solutions for infusion were authorised 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.

HES solutions belong to a 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 are solutions of low molecular weight substances and include saline and Ringer's solutions.

In the EU, HES solutions for infusion were authorised via national procedures and are available in several Member States under various trade names.

More about the procedure

EMA's Pharmacovigilance Risk Assessment Committee (PRAC), responsible for the evaluation of safety issues for human medicines, issued its recommendation after reviewing the results of a drug utilisation study that was requested as part of additional risk minimisation measures resulting from an Article 107i referral procedure concluded in 2018.

The PRAC recommendation was sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh). The CMDh, also taking into consideration additional information from the marketing authorisation holders for HES solutions for infusion and external parties, endorsed the PRAC recommendation and adopted its position.

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

The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

Related content

- Hydroxyethyl starch (HES) containing medicinal products: Article 107i procedures

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