Hydroxyethyl-starch solutions for infusion recommended for suspension from the market

15.07.2022 | Circular Number P05/2022

Information on hydroxyethyl-starch solutions

- 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.

The following product is authorised via national procedure.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Poly(o-2-hydroxyethyl)starch potassium chloride magnesium chloride hexahydrate sodium acetate trihydrate sodium chloride	Volulyte	Solution for infusion	POM	MA1123/02201	Fresenius Kabi Austria Gmbh

Information from the EMA about the safety concern

- EMA's Pharmacovigilance Risk Assessment Committee (PRAC), responsible for the evaluation of safety issues for human medicines, issued its recommendations after reviewing the results of a drug utilisation study that was requested as part of additional risk minimisation measures resulting from Article 107i referral procedure concluded in 2018.
- The PRAC recommendations were sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), to adopt a position. 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.

- The PRAC, has 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 several 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 has 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) for consideration The PRAC recommendations were sent to the CMDh which endorsed them and adopted its position during the February 2022 meeting.
- On 24 May 2022, the European Commission issued a legal decision confirming the suspension of the marketing authorisations of HES solutions for infusion. 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.

In Malta

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.

Advice 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.

For more information please see the European Medicines Agency's press release.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with hydroxyethyl-starch solutions. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

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.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

We thank you for your interest and look forward to hearing your opinion.

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Pharmacovigilance Section

Post-Licensing Directorate

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