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

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Information on Medicinal Product

Infusion solutions containing Hydroxyethyl starch (HES) are frequently used for volume replacement in situations of blood and fluid loss and belong to the class known as colloid solutions.

As per information in Medicines Authority circulars **P04/2013** and **P16/2013** a review of all available safety and efficacy data, on HES solutions was ongoing by the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) due to concerns raised by studies [1,2,3] which showed that patients with severe sepsis treated with HES were at a greater risk of kidney injury requiring dialysis and at a greater risk of mortality.

HES colloid solutions are authorised nationally and marketed in Malta as Volulyte 6% Solution for Infusion (Fresenius Kabi) and Plasma Volume Redibag 6% Solution for Infusion (Baxter Healthcare).

Information from European Medicines Agency about the safety concern

The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)[*],has endorsed by majority the recommendations of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that HES solutions should 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.

The CMDh also agreed with the PRAC recommendation that HES solutions may continue to be used in patients to treat hypovolaemia (low blood volume) caused by acute 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, It is recommended that HES solutions are not 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 (by the marketing authorisation holders) on the use of these medicines in elective surgery and trauma patients.

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As the CMDh position has been adopted by majority vote, it will now be sent to the European Commission, which will take a final legally binding decision that will be valid throughout the European Union (EU).

In Malta

For Healthcare Professionals

- Because of the risk of kidney injury and mortality, HES solutions should no longer be used in patients with sepsis, burn injuries or critically ill patients.
- It is recommended that HES solutions are 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.

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

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For more information please visit **www.ema.europa.eu**

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Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Hydroxyethyl Starch solutions. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Dr John J Borg PhD (Bristol)

Post-licensing Director

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.

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