Restriction of use of HES
(hydroxyethyl starch containing medicinal products)

Voluven 6% Solution for Infusion (500ml) PL 08828/0145
Voluven 10% Solution for Infusion (500ml) PL 08828/0207
Volulyte 6% Solution for Infusion (500ml) PL 08828/0174

Dear Healthcare Professional,

The licences of all hydroxyethyl starch (HES) products were suspended in the UK in June 2013. A European regulatory review of the benefits and risks of HES that was ongoing at that time has since been completed. Following the review, the suspension of the licenses for HES products in the UK has been lifted. The use of HES is subject to new contraindications and warnings in the product information.

Summary of the new recommendations

- HES products should only be used for the treatment of hypovolaemia due to acute blood loss when crystalloids alone are not considered sufficient

- HES products 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 products are now contraindicated in
  o Sepsis
  o Burns
  o Renal impairment or renal replacement therapy
  o Intracranial or cerebral haemorrhage
  o Critically ill patients (typically admitted to the ICU)
- Hyperhydrated patients, including patients with pulmonary oedema
- Dehydrated patients
- Severe coagulopathy
- Severely impaired hepatic function

- 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.

- Large randomised clinical trials have reported an increased risk of renal dysfunction in the critically ill, including patients with sepsis. Therefore HES should no longer be used in these patients.

- Monitoring of renal function in patients receiving HES is recommended and HES must be discontinued at the first sign of renal injury.

This letter is being sent in agreement with the EMA (European Medicines Agency) and the Medicines and Healthcare Products Regulatory Agency.

**Further information on the safety concern:**

Infusion solutions containing HES belong to the class of colloids. In the EU, HES-containing solutions for infusion are approved via national procedures.

Two large clinical trials in patients who were critically ill, mainly with sepsis, showed a greater risk of adverse renal effects in patients treated with HES compared with crystalloid (1, 2). The study of patients with sepsis (1) also showed a greater risk of mortality in patients treated with HES.

Based on the results of these randomised controlled trials, the European Medicines Agency (EMA) in November 2012, initiated a safety review of all HES-containing products on the EU market. The review included data from the scientific literature, data submitted by the companies, data from the authors of the studies and from stakeholders.

In June 2013, the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) and the UK Commission on Human Medicines recommended that the benefits of HES solutions no longer outweigh their risks and that HES-containing products should be suspended from the market.

Since then, the PRAC has analysed and considered new evidence that was not available at the time of the initial recommendation, including new studies and new proposals for additional risk minimisation measures. The companies have also committed to conduct additional studies to examine efficacy and long-term safety.
On the basis of the data available to date, the PRAC has concluded that HES products should only be used in a restricted patient population. This conclusion, ratified by the European Commission, applies across the European Union. New contraindications and warnings are being introduced and the marketing authorisation holders are required to perform further studies. The product information will be updated with the new information.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Cards website:

www.mhra.gov.uk/yellowcard.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.
Company contact point:
For further information, please contact Fresenius Kabi Ltd on ++44 (0)1928 533612 or email pharmacovigilance.GB@fresenius-kabi.com. Alternatively, contact can be made by post at the following address:

Fresenius Kabi Ltd
Regulatory Affairs
Cestrian Court
Eastgate Way
Manor Park
Runcorn
Cheshire
UK
WA7 1NT

Yours sincerely,
Fresenius Kabi Ltd

Mr Chris Harrison
Executive Vice President
Northern Europe, Southern Africa, Australia and New Zealand

Mr Tony Rigden
Head of Regulatory Affairs

Literature:


▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.