Notice to Hospitals - Health Canada Endorsed Important Safety Information on Hydroxyethyl starch containing solutions, Voluven® and Volulyte®

FRESENIUS KABI

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Dear Health Care Professional,

Please distribute to relevant Departments [Surgery, Emergency Medicine, Pharmacy, Anaesthesia, Intensive Care, Nephrology, and/or other Departments as required], and other involved professional staff and **post this notice** in your institution.

Subject: **Association of hydroxyethyl starch (HES) solutions with increased mortality and severe renal injury.**
Voluven® (6% Hydroxyethyl Starch 130/0.4 in 0.9% Sodium Chloride Injection) and
Volulyte® (6% Hydroxyethyl Starch 130/0.4 in an isotonic electrolyte injection)

New published investigator-initiated trials have demonstrated the use of HES solutions in critically ill patients to have increased risks of renal injury, mortality (in septic patients), and liver failure.[1.2.3]

- Increased mortality, renal injury and liver failure have been associated with the use of HES solutions
- Health Care Professionals should be aware that a new boxed warning advises that in patients requiring intensive or emergent care, the use of crystalloid solutions in preference to HES solutions should be considered.
- HES solutions are now contraindicated in patients with a) sepsis, b) severe liver disease and c) with renal impairment with oliguria and anuria, not related to hypovolemia.

Voluven® and Volulyte® are indicated for the treatment of hypovolemia when plasma volume expansion is required. It is not a substitute for red blood cells or coagulation factors in plasma.

The Product Monographs for Voluven® and Volulyte® have been modified:

New CONTRAINDICATIONS

- In patients with sepsis
- In patients with severe liver disease, and
- In patients with renal impairment with oliguria and anuria, not related to hypovolemia.

Boxed Serious Warning and Precautions

In patients with hypovolemia requiring intensive or emergent care, a careful evaluation of the risk of sustaining renal injury or liver failure should be undertaken before instituting treatment with Voluven®/Volulyte®.

The use of crystalloid solutions in preference to Voluven®/Volulyte® should be considered in patients deemed at risk of these adverse reactions.

This new information is based on the results from three recently published investigator-initiated clinical studies [1,2,3] which compared the effects of hydroxyethyl starch solutions with crystalloids in critically ill patients. These studies report an increased use of renal replacement therapy in critically ill and septic patients receiving HES solutions compared to crystalloids. In addition, recently published meta-analyses reported increased mortality in critically ill patients exposed to HES vs crystalloids; the above trials contributed largely to the results of the meta-analyses.[4,5]

Fresenius Kabi has worked with Health Canada to implement appropriate changes to the Product Monographs to reflect this important new information.
Healthcare Professionals are advised to consider this new safety information, in addition to the current contraindications, warnings and precautions, when prescribing Voluven®/Volulyte® for their patients. Thus, please review this letter together with the current approved Voluven®/Volulyte® Product Monographs for full prescribing information. Copies of the updated Product Monographs are available from the Health Canada DPD online http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp and the Fresenius Kabi Canada website at www.fresenius-kabi.ca

If you have any questions regarding this information, please contact Fresenius Kabi Canada's Medical Information department by email to medinfo@fresenius-kabi.ca or by fax a letter to 905-770-4811.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious adverse reaction or unexpected adverse reactions in patients receiving Voluven® or Volulyte® should be reported to Fresenius Kabi Canada or Health Canada.

Fresenius Kabi Canada,
A division of Calea Ltd.
45 Vogell Road, Suite 210
Richmond Hill, ON, L4B 3P6

To correct your mailing address or fax number, contact Fresenius Kabi Canada.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

For other health product inquiries related to this communication, contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: (613) 954-6522
Fax: (613) 952 -7738

Sincerely,

Original signed by

Matthew Rotenberg
Chief Executive Officer

Ana G. Bascom
National Safety Officer

1. Perner, A. et al. Hydroxyethyl Starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med 2012; 367(2):124- 134.
2. Brunkhorst, F.M. et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med, 2008; 358(2):125-39.
3. Myburgh, J.A. et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care; N Engl J Med 2012; 367(20):1901-11.
4. Zarychanski R, Abou-Setta AM, Turgeon AF et al. Association of hydroxyethyl starch administration with mortality and acute kidney injury in critically ill patients requiring volume resuscitation: A systematic review and meta-analysis. JAMA - Journal of the American Medical Association 2013;309(7):678-688.
5. Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane database of systematic reviews (Online) 2013;2:000567.