衞生署藥物辦公室
藥物註冊及進出口管制部

香港九龍南昌街 382 號公共衞生檢測中心三樓

2319 8458

電話號碼 Tel. No.:
詢問處 Enquiries (852) 2319 8458
傳真號碼 Faxline No. (852) 2803 4962
本署檔號 OUR REF.: DH DO PRIE/7-30/15

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

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(來函請敍明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

PRAC recommends suspending hydroxyethyl-starch solutions for infusion from the market.
Review finds measures to protect patients have not been sufficiently effective.

Your attention is drawn to the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) recommendation following a review that hydroxyethyl-starch (HES) solutions for infusion should be suspended from marketing authorisations across the European Union. These products are used as plasma volume replacement following acute (sudden) blood loss, where treatment with alternative products known as 'crystalloids' alone is not considered to be sufficient.

The review was triggered by results from two drug utilisation studies indicating that HES solutions are being used in critically ill patients and those with sepsis and kidney injury despite restrictions introduced in 2013 to reduce the risks of kidney problems and deaths in these patient populations.

In 2013, the PRAC had recommended restrictions on the use of HES solutions, including that they must no longer be used to treat critically ill patients or patients with sepsis, because of an increased risk of kidney injury and mortality seen in clinical trials. The Committee requested that further studies be carried out to verify adherence to these restrictions.

The PRAC has reviewed the results from the drug utilisation studies of HES solutions for infusion together with the currently available data on benefits and risks from clinical trials and observational studies and feedback received from stakeholders and experts. Based on this review, the PRAC has concluded that the restrictions introduced in 2013 have not been sufficiently effective. The Committee explored the possibility of introducing additional measures but concluded that such measures would be ineffective or insufficient.

In view of the serious risks that certain patient populations are exposed to, the PRAC has recommended the suspension of the marketing authorisations for HES solutions. Alternative treatment options are available.

Please refer to the following website in EMA for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/01/news_detail_002882.jsp&mid=WC0b01ac058004d5c1

In Hong Kong, there are 6 registered pharmaceutical products containing hydroxyethyl starch, namely Voluven Infusion 6% (HK-50474) and Volulyte 6% Solution for Infusion (HK-58087) registered by Fresenius Kabi Hong Kong Ltd; Tetraspan 6% Solution for Infusion (HK-56978) and Tetraspan 10% Solution for Infusion (HK-56979) registered by B. Braun Medical (HK) Ltd; and Hestar-200 Inj. 10% (HK-57095) and Hestar-200 Inj. 6% (HK-57096) registered by Unico & Co. Related news on increased risks of death and kidney injury in critically ill patients was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since June 2013, with the last update posted on 30 October 2017. Letters to local healthcare professionals to draw their attention on the above risks was issued on 17 June 2013. In December 2013, the Registration Committee of the Pharmacy and Poisons Board (the Registration Committee) decided that the package inserts of the above products should be updated to contain the information endorsed by the EMA's Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) and PRAC, i.e. hydroxyethyl-starch solutions should no longer be used in patients with sepsis or burn injuries or in critically ill patients, and are contraindicated in sepsis, renal impairment or renal replacement therapy and critically ill patients.

So far, DH has not received any adverse drug reaction case related to hydroxyethyl starch. As the concerned companies in the EU have the rights to request the PRAC to re-examine its recommendations before sending to CMDh and EMA for endorsement, DH will continue to remain vigilant on the development of this issue and safety updates on hydroxyethyl starch by other overseas health authorities.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)