副本

檔　　號：
保存年限：

衛生福利部食品藥物管理署　函

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受文者：中華民國西藥代理商業同業公會

發文日期：中華民國107年3月1日
發文字號：FDA藥字第1071401670號
速別：普通件
密等及解密條件或保密期限：
附件：附件1.103年8月部授食字第1031407108A號公告。附件2.105年6月部授食字第1051403270A號公告。附件3.歐盟警訊。

主旨：有關Hydroxyethyl-starch (HES)類成分藥品之臨床效益及安全性再評估相關事宜，詳如說明段，請查照。

說明：

一、因Hydroxyethyl-starch (HES)類成分藥品使用於重症及敗血症患者有較高腎損傷及死亡風險，故我國業於103年8月及105年6月公告該類成分藥品之中文仿單應加註相關警語(如附件1及2)，現本署擬重新審視並評估其執行成效。另，歐盟亦於107年1月重新審視該類藥品限縮使用之實行成效，認為其成效不彰因此建議暫停銷售(警訊內容如附件3)。

二、為進行含HES類成分藥品臨床效益及安全性之再評估，貴公司倘有相關意見或下列相關研究文獻等資料，請於107年3月31日前檢送至本署，逾期未提具資料者，視同無意見。

(一) 請提供貴公司該類藥品97年至106年間之國內銷售資料(依年度及醫療機構層級分列之)。

(二)請提供該類藥品整體風險效益分析報告，包括近五年內發表之臨床文獻(如臨床報告、上市後臨床試驗、觀

察性研究、處方型態研究等)之資料分析，並附上所引用資料之原始文獻。該文獻報告需以中、英文為主，且應裝訂成冊並附摘要，一式4份(臨床報告文獻之研究設計應至少具備適當之對照組比較或雙盲設計，一般敘述性質與個案報告不列入考慮)。

(三)請說明自103年8月本署公告含HES類成分藥品再評估結果相關事宜之風險管控措施後，貴公司對於國內臨床醫療人員之通知或教育訓練相關措施。

正本：信東生技股份有限公司、杏林新生製藥股份有限公司、台裕化學製藥廠股份有限公司、臺灣費森尤斯卡比股份有限公司、安強藥業股份有限公司、台灣柏朗股份有限公司、和聯生技藥業股份有限公司、麥迪森醫藥股份有限公司

副本：全國藥物不良反應通報中心、台灣製藥工業同業公會、台北市西藥代理商業同業公會、中華民國西藥代理商業同業公會、台灣藥品行銷暨管理協會、中華民國開發性製藥研究協會、中華民國製藥發展協會、中華民國西藥商業同業公會全國聯合會、社團法人中華民國學名藥協會(均含附件)

署長吳秀梅

檔　號：
保存年限：

附件1.

衛生福利部　公告

發文日期：中華民國103年8月11日
發文字號：部授食字第1031407108A號
附件：「含Hydroxyethyl starch類成分藥品之中文仿單修訂內容」一份

主旨：含Hydroxyethyl starch類成分藥品之再評估結果相關事宜。

依據：藥事法第四十八條。

公告事項：

一、依據國外文獻，含Hydroxyethyl starch類成分藥品使用於重症及敗血症患者有較高的腎損傷及死亡風險，為保障民眾用藥安全，經本部彙集國內、外相關資料及臨床相關文獻報告進行整體性評估，評估結果為：

(一)含Hydroxyethyl starch類成分藥品，其適應症統一修訂為「單獨使用晶質輸注液無法治療之急性出血導致之低血容積病人，本品無法取代紅血球及血漿中的凝血因子」。

(二)中文仿單應依本公告附件之仿單內容修正，增修內容包括起首之黑框警語、用法用量、禁忌、警語及注意事項等項目，詳如本公告附件。

二、凡持有前項藥品許可證之藥商，請於本公告日起2個月

內，依本公告附件向本部食品藥物管理署辦理中文仿單變更事宜(毋需繳交規費，可自本署網站http://www.fda.gov.tw下載本公告附件內容)，逾期未辦理者，依藥事法有關規定處理。

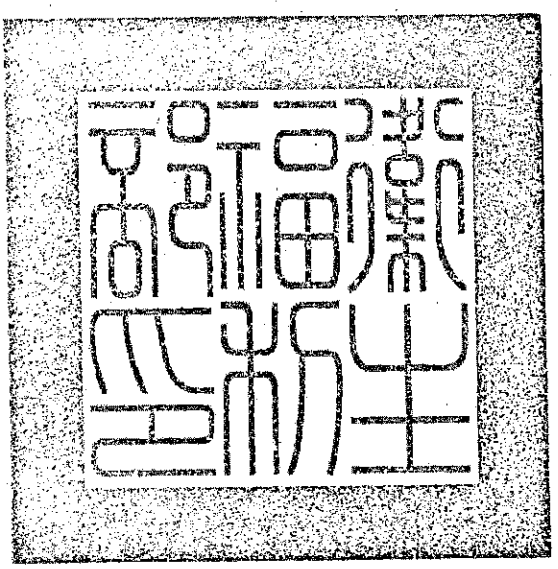
部長 邱文達

本案依分層負責規定
授權組室主管決行

檔　號：
保存年限：

附件2.

衛生福利部　公告



發文日期：中華民國105年6月15日
發文字號：部授食字第1051403270A號
附件：

裝

訂

線

主旨：修訂本部103年8月11日部授食字第1031407108A號公告「含Hydroxyethyl starch類成分藥品之再評估結果相關事宜」。

依據：藥事法第48條、第75條及本部103年8月11日部授食字第1031407108A號公告。

公告事項：

一、含Hydroxyethyl starch類成分藥品，經本部彙集國內、外相關資料及臨床相關文獻報告進行整體性評估，考量原公告「禁忌症」欄位所列「重症患者」之定義不明確，其中文仿單之「禁忌症」欄位，修訂如下：

(一)已知對羥基乙基澱粉或本品賦形劑過敏者。

(二)下列重症患者：

1、敗血症
2、嚴重燒燙傷
3、嚴重肝臟疾病
4、體液超過負荷(體內水分過多)，尤其是肺水腫與鬱血性心衰竭
5、嚴重凝血或出血性疾患
6、腎衰竭且併有非血液容積過低導致的寡尿症或無尿症
7、接受腎臟透析治療

8、嚴重高鈉血症或嚴重高氯血症
9、顱內出血
10、器官移植
11、嚴重高鉀血症(僅適用於含鉀離子之產品)

二、持有前項成分藥品許可證者，應依本公告事項修訂仿單，於本公告日起2個月內向本部食品藥物管理署依藥品查驗登記審查準則辦理中文仿單變更事宜(須以紙本送件，於期限內毋需繳交規費，逾期則需繳交規費)。逾期未辦理者，依違反藥事法第75條相關規定處辦。

三、仿單變更核備前製造（或輸入）之產品，無須回收。

副本：衛生福利部食品藥物管理署藥品組

衛生福利部食品藥物管理署 校對之章

部長林奏延

裝 訂 線

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

318743.

12 January 2018
EMA/4068/2018

PRAC recommends suspending hydroxyethyl-starch solutions for infusion from the market

Review finds measures to protect patients have not been sufficiently effective

EMA s Pharmacovigilance Risk Assessment Committee (PRAC) has recommended the suspension of the marketing authorisations for hydroxyethyl-starch (HES) solutions for infusion 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.

The PRAC recommendation will now be sent to the Coordination Group for Mutual Recognition and Decentralised Procedures Human (CMDh)[1] for consideration at its meeting on 22-25 January 2018.

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

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More about the medicines

HES solutions for infusion are used 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. They are given by infusion (drip) into a vein and are used as blood volume expanders to prevent shock following acute bleeding. They belong to the 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, such as saline or Ringer's solutions, are pure electrolyte solutions.

In the European Union, HES solutions for infusion have been approved via national procedures and are available in the Member States under various trade names.

More about the procedure

The review of HES solutions for infusion was initiated on 17 October 2017 at the request of the Swedish Medical Products Agency, under Article 107i of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. The PRAC recommendations will now be sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will 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.