



MEMORANDUM

To: Medical Director
Administrator
Clinic Manager

From: Shean Strong, QI Director
Lisle Mukai, QI Coordinator

Subject: **FDA Alert: Heparin Sodium**

Date: April 8, 2010

FDA Drug Safety Communication: Update: Follow up to the Public Health Alert about Changes to the Heparin Sodium USP Monograph

Safety Announcement: [04-07-2010] Laboratory studies performed at the request of the U.S. Food and Drug Administration (FDA) have shown that Heparin Sodium, USP (heparin) made under the new United States Pharmacopeia (USP) Monograph ("new heparin") has approximately 10% less blood-thinning (anticoagulant) activity compared to heparin prepared using the previous ("old") USP Monograph. The studies were performed in order to better understand the clinical impact of the change in potency for heparin.

The FDA first alerted the public to changes in the potency of heparin in a Public Health Alert in October 2009.

The results of these studies reinforce FDA's previous recommendation for healthcare professionals to exercise clinical judgment in determining the dose of heparin for a patient and consider the clinical circumstances where the potency decrease may require dosage adjustments and more frequent monitoring.

Healthcare professionals should be aware that heparin products, i.e., those made using both the old and the new USP standards may be available for some time. Healthcare professionals may wish to consider not using the products interchangeably. Pharmacies and hospitals may wish to consider separating the supplies of old and new heparin and exhausting the supplies of "old" heparin before transitioning to the "new" product (**See Table Below, "How to Identify Heparin Products made to the New USP Standard"**).

Additional Information for Patients

Patients should:

- Talk to a healthcare professional about any concerns with heparin.

Additional Information for Healthcare Professionals

FDA recommends that healthcare professionals:

- Be aware that there is an approximate 10% decrease in the anticoagulant activity (potency) of the "new heparin" compared with the "old heparin"
- Continue to exercise clinical judgment in determining the dose of heparin.
- Continue to individualize heparin dosing to the specific patient/patient-specific clinical situation
- Understand that the labeling for heparin, including the recommended doses for heparin has not changed
- Consider those clinical circumstances where the potency decrease may require dosage adjustments and more frequent monitoring, such as where aggressive anticoagulation is essential to the treatment of the patient, including:
 - Pediatric patients undergoing extracorporeal membrane oxygenation

- Adults and children undergoing cardiopulmonary bypass
- The treatment or prevention of life-threatening thromboses
- Report any adverse events associated with the use of heparin to FDA's MedWatch program using the information in the "Contact Us" box at the bottom of the page

Data Summary: Studies to assess differences in heparin activity were performed in animals (*in-vivo*) and in human plasma (*in-vitro*). The results of the human plasma and animal studies were consistent in demonstrating an approximate 10% decrease in heparin activity of the "new" heparin products compared to "old" heparin products. The average **Activated Partial Thromboplastin Time (aPTT)** response to a dose of heparin changed in a dose-proportional manner.

The same studies also demonstrated that there were large individual variations in aPTT responses to a given dose of heparin. Therefore, in a clinical setting, a 10% decrease in heparin dose might not be reflected in the results of an aPTT or ACT (Activated Clotting Time) for an individual patient.

Given the inherent individual variability in response to a dose of heparin, a 10% decrease in heparin activity (potency) is not likely to have clinical significance. However, special clinical situations such as cardiac surgery and/or use in pediatric patients may require more intensive monitoring to achieve optimal therapeutic response. Since heparin therapy is routinely titrated to each patient (there are many patient-specific factors that can influence heparin dosing) the usual method of individualizing dosing will continue to ensure patient safety.

Table to Distinguish Between "New" and "Old" Heparin: Since new heparin will be available, starting October 2009 there will likely be supplies of both the old and new heparin stocked for use in hospitals and pharmacies for a period of about three years. Facilities that have stocks of old and new heparin may wish to consider segregating stores of the old heparin from the new and using the "old" heparin products first. The table below provides information on how to distinguish between the old and new product and company website for additional information.

How to Identify Heparin Products made using the New USP Standard

Manufacturer	(Date) Availability of Lots Made to the New USP Standard	How to Identify the New Product	Additional Information/Company Contact
APP	October 2009	"N" will appear after the Expiration Date	http://www.appdrugs.com
B. Braun	October 2009	"N" will appear after the Lot Number	http://www.bbraunusa.com
Hospira	October 2009	Lot Numbers will begin with the number "82" or higher	http://www.hospira.com/Files/HeparinUSP.pdf ³
Baxter	October 2009	"N" will appear before the Lot Number	http://www.baxter.com/index.html

Report a Serious Problem:

- Phone: (800) 332-1088
- Fax: (800) FDA-0178
- **Regular Mail:** Use postage-paid FDA Form 3500¹⁵
- **Mail to:** MedWatch 5600 Fishers Lane
Rockville, MD 20852-9787