



Seton Network Notes

A Publication of the Pharmacy and Therapeutics Committee

FDA Public Health Alert: Change in Heparin USP Monograph

The U.S. Food and Drug Administration (FDA) is alerting health care providers of a change to the United States Pharmacopeia (USP) monograph for heparin, effective Oct. 1, 2009. The manufacturing and testing requirements under the new monograph will lessen the potential for contamination of heparin and enhance the production of a high-quality drug. The monograph change will also harmonize the USP unit dose with the WHO International Standard (IS) unit dose. **However, harmonization of the standard will result in approximately a 10 percent reduction in the potency of the heparin marketed in the United States.**

The change in heparin potency may have clinical significance in some situations, such as when heparin is administered as a bolus intravenous dose and an immediate anticoagulant effect is clinically important. In such situations, health care providers should consider the change in potency of heparin when making decisions about what dose to administer. The change in heparin potency is expected to be less clinically significant when it is administered subcutaneously due to the low and highly variable bioavailability of heparin when administered by this route. Health care providers should also be aware of the decrease in heparin potency as they monitor the anticoagulant effect of the drug; more heparin may be required to achieve and maintain the desired level of anticoagulation in some patients.

Important information and clinical recommendations during this time of transition:

- ***There will be simultaneous availability of heparin manufactured to meet the "old" and "new" USP monograph, with potential differences in potency.*** This overlap of products on the market is necessary to make certain that an adequate supply of heparin is available for all patients. Products using the new "USP unit" potency definition are anticipated to be available on or after Oct. 8. The FDA is working with the manufacturers of heparin to ensure that an appropriate identifier is placed on heparin made under the new USP monograph.
- ***Consider the potential potency variation when administering heparin,*** particularly in situations where assurance of aggressive anticoagulation is essential to treat or prevent life-threatening thromboses. Clinicians should now consider the potential for up to 10 percent estimated decrease in heparin activity per "USP unit" when deciding what dose to administer in such cases.
- ***The potency change may require more frequent or intensive aPTT or ACT monitoring.***
- ***Clinical judgment is essential in determining dose of heparin.*** Heparin dosing is always individualized to the patient-specific situation. The FDA-approved labeling for heparin has not changed, including the recommended doses. Individualization of heparin dosing has long been the standard for clinical use of the drug and the FDA reiterates the importance of clinical judgment in heparin dosing.

The FDA is working with the heparin manufacturers to study the impact of this variation in potency and will make the results available when the studies have concluded.

For additional information on the heparin monograph change, go online to www.usp.org.

SFH HMG-CoA Reductase Inhibitor (Statin) Therapeutic Interchange

The Network Pharmacy & Therapeutics Committee revisited the HMG-CoA reductase inhibitor class (statin) therapeutic interchange proposal. In August 2007, the committee completed a thorough review to determine the feasibility of streamlining the class and developing a therapeutic interchange protocol. Adverse events, drug interactions, effects on LDL and total cholesterol, and cost were taken into consideration. At that time, the committee voted in favor of the interchange, but implementation was stalled until the Department of Pharmacy had successfully implemented a network warfarin monitoring program. Findings from the class review include the following:

- Although the effect of statins may vary with regard to LDL and total cholesterol reduction, short-term therapy during an acute hospitalization should not have a clinically significant effect on the patients' long term outcomes.
- Based upon a thorough literature review, no single statin had a statistically significant number of adverse events when compared to others in the class.

(Statin interchange continued)

- Drug interactions varied among the statins. When atorvastatin, simvastatin or lovastatin are used concomitantly with drugs metabolized by CYP-3A4, there is an increased risk of adverse events.
- From a contractual standpoint, simvastatin and pravastatin are the least-expensive agents.
- Current statins on formulary include atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®), pravastatin (Pravachol®), rosuvastatin (Crestor®) and simvastatin (Zocor®).

After careful consideration of the literature, utilization data, physician preferences, safety and costs, the Network P&T approved the following recommendations:

- Simvastatin will be the statin of preference on formulary.
- Other statins that will remain on formulary include atorvastatin 80 mg and pravastatin 10 mg, 20 mg, and 40 mg.
- All patients receiving lovastatin, fluvastatin, pravastatin, atorvastatin or rosuvastatin prior to admission will be transitioned to an equivalent dosage of simvastatin during their hospitalization (exceptions noted below).
 - If a significant drug interaction exists (as determined by COMPASS via an interaction discern alert pop-up) with simvastatin, an equivalent dose of pravastatin will be dispensed.
 - If atorvastatin 80 mg or rosuvastatin 40 mg is ordered and no significant drug interactions exist, atorvastatin 80 mg will be dispensed.
 - If a patient is admitted on pravastatin, pravastatin will be continued.
 - If a patient is admitted on darunavir, atorvastatin (not to exceed 20 mg) is recommended.
- Once the HMG-CoA reductase inhibitor conversion is made, the pharmacist will document the therapeutic interchange in a Medication Administration Record (MAR) message and the Order Comments Section in the electronic MAR.
- If the physician feels that the prescribed medication is unique and medically necessary, the physician may override the automatic interchange by writing, "Do not substitute" (DNS).
- ***The statin therapeutic interchange will begin Tuesday, Dec. 1, 2009.***

Seton Family of Hospitals' Adult Vancomycin Dosing Guidelines

In October 2009, the Anti-Infectives Monitoring Subcommittee (AIMS) approved the Seton Family of Hospitals' (SFH) Adult Vancomycin Dosing Guidelines. The Vancomycin Dosing Guidelines were based on the principles of vancomycin pharmacokinetics and the 2009 national guidelines for therapeutic monitoring of vancomycin endorsed by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America and the Society of Infectious Diseases Pharmacists.

Upon initiation of intravenous vancomycin therapy, a loading dose of approximately 20-25 mg/kg (see SFH Adult Vancomycin Dosing Guideline for specific dosage recommendations) followed by maintenance doses of approximately 15-20 mg/kg is now recommended with dosage interval guided by estimated creatinine clearance. A loading dose will allow for a more rapid attainment of therapeutic serum concentration and may prevent the emergence of bacterial resistance. Loading doses greater than 3 grams have not been studied and are not routinely recommended by the SFH guidelines. Although the 2009 national therapeutic monitoring guidelines suggest considering a loading dose of 25-30 mg/kg in critically ill patients, this recommendation should be used with caution and is not routinely recommended by the SFH Adult Vancomycin Dosing Guidelines due to limited available literature regarding the safety and efficacy of this dosage. Extreme caution should be used when calculating creatinine clearance in the elderly, malnourished, paraplegic or quadriplegic, amputees, very low-weight/bed-bound patients or patients with decreased muscle mass as this may overestimate renal function.

Vancomycin doses will be adjusted according to serum trough concentrations. The recommended trough level for seriously ill patients is about 15-20 mg/L; however 10-15 mg/L may be appropriate for treatment of cellulitis, urinary tract infections or infections caused by *Staphylococcus epidermidis* or *Enterococcus* sp. depending on the infection site. Most vancomycin serum steady state concentrations are achieved by the fifth dose; therefore, trough concentrations should be drawn within 30 minutes prior to the fifth dose in stable patients. Patients who are morbidly obese, paraplegic, elderly, seriously ill or in acute renal failure may require earlier vancomycin trough evaluation. Patients may begin to accumulate vancomycin after seven to 14 days, leading to supratherapeutic serum levels and potentially increase the risk of toxicity.

- Please refer to the SFH Adult Vancomycin guidelines for more details on recommended loading doses, maintenance doses, dosing intervals, dosing adjustments and special populations.
- The guidelines will be located on the Antimicrobial Management Web site under clinical resources on the Seton intranet. Please refer to these guidelines for specific dosing recommendations.
- You may also contact either SFH Infectious Disease pharmacist (Kate Shea, PharmD, or Terry Jaso, PharmD) for more information.