UPDATE ON ANTICOAGULANT SAFETY

As described in the October 2011 issue of the P&T Committee Newsletter (Anticoagulant Safety at MGH), anticoagulation safety is a major area of focus regarding medication safety. One of the more recent actions by the P&T Committee involved the creation of upper hard limits (UHL) for unfractionated heparin drips (40 units/kg/hr) and modifications to the bivalirudin UHLs (2 mg/kg/hr) in the Alaris® pump libraries (see the April 2013 issue of the P&T Committee Newsletter for further details).

Overall, several anticoagulation agents are available on the MGH Formulary and are recognized in the Anticoagulation Monitoring and Safety policy (#100-228) including:
- Vitamin K antagonist: warfarin (Coumadin®)
- Low-molecular weight heparin: enoxaparin (Lovenox®)
- Pentasaccharide: fondaparinux (Arixtra®)
- Oral direct thrombin inhibitor: dabigatran (Pradaxa®)
- Intravenous direct thrombin inhibitors: argatroban, bivalirudin (Angiomax®)
- Factor Xa inhibitor: rivaroxaban (Xarelto®)
- Unfractionated heparin

Medication guidelines for the individual agents listed above are available on the Online Formulary and are recognized in the Anticoagulation Monitoring and Safety policy (#100-228) including:
- Vitamin K antagonist: warfarin (Coumadin®)
- Low-molecular weight heparin: enoxaparin (Lovenox®)
- Pentasaccharide: fondaparinux (Arixtra®)
- Oral direct thrombin inhibitor: dabigatran (Pradaxa®)
- Intravenous direct thrombin inhibitors: argatroban, bivalirudin (Angiomax®)
- Factor Xa inhibitor: rivaroxaban (Xarelto®)
- Unfractionated heparin

Dabigatran MUE

In January 2013, the Committee reviewed dabigatran usage data collected between January 1, 2011 and December 18, 2012. Overall, 21 patients received dabigatran. Seventeen of the twenty-one patients (81%) evaluated had a documented indication that was consistent with the guidelines for use. Additionally, 19 patients received a dose consistent with the guidelines for use. Monitoring was also reviewed against the Hospital Anticoagulation Policy. Only one patient’s therapy did not meet monitoring criteria. Specifically, this
patient had a five day lapse without a complete blood count (CBC). The results of this MUE indicate that majority of patients (81%) met the indication for the use of dabigatran and only two patients received dabigatran during their hospital stay had dosing incorrectly adjusted for renal function (neither had a cardiology consult). Overall, 33% of the patients reviewed were initiated on dabigatran in the hospital. Of those patients reviewed, only 57% had a cardiology consult, which is required by the guidelines for use.

Rivaroxaban MUE
The Committee also reviewed rivaroxaban usage data collected between January 1 and December 18, 2012. Overall, thirteen patients received rivaroxaban in which all patients had a documented indication that was consistent with the P&T Committee’s guidelines for use. The dose of rivaroxaban was also evaluated in which 12 patients received a dose consistent with the dosing criteria guidelines provided by the P&T Committee. In regards to monitoring, 9 out of 13 (69%) patients had monitoring done as recommended per the Hospital Anticoagulation Policy. The four patients who did not meet monitoring criteria did not have baseline complete blood counts (CBC).

Additionally, the bioavailability of rivaroxaban can be affected by the administration time in respect to meals. Only 38% (5/13) of patients had rivaroxaban ordered for the evening mealtime. As a result, the Committee agreed to standardize the rivaroxaban administration time to 1800. The Committee also modified the usage guidelines to include additional uses of rivaroxaban based on available published literature (i.e., use by the orthopedic service).

Enoxaparin MUE
In December 2012, the Committee reviewed enoxaparin usage data collected between August 1 and August 22, 2012. Approximately 413 patients were identified as receiving enoxaparin. Of those patients, approximately 342 received prophylaxis doses while approximately 71 received treatment doses. Among these patients, 40 patients were selected for review, 25 (7%) patients receiving prophylaxis doses and 15 (21%) patients receiving treatment doses. Overall, enoxaparin was utilized in accordance with the guidelines set forth by the P&T Committee and the hospital Anticoagulation Monitoring Policy the majority of the time. Enoxaparin was appropriately dosed in all but six patients evaluated (inappropriate doses determined for 5 prophylaxis cases and 1 treatment case). The relatively small sample size reviewed limits the generalizability of the results, but does provide a general overview of prescribing patterns. Some potential issues identified by this MUE include discontinuation of enoxaparin when no longer appropriate, selection of the renal dose when unnecessary, and initiating enoxaparin prophylaxis in ambulatory patients not otherwise candidates for pharmacological prophylaxis of DVT. However, in depth analysis of these or other specific prescribing patterns would require a more targeted MUE. Currently, a more targeted MUE focused on anticoagulant bridging with enoxaparin is underway.

In addition to specific corrective actions mentioned above, the Committee agreed to continue to monitor use of these agents to evaluate prescribing patterns and appropriateness of current guidelines.

For more detailed information regarding these MUEs, including the prescribing services and number of patients from each service who received medication therapy in a manner consistent with the guidelines for use, please contact the Pharmacy Department.

MEDICATION MANAGEMENT
This section of the P&T Committee Newsletter focuses on medication management issues as highlighted primarily by The Joint Commission (TJC) and the Institute for Safe Medication Practices (ISMP).

Question: What is the National Patient Safety Goal 3E (NPSG 3E) as defined by the Joint Commission?
Answer: NPSG.03.05.01 was implemented in 2008 in an effort to reduce the likelihood of patient harm associated with the use of anticoagulation therapy involving unfractionated heparin, low molecular weight heparin, warfarin, and other anticoagulants.

RECENT FDA ALERTS/WARNINGS
The following links provide additional information on Drug Safety Communications that have been recently issued from the U.S. Food and Drug Administration.

- FDA approves new label changes and dosing for zolpidem products and a recommendation to avoid driving the day after using Ambien CR 5/14/2013
- Valproate Anti-seizure Products Contraindicated for Migraine Prevention in Pregnant Women due to Decreased IQ Scores in Exposed Children 5/6/2013
- FDA warns about potential medication errors resulting from confusion regarding nonproprietary name for breast cancer drug Kadcyla (ado-trastuzumab emtansine) 5/6/2013

DRUG SHORTAGES
As of May 30, 2013, there remain over 200 drug shortages listed on ASHP’s Drug Shortage website and many continue to impact MGH which are listed on the MGHS Online Formulary. Those currently in critical supply necessitating selected restrictions and/or other actions at MGH include:

- Acetylcysteine inhalation
- Aminocaproic acid injection
- Caffeine and sodium benzoate injection
- Diltiazem injection
- Ketorolac injection
- Magnesium sulfate injection
- Multivitamins for injection
- Potassium acetate injection
- Propofol injection

DRUG SHORTAGES CONTINUED

- Selenium injection
- Sodium phosphate injection
- Trace elements injection
- Tromethamine (THAM) injection
- Zinc injection

Additional information is also available at the Food and Drug Administration Drug Shortage website. For additional information regarding ongoing drug shortages, please visit the MGHS Online Formulary or contact the Pharmacy Department at 225-3495.

COMPOUNDING PHARMACY UPDATE

As described in the April 2013 issue of the P&T Committee Newsletter, the FDA has inspected several compounding pharmacies across the country that were identified as producing high-risk sterile drug products. Additionally, three more voluntary recalls have been issued by compounding pharmacies including:

- May 28, 2013 Main Street Family Pharmacy, LLC Issues Voluntary Nationwide Recall of All Sterile Compounded Products
- May 15, 2013 Pentec Health Announces Limited Voluntary Recall of Certain Compounded Prescription Therapies for Renal Patients
- May 06, 2013 In Cooperation with FDA, The Compounding Shop, LLC Declares a Voluntary Recall of All Lots of Sterile Compounded Products Due to a Lack of Sterility Assurance Distributed Within its Local Market Area

The most recent recall issued on May 28th involves the Main Street Family Pharmacy, LLC based out of Newbern, TN. The recall updates an FDA press release issued May 24, 2013. At this time, the recall involves all lots of all sterile products compounded by the pharmacy. The compounded products that are subject to the recall are those products with a use by date on or before November 20, 2013. The recall is being initiated due to seven (7) reported cases of adverse events in the form of skin abscesses, one of which appears to be fungal in nature. An investigation into the exact source of the adverse events is still ongoing. This announcement updates a press release that was issued by the FDA on May 24, 2013.

Additionally, a draft proposal on pharmaceutical compounding from the US Senate Committee on Health Education Labor and Pensions is currently under review (click here). This proposal is intended to provide more comprehensive regulation of pharmaceutical compounding.

FORMULARY UPDATES

The P&T Committee did not meet in May 2013 and will reconvene in June 2013. A summary of activities will be made available through the MGHSnet Online Formulary (https://mghsnet.mgh.org/).