In April 2012, the Pharmacy and Therapeutics Committee reviewed three different new items of business:

1. Medication Use Evaluation: Argatroban, Justinne Guyton, PharmD
2. Medication Use Evaluation: Anticoagulation Monitoring, Lindsey Tillman, PharmD
3. Ofirmev (intravenous acetaminophen) Restriction Order Form

A brief background, conclusion, and approved recommendations are below for each medication use evaluation report. The complete report can be reviewed by clicking the title.

**Argatroban**

**Purpose**

The purpose of this report is to evaluate the use of argatroban within the University of Mississippi Medical Center. Argatroban is an IV anticoagulant which is approved for use with limited indications. This evaluation will provide information about the usage and safety of argatroban at this medical center.

**Conclusion**

Documentation of heparin allergy occurred inconsistently among patients treated with argatroban, regardless of method used to determine the likelihood of HIT or use of the protocol. The 4T test an initial screening tool and the delay of laboratory results for the ELISA antibody test or the serotonin release assay make it difficult to determine the presence of HIT upon initial suspicion, which justifies the automatic selection of the heparin allergy on the argatroban protocol. If a patient truly has HIT, there is a high risk for thrombosis with continued heparin exposure. These patients may also experience a lag in platelet recovery and are at risk for developing rapid-onset HIT upon heparin re-exposure as heparin antibodies can last up to 50-80 days. The American College of Chest Physicians recognizes that there are certain circumstances where future use of heparin may be considered, for example individuals who are antibody negative requiring heparin for less than four days. However, in patients who have experienced HIT who require prophylaxis or treatment of thrombosis, heparin products should generally be avoided.

There was noted inconsistency in the documentation of argatroban rate changes. In several instances an “argatroban flow sheet” was created from a “heparin flow sheet”, which improved documentation. The aPTT was not monitored as recommended every 2 hours, and may have been confused with heparin monitoring which is every 6 hours.

There is a great need for improvement during the transition to warfarin therapy. The details are outlined on the second page of the argatroban protocol; however this did not improve the rate of adherence to the recommendations. Failure to transition appropriately to warfarin was also evaluated in clinical literature and is generally thought to be due to misinterpretation of the high INR caused by argatroban.

As presented in Table 3, there were 18 patients identified who received a dose of argatroban less often than the frequency recommended to ensure sterility (q 24 hours). Further investigation revealed that label comments on some of the argatroban doses state “***STABLE 96 HOURS***”. This may have led to the dose being replaced less often than the 24 hour recommendation.
Approved Recommendations

1. Increase education (physician and/or pharmacist) about documentation of heparin allergy in the patient record.
2. Create a standardized flow sheet or alter MAR for standardization of Argatroban documentation.
   a. Educate pharmacy and nursing staff about any changes that are instituted.
3. Include aPTT monitoring recommendations to a standardized argatroban flow sheet.
4. Consider education (physician and/or pharmacist) about the transition from argatroban to warfarin.
5. Add the following label comments to Argatroban: “CHANGE IV EVERY 24 HOURS”.
6. When Argatroban is initiated, a clinical pharmacist consult for anticoagulation monitoring will be placed with ordering privileges. The consult parameters are delineated in an updated version of the pharmacy anticoagulation protocol (pg 10-11)
7. Pharmacist will be authorized to order any labs needed to monitor patients on argatroban.

Anticoagulation Monitoring

Purpose

This medication use evaluation (MUE) is a retrospective review of the use of three anticoagulants and a warfarin-reversal agent – warfarin, heparin, enoxaparin, and phytonadione (vitamin K). The Joint Commission (TJC) National Patient Safety Goal 3E 3.05.01 is “to reduce the likelihood of patient harm associated with the use of anticoagulation therapy.”1 The University of Mississippi Medical Center (UMMC) has implemented the Therapeutic Anticoagulation Management Policy to assess compliance with this TJC Goal.2 Compliance with this policy will be evaluated.

Conclusion

According to the evaluation, there are several areas of improvement for the appropriate use of anticoagulants in the institution. While the new ACCP guidelines recommend 2 days of 10 mg initially (Evidence Level 2C), our policy does not recommend loading doses.3 Six percent of patients were inappropriately prescribed loading doses, compared to only three percent last year. Baseline and follow-up INR monitoring with appropriate dose adjustment also needs to be addressed. Last year, baseline INR was obtained in 83% of patients, compared to only 78% this year. Appropriate INR monitoring was performed in 98% of patients in last year’s evaluation, compared to only 85% this year. These results may potentially worsen with the new limits to routine lab ordering.

As a whole, the institution does very well at utilizing the standardized heparin order set and standardized concentration. However, the order sets were not always completed correctly or calculated correctly. Proper aPTT monitoring (defined as aPTT q 6 hours until the first 2 therapeutic aPTTs) occurred during initial dose titration in 68% of patients, a slight improvement from only 60% last year. Because only a few charts (14/25) had the heparin dosing flowsheet still in the chart, it was not always evident how or if the dose was changed for an inappropriate aPTT.
Enoxaparin dosing was corrected for weight and renal function in most cases. Patient weights were not always readily available in the chart. Because proper injection technique is vital for proper treatment of thrombotic events, education of injection should be emphasized.

According to the CHEST guidelines, vitamin K should only be given by oral and IV routes with IV only recommended in patients with serious active bleeding at any elevation of INR.4 Most of the doses of vitamin K were given by the appropriate route per the guidelines (81.25%). Only 3 of the 16 doses were given by routes not recommended by the guidelines (2 SC, 1 IM).

Approved Recommendations

1. Allow pharmacists to order coagulation studies and other labs that are necessary for safe anticoagulant treatment when appropriate per the policy (INR, aPTT, PT, CBC, SCr, anti-Xa). The primary team will be contacted when such orders are written. The ordering parameters will be delineated in an updated version of the pharmacy anticoagulation protocol (pg 12).
2. Improve the Heparin flowsheet or the MAR to include times that the next aPTT is due.
   a. Educate pharmacy and nursing staff about any changes that are instituted.
3. Improve interventions in regards to accuracy of Heparin orders (calculations) when appropriate.
4. Educate pharmacy and nursing staff about the importance of documenting teaching enoxaparin injection technique.

Ofirmev (intravenous acetaminophen) Restriction Order Form

A restriction order form for intravenous acetaminophen was reviewed and accepted for use by the committee. Per the form, the patient must meet all of the following requirements to receive intravenous acetaminophen:

1. Pediatric patient
2. Unable to tolerate PO administration (Intractable vomiting, Grade 3 or 4 mucositis)
3. Unable to tolerate PR administration (Immunosuppressed patient, Past rectal surgery)
4. Fever

Since the agent is being restricted to fever, the restriction for "no PRN orders" will no longer be valid.