



Family Medicine Clinical Pharmacy Forum

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Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

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Updated CHEST 2008 guidelines - anticoagulation

1. Warfarin Dosing

- Doses of 5 or 10 mg for 1st and 2nd doses for most individuals
- Elderly, debilitated, malnourished, or CHF may need to start at ≤ 5 mg
- If on a stable dose, monitoring intervals should not exceed 4 weeks

2. DVT/PE Treatment

- Initial treatment with SC LMWH, IV UFH, or SC fondaparinux should be for at least 5 days AND until the INR is ≥ 2.0 for 24 hours.
- Start warfarin therapy on day 1
- Warfarin duration of therapy should be 3 months for 1st episode due to transient risk factors. If the first episode is idiopathic, treatment should continue for at least 3 months. After 3 months of treatment, risk vs benefit ratio should be considered for long term therapy in patients with unprovoked DVT. For patients with unprovoked VTE that is a proximal DVT and risk factors of bleeding are absent, long-term therapy is recommended. However, for patients with unprovoked distal DVT, 3 months of treatment is preferred over indefinite therapy

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(Special thanks to Juli Kula, Pharm.D. for helping with this issue)



3. Atrial Fibrillation/Flutter

Patients	Treatment
Prior stroke or TIA	Warfarin (INR 2.0-3.0)
Two or more risk factors (including moderately or severely impaired LV function, CHF, HTN, diabetes or age > 75)	Warfarin (INR 2.0-3.0)
1 risk factor	Warfarin or aspirin (75-325 mg/day)
No risk factors and age \leq 75	Aspirin (75-325 mg/day)

“Refresher” on Approved Lovenox (enoxaparin) Dosing Regimens

Indication	Standard Regimen	Severe Renal Impairment (< 30 ml/minute)
DVT prophylaxis in abdominal surgery	40 mg SC daily	30 mg SC daily
DVT prophylaxis in knee surgery	30 mg SC twice daily	30 mg SC daily
DVT prophylaxis in hip replacement surgery	30 mg SC twice daily or 40 mg SC daily	30 mg SC daily
DVT prophylaxis in medical patients	40 mg SC daily	30 mg SC daily
Inpatient treatment of acute DVT with or without PE	1 mg/kg SC twice daily or 1.5 mg/kg daily	1 mg/kg SC daily
Outpatient treatment of acute DVT without PE	1 mg/kg SC twice daily	1 mg/kg SC daily

Lovenox Package Insert 2008.

Generics Available

In the last couple of months, there have been some brand name drugs that finally have a generic equivalent. Lamotrigine is still only available as the "blue, green, and orange starter kits" in the brand Lamictal. The chewable tablets are also only available as brand name Lamictal. Alendronate oral solution is still only available as Brand Fosamax.

DRUG	BRAND	GENERIC
Lamotrigine (Lamictal)	25 mg (30): \$140.00	25 mg (30): \$115.79
	100 mg (30): \$160.00	100 mg (30): \$120.00
	100 mg (60): \$319.99	100 mg (60): \$240.00
	200 mg (30): \$194.99	200 mg (30): \$161.57

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Alendronate (Fosamax)	5 mg (30): \$85.99	5 mg (30): \$76.79
	10 mg (30): \$88.99	10 mg (30): \$70.50
	35 mg (4): \$81.99	35 mg (4): \$49.99
	70 mg (4): \$83.99	70 mg (4): \$32.99
Zofran (ondansetron) <i>(has been available as generic for some time)</i>	8mg (#10): \$391.67	8mg (#10): \$349.65

Drugstore.com 10.27.08

Influenza Vaccine Recommendation Updates

The new CDC guidelines are out for the influenza vaccine. Here are this year's highlights.

- Annual vaccination of all children aged 5 to 18 years is recommended.
- Annual vaccination of all children aged 6 months to 4 years (59 months) and older children with conditions placing them at increased risk for complications of influenza should continue.
- Children 6 months to 8 years of age should receive two doses of vaccine at least 4 weeks apart if receiving influenza vaccine for the first time.
- All adults greater than 50 years of age and older should continue to be vaccinated.
- All nursing home patients should be vaccinated.
- All patients with chronic medical conditions and cardiopulmonary disorders should be vaccinated.
- Immunosuppressed patients should be vaccinated.
- Pregnant women should be vaccinated and it is recommended that household contacts of all children less than 5 years of age be vaccinated.
- Health care workers should be vaccinated.
- Contacts of high risk individuals should all be vaccinated.

2008 Immunization Administration: A Certificate Program for Pharmacists live seminar.

Proton Pump Inhibitor Use and Risk of Community-Acquired Pneumonia

In a recent article in the Annals of Internal Medicine, proton pump inhibitors (PPIs) were investigated as having a potential association with an increased risk for community-acquired pneumonia. The study was a case-control study performed between 1987 and 2002 in the United Kingdom. Patients were 18 years of age or older with at least 6 months of initial pneumonia-free follow up. Case patients were defined as patients who had received an incident diagnosis of community-acquired pneumonia (CAP) and were compared to a control group.

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Overall, current PPI use was not associated with an increased risk for CAP. However, there was an impressive increase in risk for CAP in patients who had started PPI therapy within the previous 2 days (adjusted OR 6.53 [CI 3.95-10.80]), 7 days (adjusted OR 3.80 [CI 2.70-5.41]), and 14 days (adjusted OR 3.16 [CI 2.45-4.08]). There was no statistically significant association between long term PPI use and risk for CAP. Similar results were seen in patients who received histamine-2 receptor antagonists 2, 7, and 14 days prior to incident diagnosis of CAP.

Sarkar, Monika et al. Proton-pump inhibitor use and the risk for community-acquired pneumonia. *Ann Intern Med.* 2008;149:391-398.

Inhaled Anticholinergic Medications and Risk of Cardiovascular Events

Two recent publications reported increased risk for mortality and/or cardiovascular events in patients who received tiotropium or inhaled anticholinergics.

Singh et al performed a meta-analysis of 17 clinical trials enrolling 14,1783 patients treated with anticholinergic drugs for COPD. Cardiovascular death, MI or stroke occurred in 1.8% of patients receiving inhaled anticholinergics compared to 1.2% of patients receiving control therapy. MI risk was increased (RR 1.53 (95%CI 1.05-2.23)) as was risk of cardiovascular death (RR 1.80 (1.17-2.27)).

Lee et al performed a case-control study of 32,130 patients (320,501 controls) with COPD who received care in the VA healthcare system. Ipratropium use was associated with increased cardiovascular deaths (OR 1.34 (1.22-1.47)), and increased all-cause mortality (OR 1.11 (1.08-1.15)).

On March 18, 2008, the FDA issued a communication that Boehringer-Ingelheim had identified a small increased risk of stroke (2 cases per 1000) with Spiriva (tiotropium) over placebo in a pooled analysis of 29 trials. However, in October 2008, the UPLIFT study was published which was a 4-year placebo-controlled trial with tiotropium in 6000 patients with COPD and there was no increased stroke or cardiovascular risk observed with tiotropium.

The bioavailability of inhaled anticholinergics is quite low. Increased heart rate and tachyarrhythmias are one of the theorized mechanisms for increased cardiovascular events. However, it appears that there is no need to discontinue inhaled anticholinergics or change your practice given the conflicting evidence at present.

Tashkin et al. *NEJM* 2008;359:1543-54., Lee TA et al. *Ann Intern Med* 2008;149:380-90., Singh S et al. *JAMA* 2008;300(12):1439-50.

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In the Pipeline: Rivaroxaban as a New Alternative to Warfarin?

Rivaroxaban is a new, oral direct factor Xa inhibitor being developed by Bayer. It is being evaluated for conditions such as DVT prophylaxis and treatment, atrial fibrillation, and acute coronary syndromes.

It has a half-life of 9 hrs, fast onset of action, and has predictable pharmacodynamics such that no regular anticoagulant monitoring is required with its use (i.e. no INR or aPTT needed). The RECORD3 trial compared rivaroxaban 10mg PO daily to Lovenox 40mg SC daily for 10-14 days in 2531 patients after total knee arthroplasty. Death, nonfatal PE, or any DVT occurred in 18.9% of Lovenox patients and 9.6% of rivaroxaban patients ($p < 0.001$). Risk of major bleeding was similar in the two groups.

The RECORD1 trial compared rivaroxaban 10mg PO daily to Lovenox 40mg SC daily for 35 days in 4541 patients after total hip arthroplasty. Death, nonfatal PE or any DVT occurred in 3.7% of Lovenox patients and 1.1% of rivaroxaban patients ($p < 0.001$) with a similar risk of major bleeding.

Rivaroxaban appears to be more efficacious than Lovenox prophylaxis for DVT prevention after orthopedic surgery. How it will compare to warfarin in prevention of stroke in patients with atrial fibrillation is being evaluated in the ROCKET AF study (N=16,000) which is underway.

Ximelagatran was an oral, direct thrombin inhibitor which showed initial promise as an alternative to warfarin but was later withdrawn due to hepatotoxicity. It is different from rivaroxaban. Other oral, factor Xa inhibitors (in addition to rivaroxaban) are also under development and in phase II-III trials.

NEJM 2008;358:2776-86, NEJM 2008;358:2765-75, J Clin Pharmacol 2006;46:981-90.

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