



Family Medicine Clinical Pharmacy Forum Vol. 5, Issue 2 (March/April 2009)

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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Heart Failure Guidelines

The ACCF/AHA recently released a focused update for the diagnosis and management of heart failure in adults. Key medication points from the update:

- Continued recommendation of diuretics, angiotensin-converting enzyme inhibitors (ACEI) and beta blockers for patients with current or prior symptoms of HF and reduced LVEF
- Use of hydralazine and nitrates in combination for African Americans on optimal therapy having moderate-to-severe symptoms
- Recommendation to either control ventricular rate or maintain sinus rhythm in patients with atrial fibrillation and heart failure
- Medication recommendations for patients hospitalized with heart failure:
 - Intravenous loop diuretics should be initiated without delay
 - Intensify diuretic regimen with higher doses of loops, addition of second diuretic (i.e. metolazone, spironolactone or IV chlorothiazide or continuous infusion of a loop diuretic)
 - ACEI and beta-blocker therapy should be continued in most patients in the absence of hemodynamic instability or contraindication. Patients not on these treatments at admission should be started prior to discharge. Beta-blocker therapy should be started at a low dose in stable patients after volume status resolves and IV diuretics have been discontinued.

Jessup M, Abraham WT, Casey DE, et al. Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation published online Mar 26, 2009.

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Aspirin Guidelines

The U.S. Preventive Services Task Force (USPSTF) has updated their recommendations about the use of aspirin for the prevention of coronary heart disease.

Use of aspirin is encouraged when potential CVD benefit (MI for men, stroke for women) outweighs potential harm of GI hemorrhage

- Men age 45-79 for prevention of myocardial infarction
- Women age 55-79 for prevention of ischemic stroke
- Insufficient evidence for persons older than 80 years

Risk Level at Which CVD Events Prevented (Benefit) Exceeds GI Harm			
Men		Women	
Age	10 yr CHD Risk	Age	10 yr CHD Risk
45-69	≥ 4%	55-59	≥ 3%
60-69	≥ 9%	60-69	≥ 8%
70-79	≥ 12%	70-79	≥ 11%

This is in slight contrast to the ADA Diabetes Treatment Guidelines (75mg – 162mg per day) as primary prevention in patients with diabetes who are at increased CV risk

- 40 years or older
- Family history, HTN, smoking, dyslipidemia, or albuminuria

U.S. Preventive Services Task Force: Aspirin for the prevention of cardiovascular disease. Ann Intern Med 2009;150:396-404.

NICE-SUGAR trial questions tight blood glucose control in hospitalized patients

The debate of glucose in hospitalized patients continues. The most recent trial, NICE-SUGAR examined 6000 patients in the intensive care unit. The endpoint of the trial was death from any cause within 90 days. The trial is summarized below:

- Intensive control patients had a goal of 81-108 mg/dL
- Conventional control patients had a goal of <180 mg/dL
- Mortality rates were 27.5% (intensive) vs. 24.9% (conventional)
- Intensive control relative risk was 1.14 (1.02-1.28) p = 0.02

The NICE-SUGAR Study Investigators. Intensive versus Conventional Glucose Control in Critically Ill Patients. NEJM 2009;360:1283-97.

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Polypill for prevention of cardiovascular disease?

A pill with five generic drugs is being studied to prevent cardiovascular disease. The Indian Polycap Study is examining a once-daily pill, called the polypill, with low to moderate doses of thiazide, atenolol, ramipril, simvastatin and aspirin. The study has enrolled 2000 people ages 45-80 without cardiovascular disease but with one risk factor such as hypertension or smoking. Their first study was VERY short, only 12 weeks, but showed the polypill was noninferior to its individual components in lowering blood pressure and heart rate with cholesterol and antiplatelet activity slightly in favor of the combination pill. A study with more patients and a longer follow-up including outcomes should follow but watch to see if this is the pill many have waited for.

The Indian Polycap Study (TIPS) Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomized trial. Lancet published online March 30, 2009.

The new warfarin? Rivaroxaban recommended for FDA approval

An FDA advisory panel has recommended approval of rivaroxaban (Xarelto[®]) for the prophylaxis of pulmonary embolism (PE) and deep vein thrombosis (DVT) in patients undergoing hip and knee-replacement surgery. Rivaroxaban would be used in place of warfarin or low molecular weight heparin in these patients. Rivaroxaban is a factor Xa inhibitor that would require significantly less monitoring than warfarin. There is still a concern with the safety of the drug including bleeding risks, hepatotoxicity and possible thrombotic events with discontinuation.

Secondary prevention and long term safety and efficacy of rivaroxaban in patients with a history of DVT/PE are being studied (EINSTEIN) as well as a study in hospitalized patients (MAGELLAN). The drug is expected to be filed for approval of atrial fibrillation and prevention of acute coronary syndrome in 2010. Rivaroxaban is one of many oral anticoagulants in the drug development pipeline.

The new amiodarone? Dronedarone recommended for FDA approval

An FDA advisory panel has voted to recommend approval of dronedarone for the treatment of atrial fibrillation (AF). Dronedarone is being studied in hopes to replace amiodarone, known for its unfavorable side effects and toxicities despite its effectiveness. The decision was based largely on the ATHENA trial which showed a 24% decrease in the primary end point of death from any cause or cardiovascular hospitalization compared to placebo treatment. The committee had previously not voted for the drug due to increased mortality risk in patients with severe systolic heart failure.

Raptiva[®] (efalizumab) recalled

Drugmaker Genentech has announced it will voluntarily withdraw efalizumab (Raptiva[®]) from the U.S. market. The psoriasis drug has been associated with an increased risk of developing progressive multifocal leukoencephalopathy (PML).

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Metoclopramide-containing drugs

A new black box warning will be added to metoclopramide due to risk of its long-term or high-dose use. Tardive dyskinesia, including voluntary and repetitive movements of the body, has been associated with chronic use of metoclopramide. Even after discontinuation of metoclopramide the symptoms can persist as they are rarely reversible and no treatment has been currently identified. The warning is specifically for long-term or high-dose use. Keep this in mind while prescribing various formulations of metoclopramide and consider using the lowest dose for the shortest time needed.

Narcotics in short supply

Many narcotics have been in short supply over the past months. Even though pharmacies supply it, currently, the morphine sulfate oral solution 20 mg/ml products being marketed in the U.S are not approved by the FDA. The FDA is working closely with the manufacturers to either stop supplying the drug or apply for drug approval. Oxycodone and hydrocodone have seen sporadic supply concerns over the past few months. Keep in mind the dose conversion of analgesic products if these issues arise for you in your own practice.

Equianalgesic Table

Medication	Equianalgesic dose (parenteral)	Equianalgesic dose (oral)
Codeine (various)	130 mg	200 mg
Fentanyl -parenteral: Sublimaze® -transdermal: Duragesic®	-0.1 mg -N/A	-N/A -20-30 mcg/hour ≈ SR morphine 60 mg/day
Hydrocodone (various)	N/A	30 mg
Hydromorphone (Dilaudid®)	1.5 mg	7.5 mg
Methadone (various)	Varies (see below)	Varies (see below)
Levorphanol (Levo-Dromoman®)	2 (acute) 1 (chronic)	4 (acute) 1 (chronic)
Meperidine (Demerol®)	75	300
Morphine (MS Contin®, Roxanol®, others)	10 mg	30 mg
Oxycodone (OxyContin®, others)	N/A	30 mg

Methadone Conversion

Oral Morphine Dose	Conversion Ratio	Example
30-90 mg	4:1	30 mg morphine = 7 mg methadone
91-300 mg	8:1	300 mg morphine = 35 mg methadone
>300 mg	12:1	400 mg morphine = 35 mg methadone