



Family Medicine Clinical Pharmacy Forum Vol. 3, Issue 2 (March/April 2007)

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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NEW DRUG for hypertension: Aliskiren (Tekturna[®])

Aliskiren (Tekturna[®]) represents the first drug in a new class of agents called direct renin inhibitors. Aliskiren is indicated for the treatment of hypertension alone or in combination with other antihypertensive agents. It acts by inhibiting the production of renin higher in the cascade than ACE inhibitors and angiotension receptor blockers (ARBs). It is indicated for once daily dosing and recommended at doses of 150mg daily or 300mg once daily.

A trial of 3,961 patients comparing aliskiren with placebo over eight weeks showed aliskiren had significant blood pressure lowering effects compared to placebo at doses of 150-300mg, but no further increase at a dose of 600mg. Aliskiren showed comparable efficacy to other agents such as hydrochlorothiazide, valsartan and amlodipine with excellent tolerability and safety.

NEW DRUG for ADHD: Lisdexamfetamine dimesylate (Vynase[®])

Vynase[®], or lisdexamfetamine dimesylate, is a prodrug in which dextroamphetamine is covalently linked to L-lysine. This combination is rapidly absorbed by the GI tract and converted to dextroamphetamine, the compound responsible for its activity. One study showed that at six months, 95% of children taking the drug had a “much improved” or “very much improved” rating on the Clinical Global Impressions – Improvement score.

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(Special thanks this edition also to contributors: Abby Beane and Talia Ruble, Pharm.D. candidates at The University of Iowa College of Pharmacy.)



Vynase[®] may have advantages over other currently available treatment options for ADHD. Clinical trials have shown that all dosages (**30mg, 50mg and 70mg**) provide significant efficacy compared to placebo for a full treatment day, up through and including 6:00pm. All dosage strengths are indicated for once daily dosing. Another advantage is that it has lower potential for abuse compared with other stimulant medications used to treat ADHD, however the FDA has proposed it be classified as a schedule II controlled substance. A final scheduling decision by the DEA is expected in about a month and then product launch will follow.

FDA Requests Label Change for All Sleep Disorder Drug Products

The U.S. Food and Drug Administration (FDA) has requested that all manufacturers of sedative-hypnotic drug products, a class of drugs used to induce and/or maintain sleep, strengthen their product labeling to include stronger language concerning potential risks. These risks include severe allergic reactions and complex sleep-related behaviors, which may include sleep-driving. Sleep driving is defined as driving while not fully awake after ingestion of a sedative-hypnotic product, with no memory of the event. In addition, FDA has requested that manufacturers of sedative-hypnotic products develop Patient Medication Guides for the products to inform consumers about risks and advise them of potential precautions that can be taken. Although all sedative-hypnotic products have these risks, there may be differences among products in how often they occur. The medications that are the focus of the revised labeling include products such as: Ambien/Ambien CR, Halcion, Lunesta, Restoril, Rozerem and Sonata. **Additionally, this issue has caught the attention of media so be prepared to answer questions from your patients on the use of these agents.**

Read the complete MedWatch 2007 Safety summary, including a link to the FDA press release, at: <http://www.fda.gov/medwatch/safety/2007/safety07.htm#Sedative>

Pioglitazone (Actos[®]) and risk of fractures

Takeda and FDA notified healthcare professionals of recent safety data concerning pioglitazone-containing products. The results of an analysis of the manufacturer's clinical trial database of pioglitazone showed more reports of fractures in female patients taking pioglitazone than those taking a comparator (either placebo or active). Interestingly, the majority of fractures observed in female patients were in the distal upper limb (forearm, hand and wrist) or distal lower limb (foot, ankle, fibula and tibia). There were more than 8100 patients in the pioglitazone-treated groups and over 7400 patients in the comparator-treated groups. The duration of pioglitazone treatment was up to 3.5 yrs. Although unlikely, physicians should consider this risk when initiating or treating female patients with type 2 diabetes mellitus with pioglitazone.

Read the complete MedWatch 2007 Safety summary regarding this issue at: <http://www.fda.gov/medwatch/safety/2007/safety07.htm#Actos>

Future directions in OTC and supplement safety

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Manufacturers, packers, and distributors of dietary supplements and nonprescription drug products this year must start reporting "serious" adverse events to FDA within 15 business days of learning of such events. The Dietary Supplement and Nonprescription Drug Consumer Protection Act, signed into law December 2006, defines a serious adverse event as death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an event that requires a medical or surgical intervention to prevent an outcome. Hopefully this new legislation will help to learn more about the safety of many OTCs and supplements that our patients use every day!

Clopidogrel use and Drug-Eluting Stents

Currently, the minimum requirements of clopidogrel (Plavix[®]) use after drug-eluting stent (DES) placement is 3 months after sirolimus-coated stents and 6 months after paclitaxel-coated stents. However, the duration of antiplatelet therapy has been questioned as thromboses are occurring after discontinuation of clopidogrel.

A recent trial looked at patients receiving intracoronary stents. Patients were divided into four groups, DES with clopidogrel, DES without clopidogrel, bare metal stent (BMS) with clopidogrel, and BMS without clopidogrel. Patients were assessed for death, non-fatal myocardial infarction (MI), and death or MI at 6 and 12 months based on clopidogrel use. Patients were followed for 24 months. The results at 24 months from reported clopidogrel use at 6 months and 12 months showed DES with clopidogrel had a statistically significant lower adjusted rate of death compared to DES without clopidogrel ($p=0.03$ and $p<0.004$ respectively). This trial also evaluated BMS with and without clopidogrel, and there was no statistical difference based on clopidogrel use.

The results of this study give insight into the beneficial effects of continued clopidogrel use beyond the current guidelines. Clopidogrel use in patients with DES is suggested to continue for at least twelve months. Further research is anticipated in order to determine the appropriate length of clopidogrel use for DES.

Eisenstein EL, Anstrom KJ, Kong DF, et al. Clopidogrel Use and Long-term Clinical Outcomes After Drug-Eluting Stent Implantation. JAMA. 2007 Jan;297(2):159-168.

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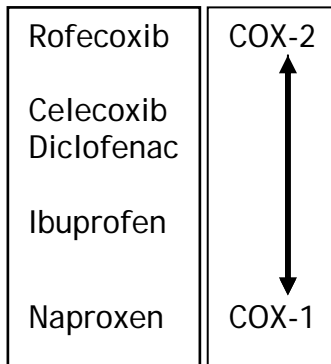
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Use of NSAIDs: Scientific Statement from the American Heart Association

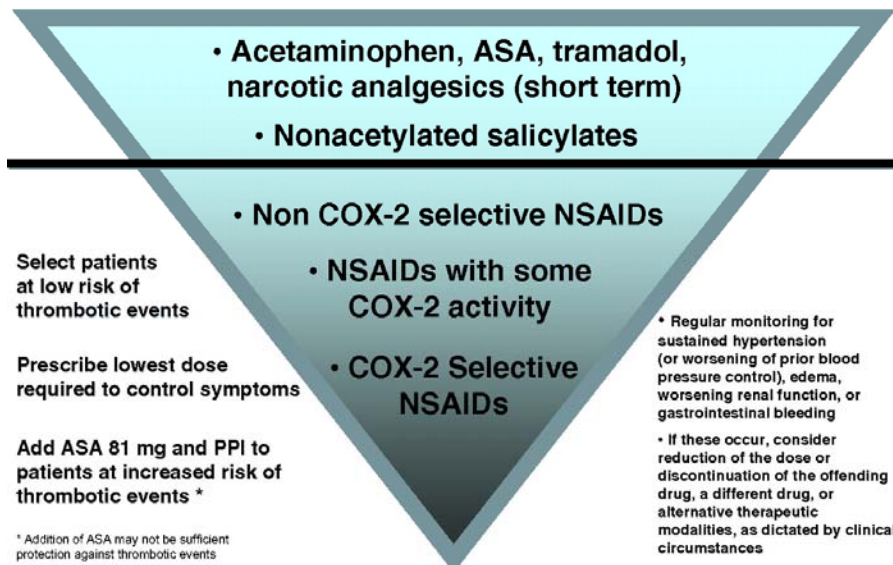
On March 27, 2007 the American Heart Association published a scientific statement on the increased cardiovascular risk of nonsteroidal anti-inflammatory drugs (NSAIDs), both COX-2 selective and non-selective NSAIDs. The group discussed the relevance of degree of selectivity of these agents as it correlates to increased risk. The group also recommended a stepped care approach for patients with known cardiovascular disease or risk factors for ischemic heart disease.



Degree of selectivity:

The available data have implicated several COX-2 inhibitors with varying degrees of selectivity. A relative lack of COX-2 selectivity does not completely eliminate the risk of cardiovascular events, and in that regard, all drugs in the NSAID spectrum should only be prescribed after thorough consideration of the risk/benefit balance.

Stepped Care Approach to Pharmacologic Therapy for Musculoskeletal Symptoms With Known Cardiovascular Disease or Risk Factors for Ischemic Heart Disease



Antman EM, Bennett JS, Alan Daugherty A, et al. Use of Nonsteroidal Antiinflammatory Drugs: An Update for Clinicians: A Scientific Statement From the American Heart Association. *Circulation* 2007;115:1634-1642.

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Smoking Cessation: Now is the time!

The recent \$1.00 tax increase for a pack of cigarettes presents us as healthcare professionals with an excellent opportunity to encourage our patients to quit smoking.

Remember the 5 As of smoking cessation when caring for your patients:

ASK, ADVISE, ASSESS, ASSIST and ARRANGE

Nicotine replacement therapies are becoming more available through prescription plans. The use of these agents for Medicaid patients requires a prior authorization (PA) which is simply a signed commitment by the patient to join the **free** state of Iowa sponsored QUITLINE program. Bupropion is available generically and varenicline (Chantix[®]) is a new oral agent that offers another option for your patients.

Some facts to share with your patients—

- *24 hours after quitting the chance of having a heart attack begins to decrease*
- *2 to 3 months after quitting blood circulation and lung function may improve*
- *1 to 9 months after quitting the lungs can start to clean themselves again and coughing and shortness of breath improve*
- *1 year after quitting the risk of a heart attack is now ½ the risk of a smoker's*
- *5+ years after quitting the risk of stroke is reduced to the same as a person who has never smoked*
- *10 years after quitting arteries in the body return to near normal*
- *10 years after quitting the risk of lung cancer and other cancers is reduced*

Adapted from <http://www.quitlineiowa.org>

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