

## Health Matters January 2007; Volume 1, Issue 6

### FDA approves 18 “new molecular entities” in 2006

The Food and Drug Administration (FDA) approved 50 new drugs or biologicals during 2006, with 18 of them being considered “new molecular entities”. A listing of these medications is included in the table below:

Brand	Generic	Indication/Use
Amitiza	lubiprostone	Chronic idiopathic constipation
Anthelios SX	ecamsule/avobenzone/octocrylene	OTC sunscreen for UVA/UVB
Azilect	rasagiline	Parkinson's disease
Chantix	varenicline	Smoking cessation
Dacogen	decitabine	Myelodysplastic syndromes
Eraxis	anidulafungin	<i>Candida</i> infections
Invega	paliperidone	Schizophrenia (metabolite of risperidone)
Januvia	sitagliptin	Type 2 diabetes
Noxafil	posaconazole	<i>Aspergillus</i> and <i>Candida</i> infections
Omnaris	ciclesonide	Allergic rhinitis
Prezista	darunavir	HIV disease
Pylera	bismacitrate/metronidazole/tetracycline	<i>H. pylori</i> therapy (combined with omeprazole)
Ranexa	ranolazine	Chronic angina
Sprycel	dasatinib	Leukemia
Sutent	sunitinib	Stomach and kidney cancer
Tyzeka	telbivudine	Hepatitis B
Veregen	kunecatechins	External genital and perianal warts
Zolinza	vorinostat	Skin cancer

In addition to the “new molecular entities”, a number of significant new biologicals were approved in 2006. Included in this group were the vaccines for human papilloma virus (Gardasil™), rotavirus (RotaTeq™) and zoster (Zostavax™).

Inside this issue	
New drugs of 2006	1
The “Triple Whammy”	2
FTC fines diet products	2
News Clips	2
FDA bans unapproved quinine	3
Use the DIC	3

More than 20 significant new dosage forms were also approved in 2006. New dosage forms are unique formulations of previously approved agents. Included in this group were combination products, transdermal preparations, and novel administration routes (Exubera™ - inhaled insulin).

For more information on the drugs and biologicals approved in 2006, please contact the Drug Information Center at 280-5100 or [druginfo@creighton.edu](mailto:druginfo@creighton.edu).

References:

1. U.S. Food and Drug Administration Center for Drug Evaluation and Research. Accessed at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>, January 4, 2007.
2. New drugs approved by the FDA in 2006. Pharmacist's Letter/Prescriber's Letter 2006.

## “Triple Whammy” effect related to drug combinations

You may have seen the term “triple whammy” referred to in recent literature. The term describes a phenomenon in which a combination of frequently used medications, Ace-Inhibitors (ACE-I) or Angiotensin Receptor Blockers (ARB), non-steroidal anti-inflammatory agents (NSAIDs, including aspirin) and/or diuretics, results in impaired renal function.

Recently published data from Australia note that between 4.7 and 7.9% of patients attending general practices in that country were on a such a combination of medications, potentially leading to renal dysfunction. Although no statistics regarding usage patterns of these medications in the United States are available, the likelihood of patients, particularly the elderly, suggest that prescribers be alert to the possible consequences of such drug combinations. Loboz and Shenfield recently published a cross-sectional study of pa-

tients admitted to a general medicine ward in an Australian teaching hospital over a three month period. Prior consumption of ACE-I/ARBs, NSAIDs (including low-dose aspirin) and diuretics was assessed and correlated with creatinine and creatinine clearance at admission. Taking two or more of the identified drugs was associated significantly with renal impairment, particularly in older patients.

Two mechanisms are thought to primarily be involved in the pathogenesis of renal dysfunction and the “triple whammy” effect. Drugs that impact the renin-angiotensin system, as well as NSAIDs, decrease afferent arteriolar vasodilation. Diuretics decrease plasma volume. Synergistically, these mechanisms can lead to decreased renal blood flow and subsequent renal dysfunction. The elderly are thought to be more susceptible to the “triple whammy” effect due to a decreasing

glomerular filtration rate, as well as decreased compensatory abilities.

Age and pre-existing renal impairment are the most likely factors to increase the risk of developing such adverse effects. Treatment considerations for this population may include the use of acetaminophen or opioids over NSAID for pain relief, low doses and slow titration of loop agents when diuresis is necessary, and cautious use of potassium-sparing diuretics in patients already receiving angiotensin agents in combination with NSAIDs.

### References:

1. The “triple whammy”. Pharmacist’s Letter/Prescriber’s Letter 2006;22(12):221202.
2. Loboz KK, Shenfield GM. Drug combinations and impaired renal function – the “triple whammy”. Br J Clin Pharmacol 2005;59:239-43.

## FTC fines diet pill makers for false claims

The Federal Trade Commission (FTC) last week fined the marketers of four diet pills millions of dollars for making false advertising claims about their products. Although products can remain on the shelves, false claims ranging from rapid weight loss to reducing the risk of cancer, osteoporosis and Alzheimer’s disease were identified.

Marketers representing the following four products were fined:

Xenadrine EFX  
One A Day Weight Smart  
Cortaslim  
TrimSpa

More than \$25 million in fines are expected to be recovered based on four separate cases involving the above products. Each suit alleged that weight-loss and weight-control claims were not supported by com-

petent and reliable scientific evidence. In the case of Xenadrine, a clinical study existed showing that persons taking placebo actually lost more weight than those taking the diet pill. Additionally, failure to disclose payments to endorsers for “testimonials” were included in the FTC complaints.

According to the FTC commissioner, it is thought millions of dollars from the civil fines would be returned to consumers.

### Reference:

1. Federal Trade Commission. Federal Trade Commission reaches “New Year’s” resolutions with four major weight-control pill marketers. Available from <http://www.ftc.gov/opa/2007/01/weightloss.htm>. Accessed January 4, 2007.

## News Clips



### More generics on the horizon....

The FDA has approved generic equivalents for Toprol XL™, Zofran™ and Wellbutrin XL™. Although not yet available in pharmacies, expect to see them over the next few months. For up-to-date information on generic equivalents currently on the market, click on to the “Generic Alternatives” link at <http://druginformation.creighton.edu>.

### Drug advertising continues to rise...

Pharmaceutical company advertising spending rose to \$2.46 billion for the first 6 months of 2006, representing an approximate 9% increase over the same period in 2005.

## FDA orders unapproved quinine products off the market

In December 2006, the Food and Drug Administration (FDA) ordered all unapproved quinine products off the market, citing serious safety concerns. Although quinine is commonly used for treatment of leg cramps, it is only approved for the treatment of malaria. The only FDA-approved quinine product allowed on the market is Qualaquin™.

In making this decision, the FDA refers to more than 665 reports of serious adverse effects, including 93 deaths, associated with quinine use since 1969. Reports of cardiac arrhythmias, thrombocytopenia and severe hypersensitivity reactions have been documented. Additionally, there is concern of significant drug interactions with quinine.

Manufacturers must cease product production within 60 days of this ruling, and shipments of the product may not continue past June 13, 2007. Following this date, Qualaquin™ will be the only quinine product available. This product costs approximately \$5 per capsule, and is only approved for treating malaria. It is not illegal to write for quinine off-label for leg cramps, and the FDA recognizes the professional judgment of physicians to identify what is in the best interest of patients. A

published legal analysis of the situation indicates however, since package labeling specifically says not to use quinine for leg cramps, this could potentially increase liability if a patient were to experience an adverse event from the drug.



Quinine is an example from a group of mainly older drugs that continue to be marketed, despite formal evaluation and approval by the FDA. The FDA will eventually require all of these drugs to prove safety and efficacy. Until this can take place, these drugs have been allowed to remain on the market if no immediate concerns exist.

### References:

1. FDA News FDA advances effort against marketed unapproved drugs. FDA orders unapproved quinine drugs from the market and cautions consumers about "off label" use of quinine to treat leg cramps. December 11, 2006. Available from <http://www.fda.gov/bbs/topics/NEWS/2006/NEW01521.html>. Accessed January 4, 2007.
2. Professional information about quinine and leg cramps. Pharmacist's Letter/Prescriber's Letter 2007;23(12):230101.
3. Legal analysis of using quinine off-label and informed consent for leg cramps. Pharmacist's Letter/Prescriber's Letter 2007.

## Have a drug question? Call the Drug Information Center

The Creighton University Drug Information Center (DIC) is a free service available to assist any health care professional in answering questions related to medications and drug therapy.

The non-emergent service, located in the Health Sciences Library on the Creighton campus, is open Monday through Friday, 8:30 am through 4:30 pm. The DIC is staffed with Drug Information Specialist pharmacists and a post-graduate specialty pharmacy resident, and serves as a teaching site for fourth year pharmacy students.

Using state-of-the art computer, Internet, serial and monograph resources, the DIC fields e-mail, fax, and phone requests from a wide spectrum of health care professionals. The scope of inquiries the center receives spans basic and advanced medication and drug therapy questions. The DIC responds to the large majority of requests within 24 hours and is committed to providing accurate, unbiased and up-to-date information not generally available in standard medical references.

The DIC has recently updated their website with a special site for UniNet providers. This site can be accessed at

<http://druginformation.creighton.edu>.

Incorporated into the site are an online drug information request form, copies of recent newsletters and headlines, and updated generic medication availability information.

The Drug Information Center can be reached locally at (402) 280-5100 or toll free at (800) 561-3728. You may also contact us via email at [druginfo@creighton.edu](mailto:druginfo@creighton.edu).



Health Matters January 2007; Issue 1, Volume 6

**Our Mission...**

**To serve the health care professional community by providing evidence-based, timely and unbiased information in an effort to contribute to comprehensive patient-based care. We also strive to provide excellent training and foundational skills to prepare our students to competently meet the challenges of providing such information throughout their careers.**

Creighton University Drug Information Center  
2500 California Plaza  
Omaha, NE 68178

**We're on the web!!**  
<http://druginformation.creighton.edu>

Contact us:

Telephone: 402-280-5100  
800-561-3728

Fax: 402-280-5149

Email: [druginfo@creighton.edu](mailto:druginfo@creighton.edu)



**Editor:**

Amy Friedman Wilson, Pharm.D.  
Director of Drug Information Services