

# AU InforMed

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## Key Inforbits

- 3 new drugs approved!
- Vocabulary - Pharmacometrics
- CAM use measured in the U.S.
- Patient information leaflets – Not so good!
- Capitalism is alive and well in pharmaceuticals
- Merry Christmas!

## NEW DRUGS, and other related stuff ...

**New Drug** ... (11/24/2008) The FDA has approved **tapentadol hydrochloride** (no trade name determined, **by Johnson & Johnson**), an immediate-release oral tablet for the relief of moderate to severe acute pain. Tapentadol is a centrally-acting synthetic analgesic that is available in doses of 50 mg, 75 mg, or 100 mg. Tapentadol acts in two ways, opioid (narcotic) and non-opioid. It affects the brain and body primarily by activating opioid receptors in the brain, spinal cord and gastrointestinal tract. In addition, tapentadol inhibits the reuptake of the brain chemical norepinephrine which possibly has an analgesic effect. The most common side effects are nausea, dizziness, vomiting, sleepiness, and headaches. The labeling includes warnings about the risk of respiratory depression; addictive depressive effects on the central nervous system when taken with alcohol, other opioids, or illicit drugs; and abuse potential. Per Federal regulation for all controlled substances, tapentadol will be reviewed by the U.S. Drug Enforcement Agency for scheduling, and it cannot be sold until it receives a scheduling classification.

<http://www.fda.gov/bbs/topics/NEWS/2008/NEW01916.html>

<http://www.investor.jnj.com/releasedetail.cfm?ReleaseID=350226> (Johnson & Johnson Press Release)

**New Drug** ... (12/15/2008) The FDA has approved **Mozobil™ (plerixafor injection** by Genzyme), a drug to be used in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the bloodstream for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM). The product has also been granted orphan drug designation. Currently, before a transplant can take place, patients may receive chemotherapy and/or growth factors to help mobilize their hematopoietic stem cells into the bloodstream. Once the cells are released into the bloodstream, they are collected in preparation for a transplant. In order for the transplant to take place, a minimum number of approximately 2 million stem cells per kg must be collected. For many patients, this process can take three or four hours over multiple days to complete. Even then, some patients are not able to mobilize enough cells, and a transplant is not possible.

<http://www.genzyme.com/> (Manufacturer web site)

<http://www.genzyme.com/corp/investors/GENZ%20PR-121508.asp> (Manufacturer press release)

**New Drug** ... (12/16/2008) The FDA has approved **fenofibric acid, delayed release (TriLipix™ by Abbott Labs)**. It is approved for use in combination with a statin to reduce triglycerides (TG) and increase HDL-C in patients with mixed dyslipidemia and coronary heart disease (CHD) or a CHD risk equivalent who are on optimal statin therapy to achieve their LDL-C goal; as monotherapy to reduce TG in patients with severe hypertriglyceridemia; as

monotherapy to reduce elevated LDL-C, Total-C, TG and Apo B, and to increase HDL-C in patients with primary hyperlipidemia or mixed dyslipidemia.

[http://www.rxabbott.com/pdf/trilipix\\_pi.pdf](http://www.rxabbott.com/pdf/trilipix_pi.pdf) (Package Insert)

[http://www.abbott.com/global/url/pressRelease/en\\_US/60.5:5/Press\\_Release\\_0660.htm](http://www.abbott.com/global/url/pressRelease/en_US/60.5:5/Press_Release_0660.htm) (Press release)

**MedWatch** ... (11/24/2008) The FDA is investigating new preliminary data regarding a potential **increased risk of serious skin reactions including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) from phenytoin therapy in Asian patients** positive for human leukocyte antigen (HLA) allele, HLA-B\*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais. Until the FDA evaluation is completed, healthcare providers should consider avoiding phenytoin and fosphenytoin as alternatives for carbamazepine in patients who test positive for HLA-B\*1502. A summary of the data currently being analyzed by FDA, and information for patients and healthcare professionals to consider, can be found in the links provided in the MedWatch safety alert.

Read the MedWatch safety summary, including links to the Information for Healthcare Professionals and FDA Drug Information pages, at:

<http://www.fda.gov/medwatch/safety/2008/safety08.htm#Phenytoin>

**MedWatch** ... (11/26/2008) Balanced Health Products, Inc. announced a **recall of STARCAPS due to the presence of an undeclared drug ingredient, bumetanide**, which is a diuretic. Risks associated with the use of bumetanide include serious fluid and electrolyte loss and an elevation in uric acid concentrations. Consumers should not take bumetanide if they are allergic to sulfonamides. Significant drug interactions with bumetanide, such as with digoxin and lithium, may lead to an increase risk of toxicity. Patients may also be at an increased risk of hypotension, fainting and resultant injury if they have normal blood pressure or are already taking an antihypertensive medication and take STARCAPS with undeclared bumetanide. Consumers who have this product should immediately discontinue taking it and return the product to the manufacturer. See the company's press release for specific lot number information.

Read the complete MedWatch 2008 Safety summary, including a link to the firm's press release, at: <http://www.fda.gov/medwatch/safety/2008/safety08.htm#Starcaps>

**MedWatch** ... (11/26/2008) Fashion Sanctuary announced a **recall of Zhen De Shou Fat Loss Capsules** because FDA analysis found the product to contain undeclared sibutramine, an appetite suppressant for weight loss. This poses a threat to consumers because sibutramine is known to substantially increase blood pressure and/or pulse rate in some patients and may present a significant risk for patients with a history of coronary artery disease, congestive heart failure, arrhythmias or stroke. The product was primarily distributed in the U.S and sold via the Internet and the recall affects all lot codes and use by dates. Consumers who may have purchased product from this company should immediately discontinue using the product.

Read the complete MedWatch Safety summary, including a link to the firm's press release, at:

<http://www.fda.gov/medwatch/safety/2008/safety08.htm#Zhen>

## **FROM THE MEDICAL LITERATURE ...**

**Vocabulary** ... **Pharmacometrics** ... is emerging as the science that quantifies drug, disease and trial information to aid efficient drug development and/or regulatory (eg, FDA) decisions. Drug models describe the relationship between exposure (or pharmacokinetics-PK), response (or pharmacodynamics-PD) for both desired and



undesired effects, and individual patient characteristics. Disease models describe the relationship between biomarkers and clinical outcomes, time course of disease and placebo effects. The trial models describe the inclusion/exclusion criteria, patient discontinuation and adherence. The typical focus of Pharmacometrics has been on drug models, also referred to as: concentration-effect, dose-response, PKPD relationships. Pharmacometrics now consists of multidisciplinary skills including clinical pharmacology, statistics, engineering/data management along with clinicians.

<http://www.fda.gov/cder/regulatory/pharmacometrics/default.htm>

**CAM use in US, 2007** ... A survey was conducted as part of the 2007 National Health Interview Survey (NHIS), an annual study in which tens of thousands of Americans are interviewed about their health/illness-related experiences. It was developed by the National Center for Complementary and Alternative Medicine (NCCAM) (part of the National Institutes of Health [NIH]) and the National Center for Health Statistics (NCHS) (part of the Centers for Disease Control and Prevention [CDC]). Approximately 38% of adults  $\geq 18$  years old and nearly 12% of children  $\leq 17$  years old use some form of **complementary and alternative medicine (CAM)**. The most common forms of CAM used include:



Nonvitamin, nonmineral, natural products (17.7%)

Most common: fish oil/omega 3/DHA, glucosamine, echinacea, flaxseed oil, ginseng  
Deep breathing exercises (12.7%); Meditation (9.4%); Chiropractic or osteopathic manipulation (8.6%) ; Massage (8.3%); and Yoga (6.1%).

<http://www.cdc.gov/nchs/data/nhsr/nhsr012.pdf> (24-page report)

<http://nccam.nih.gov/news/2008/121008.htm> (Press Release)

**Patient Medication Information Quality** ... A study released 12/16/2008 by the FDA found that the printed consumer medication information (CMI) voluntarily provided with new prescriptions by retail pharmacies does not consistently provide easy-to-read, understandable information about the use and risks of medications. Compared to the first study in 2001 on average, using two drugs (lisinopril and metformin as the study drugs) there were a few improvements in the information content but the legibility component (inadequate) remained the same over the seven years. However, only 62% of medication information sheets contained at least 60% of recommended information. While there are just a few publishers that provide this information commercially, the individual pharmacies may also edit the documents which allowed for great variation among medication/information providers. The results of these studies may determine whether the FDA will mandate specific standards for publishing and providing this information. In 1995 the FDA was poised to do just that, but Congress intervened and blocked the FDA from doing so (largely based on pleadings from publishers and some pharmacy groups, all of which promised to meet the standards voluntarily by 2008.)



<http://www.fda.gov/cder/news/CMI/default.htm> (contains links to the full report [50 pages] and executive summary of the study)

### Reviews of Note ...

- Zuraw BL. Hereditary angioedema. *N Engl J Med.* 2008 Aug 28;359(9):1027-1036.
- Balani AR, Grendell JH. Drug-induced pancreatitis: Incidence, management and prevention. *Drug Safety.* 2008;31(10):823-837.

- Gartlehner G, Thieda P, Hansen RA, Gaynes BN, DeVeough-Geiss, Krebs EE, Lohr KN. Comparative risk for harms of second-generation antidepressants: A systematic review and meta-analysis. *Drug Safety*. 2008;31(10):851-865.
- Arain FA, Cooper LT Jr. Peripheral arterial disease: Diagnosis and management. *Mayo Clin Proc*. 2008 Aug;83(8):944-950.
- Cappell MS, ed. Common hepatic emergencies (10 articles). *Med Clin N Am*. 2008 Jul;92(4):717-992.

### **FROM THE LAY LITERATURE about medicine ...**

**This may keep you up at night ...** Capitalism at its best (or worst). As an extreme example, a relatively new drug, Provigil (modafinil) by Cephalon indicated for narcolepsy (and used for other sleep disorders) costs \$8.71 per tablet. This is 74% more than 4 years ago and the company intends to raise the price further. The patent on Provigil expires in 2012, so to protect/increase profits, the company intends to launch a new, longer-acting product, Nuvigil next year. Nuvigil will be priced slightly less than Provigil so physicians will be encouraged to switch patients to the new product (along with the companies claims of superiority). The company then expects most patients to be switched to Nuvigil by 2012 when Provigil's patent expires and generic competition ensues, while the patent on Nuvigil will expire in 2023. Modafinil has significant use off-label so consequently, insurance coverage is often lacking, making for a very expensive out-of-pocket prescription. See also the new drug above, just approved, TriLipix™ (fenofibric acid). It is a slight variation of fenofibrate (TriCor®) which loses patent protection in 2011.



Rockoff JD. How a drug maker tries to outwit generics. *Wall Street Journal*. 2008 Nov 17.

<http://online.wsj.com/article/SB122696875770635577.html?mod=djemHL> (subscription only)

Wang SS. Abbott's TriLipix approved by FDA. *Wall Street Journal*. 2008 Dec 16.

<http://online.wsj.com/article/SB122938838858708977.html?mod=djemHL> (subscription only)

### **AUBURN HSOP FACULTY and STUDENTS in the literature ...**

- Eiland LS, Salazar ML. Approved and unapproved hydrocodone-containing cough products: What do you need to know? *US Pharmacist*. 2008 Nov;33(11):43-49.
- Felkey BG, Fox BI. Adopt health information technology systems now! But in what sequence? *Hosp Pharm*. 2008 Dec;43(12):1014-1015.



#### **The last "dose" ...**

"At Christmas I no more desire a rose  
Than wish a snow in May's new-fangled mirth;  
But like of each thing that in season grows."  
- William Shakespeare [1564-1616]



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