

AU InforMed

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Key Inforbits

- Publication bias exposed!
- ACEIs vs. ARBs
- Cough/cold meds continue to be abused
- Dengue fever may be coming
- Ear candling a good idea?
- Gratitude

NEW DRUGS, and other related stuff ...

New Indication ... (1/14/2008) The FDA has approved Tysabri[®] (natalizumab; Biogen Idec of Cambridge, MA and Elan of Dublin, Ireland) for the treatment of moderate-to-severe Crohn's disease in patients with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn's disease therapies. Patients, prescribers, pharmacies, and infusion centers must be enrolled in a special restricted distribution program called the Crohn's Disease–Tysabri[®] Outreach Unified Commitment to Health (CD TOUCH) Prescribing Program. Tysabri[®] was approved by the FDA in June 2006 to treat relapsing forms of multiple sclerosis. Tysabri[®] carries a boxed warning for progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection that affects the brain and can lead to death or severe disability. Tysabri[®] is administered IV at infusion centers. For more information on Crohn's Disease, visit: Crohn's Disease–National Institute of Diabetes and Digestive and Kidney Diseases www.digestive.niddk.nih.gov/ddiseases/pubs/crohns/index.htm <http://www.fda.gov/bbs/topics/NEWS/2008/NEW01775.html> (FDA News)

MedWatch ... (1/17/2008) FDA informed consumers and healthcare professionals that the Agency has completed its review of information regarding the **safety of over-the-counter (OTC) cough and cold medicines** in children under 2 years of age and recommends that these drugs not be used to treat children in this age group because serious and potentially life-threatening side effects can occur. FDA's recommendation is based on both the review of the information the Agency received about serious side effects in children in the referenced age group and the discussion and recommendations made at the October 18 -19, 2007, public advisory committee meeting at which this issue was discussed. FDA has not completed its review about the safety of OTC cough and cold medicines in children 2 through 11 years of age. See the FDA Public Health Advisory for Agency recommendations regarding this issue. Read the complete 2008 MedWatch Safety Summary including a link to the FDA Public Health Advisory and a previous MedWatch alert dated January 12, 2007, regarding this issue. <http://www.fda.gov/medwatch/safety/2008/safety08.htm#cough>

BHRT Warning ... (1/9/2008) The FDA has warned seven pharmacy operations that the claims they make about the safety and effectiveness of their "bio-identical hormone replacement therapy," or "BHRT" products are unsupported by medical evidence, and are considered false and misleading by the agency. The pharmacy operations improperly claim that their drugs, which contain hormones such as estrogen, progesterone, and estriol (which is not a component of an

FDA-approved drug and has not been proven safe and effective for any use) are superior to FDA-approved menopausal hormone therapy drugs and prevent or treat serious diseases, including Alzheimer's disease, stroke, and various forms of cancer. Compounded drugs are not reviewed by the FDA for safety and effectiveness, and FDA encourages patients to use FDA-approved drugs whenever possible. The warning letters state that the pharmacy operations violate federal law by making false and misleading claims about their hormone therapy drugs. FDA also responded today to a citizen petition from Wyeth, Madison, NJ, asking FDA to take regulatory action against compounding pharmacy operations that produce compounded "BHRT" drugs. Other stakeholders, including health care providers and consumer groups, have also raised concerns about "BHRT" drugs.

FDA takes action against compounded menopause hormone therapy drugs. *FDA News*. 2008 Jan 9.

<http://www.fda.gov/bbs/topics/NEWS/2008/NEW01772.html>

Also, see the MedWatch Safety Summary information at:

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

MedWatch ... (1/15/2008) FDA advised healthcare professionals of serious adverse events associated with **unretrieved device fragments (UDFs)**. A UDF is a fragment of a medical device that has separated unintentionally and remains in the patient after a procedure. Patients may not be aware that this has occurred. The FDA Center for Devices and Radiological Health receives nearly 1000 adverse event reports each year related to UDFs. The adverse events reported included local tissue reaction, infection, perforation and obstruction of blood vessels, and death. Contributing factors may include biocompatibility of the device materials, location of the fragment, potential migration of the fragment, and patient anatomy. During MRI procedures, magnetic fields may cause metallic fragments to migrate, and radiofrequency fields may cause them to heat, causing internal tissue damage and/or burns. See the FDA Public Health Notification for the Agency's recommendations regarding this issue.

Read the complete 2008 MedWatch Safety Summary including a link to the FDA Public Health Notification regarding this issue at:

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

FROM THE MEDICAL LITERATURE ...

Publication bias exposed ... An article published today in the *New England Journal of Medicine* indicates significant publication bias for publishing positive articles versus those with a negative result, based on a review of 74 FDA-registered studies. These studies were of 12 antidepressants involving 12,564 patients. The authors compared the studies with published literature for actual publication and agreement of results of the study with what was actually published. The findings are not surprising. Of the 74 studies, 37 were viewed by the FDA as positive and all but one were published. Studies viewed by the FDA as negative numbered 34; one was published, 22 were not published, and 11 were published with a positive spin. Overall, based only on published studies it would appear that 94% of the trials were positive. Based on all the relevant studies, 51% were positive. While there are limitations to interpretation of these results, it would appear a disservice is being done.

Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. *N Engl J Med*. 2008 Jan 17;358(3):252-260.

ACEIs + ARBs better ... in a meta-analysis of 49 studies involving 6181 patients the combinations of angiotensin receptor blockers (ARBs) vs. placebo, angiotensin-converting

enzyme inhibitors (ACEIs), calcium-channel blockers or a combination of ACEI + ARB were assessed using measurements of proteinuria and microalbuminuria. Self reported limitations included that most studies were small and varied in quality; adverse effect reporting was inconsistent. Conclusions were that all single therapies were approximately equal. However, the combination of ACEIs and ARBs were more effective than either alone.

Kunz R, Friedrich C, Wolbers M, Mann JFE. Meta-analysis: Effect of monotherapy and combination therapy with inhibitors of the renin-angiotensin system on proteinuria in renal disease. *Ann Intern Med.* 2008 Jan 1;148(1):30-48.

OTC Cough/Cold Meds Abused ... The 2006 National Survey on Drug Use and Health (NSDUH) focused on persons aged 12 and older and their use of OTC cough or cold medications



during their lifetime and the past 12 months, for the purpose of “getting high.” Some results included that about 3.1 million (5.3%) in this group misused these agents and 1 million (1.7%) had done so in the past year. In the younger end of this spectrum, females were more likely to be the abusers, but switched to males in the older end. The three most common products misused were NyQuil[®] products, Coricidin[®] products and Robitussin[®] products. The presumed active drug sought is dextromethorphan, a cough suppressant which in high doses can produce hallucinations or dissociative experiences similar to phencyclidine and ketamine.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies. (January 10, 2008). *The NSDUH Report: Misuse of Over-the-Counter Cough and Cold Medications among Persons Aged 12 to 25.*

Rockville, MD. <http://oas.samhsa.gov/2k8/cough/cough.cfm>

Dengue fever a growing threat ... A recent report has raised the alarm of a possible invasion of dengue fever in the U.S. It is likened to the attention given (little) and quick-growing threat of West Nile virus a few years ago. It is emerging in the Texas-Mexico border areas and could spread to other temperate climates in the U.S. Symptoms resemble influenza and are largely mild and uncomplicated. However, some cases can progress to severe and fatal forms of dengue hemorrhagic fever and shock syndrome. Worldwide, dengue fever, spread by mosquitoes, is among the most important re-emerging infectious diseases with an estimated 50 to 100 million cases causing 500,000 hospitalizations and 22,000 deaths (mostly in children). It is caused by 4 related flaviviruses (same family as Yellow Fever, West Nile and Japanese Encephalitis viruses). A vaccine is in the works, but several challenges are delaying development. There is no specific drug therapy and treatment is largely symptomatic. *Topic submitted by Maggie Phillips.*

Morens DM, Fauci AS. Dengue and hemorrhagic fever: A potential threat to public health in the United States.

JAMA. 2008 Jan 10;299(2):214-216.

Reviews of Note ...

- O'Brien JM, Ali NA, Aberegg SK, Abraham E. Sepsis. *Am J Med.* 2007 Dec;120:1012-1022.
- Nestler JE. Metformin for the treatment of the polycystic ovary syndrome. *N Engl J Med.* 2008 Jan 3;358(1):47-54.
- Belmaker RH, Agam G. Mechanism of Disease: Major depressive disorder. *N Engl J Med.* 2008 Jan 3;358(1):55-68.
- Thakur RK, Natale A, eds. Atrial fibrillation. *Med Clin N Am.* 2008 Jan;92(1):1-264. (14 articles)

FROM THE LAY LITERATURE about medicine ...

Vocabulary ... Ear Candling ... a.k.a., coning, uses hollow candles made from a cylinder of fabric covered with wax. They are placed in the ear canal, lit, and burned down; it is intended to create a negative pressure in the ear that sucks out impurities (wax, fungus, etc). Scientific evidence, of which there is very little, implies the procedure is at best placebo and at worst, dangerous (candle wax in the ear, burns, punctured ear drum). Practitioners of course, tout its benefits (relaxing, alteration of “life energy”). Candles cost \$1-\$3 for home use, or \$25-\$75 if part of a spa experience. I’ll stick with the massage ...



Johannes L. Clearing wax buildup with a candle in the ear. *Wall Street Journal*. 2008 Jan 8; p. D2.

<http://online.wsj.com/article/SB119975907892973813.html?mod=djemHL> [subscription only]

Fibromyalgia ... real or manufactured ... The question of whether fibromyalgia is a real disease is still being hotly debated. Many in the medical profession, including the physician that defined fibromyalgia in 1990, think it is now more a function of marketing than disease. They also fret that giving these symptoms a name legitimizes what otherwise would be vague complaints of chronic pain. Considering that the typical fibromyalgia patient does not respond to standard analgesics clouds the issue and has stimulated research into drugs such as pregabalin that act via other mechanisms, yet unknown. Depending if you are a detractor or advocate, the approval of Lyrica® (pregabalin) last summer for fibromyalgia has either worsened or improved the problem. Despite one’s perspective, one thing is certain, Lyrica® has real side effects. As the article is ended, referring to the pharmaceutical companies investigating and marketing these drugs, they are “going to make a fortune.”



Berenson A. Drug approved, is disease real? *New York Times*. 2008 Jan 14.

<http://www.nytimes.com/2008/01/14/health/14pain.html? r=1&oref=slogin&ref=health&pagewanted=print>

NEW RESOURCES in the DILRC ...

- Baxter K, ed. *Stockley’s Drug Interactions*. 8th ed. London: The Pharmaceutical Press, 2008.
- Pichler WJ. *Drug Hypersensitivity*. Basel: Karger, 2007.
- Bartlett JD, Jaanus SD, eds. *Clinical Ocular Pharmacology*. 5th ed. St. Louis: Butterworth Heinemann Elsevier, 2008.
- Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, eds. *Williams Textbook of Endocrinology*. 11th ed. Philadelphia: Saunders Elsevier, 2008.
- *Directory of Residencies, Fellowships, and Graduate Programs 2008*. Lenexa, KS: American College of Clinical Pharmacy, 2008.



The last “dose” ...

Gratitude is the sign of noble souls.

~Aesop [~550 B.C.]

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