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Key Inforbits

- 2 new drugs
- MedWatches
- NEW electronic labels coming from FDA
- Tamiflu® stretching exercises
- An NSAID makes it worse?!
- National Diabetes Month

NEW DRUGS, and other related stuff …

New Drug … The FDA approved **nelarabine (Arranon®** by GlaxoSmithKline) on October 28, 2005. Its labeled indications are for treatment of T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma that has not responded or has relapsed after treatment with at least two chemotherapy regimens. Nelarabine is a prodrug of 9-β-*D*-arabinofuranosylguanine (ara-G) and carries a Black Box Warning for severe neurological events including severe somnolence, seizures and peripheral neuropathy. It is available as a 250 mg vial.
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Overview&DrugName=ARRANON (FDA web site)
http://www.gsk.com/index.htm (GlaxoSmithKline web site with press release)

New Drug … The FDA approved **deferasirox (Exjade®** by Novartis) on November 9, 2005. It is the first once-daily oral iron chelator. Deferasirox is indicated for the treatment of chronic iron overload due to blood transfusions in adults and children ≥2 years of age. It is the only iron chelator administered as a drink (the tablets are dispersed in a glass of orange juice, apple juice or water). The current standard of care is a subcutaneous infusion of 8 to 12 hours per night, for five to seven nights a week for as long as the patient continues to receive blood transfusions or has excess iron within the body. Deferasirox was approved under FDA's accelerated approval program, and it also received Orphan Drug Designation.
http://www.fda.gov/bbs/topics/news/2005/NEW01258.html (FDA News)
http://www.novartis.com/ (Novartis press release)

MedWatch … Ligand Pharmaceuticals Inc. and FDA notified healthcare professionals of revisions to Boxed Warning, Warnings, Precautions, Clinical Pharmacology, and Dosage and Administration sections of the prescribing information to highlight and strengthen the warning that patients should not consume alcohol while taking Avinza® (extended release morphine). Additionally, patients must not use prescription or non-prescription medications containing alcohol while on Avinza® therapy. This ranks up there with "Don't eat yellow snow."
Read the complete MedWatch 2005 Safety Summary, including links to the Dear Healthcare Professional letter and revised label, at:
http://www.fda.gov/medwatch/safety/2005/safety05.htm#Avinza

MedWatch … The FDA notified healthcare professionals of the potential for life-threatening falsely elevated glucose readings in patients who have received parenteral products containing maltose or galactose, or oral xylose, and are subsequently tested using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) based glucose monitoring systems. There have been reports of the inappropriate administration of insulin and consequent life-threatening/fatal hypoglycemia in response to erroneous test results obtained from patients receiving parenteral products containing maltose. Cases of true hypoglycemia can go untreated if the hypoglycemic state is masked by false elevation of glucose readings. A preliminary listing of U.S. products that may cause glucose test interference is provided. Read the complete MedWatch 2005 Safety Summary, including links to the FDA Notices, at:
http://www.fda.gov/medwatch/safety/2005/safety05.htm#maltose

FROM THE MEDICAL LITERATURE …

Electronic labels … The FDA, on November 2, 2005, began requiring drug manufacturers to submit prescription drug label information to FDA in a new electronic format called a structured product labeling (SPL) format that provides accurate, up-to-date drug information using standardized medical terminology in a readable, accessible format. This electronic format will allow healthcare providers and the general public to more easily access the product information found in the FDA-approved package inserts ("labels") for all approved medicines in the U.S. These new electronic product labels will be the key element and primary source of medication information for "**DailyMed,**" a new interagency online health information clearinghouse that will provide the most up-to-date medication information free to all, accessed through the National Library of Medicine at http://dailymed.nlm.nih.gov. In the future, this product information will also be provided through facts@fda.gov. The **DailyMed** site is up and running, but is very sparsely populated. Updated product labels will be posted on the site within one business day of an approval action by FDA or submission to FDA of a product label change that does not require prior approval. Within a year, product labels for most approved Rx medications will be posted.
FDA. FDA announces the used of new electronic drug labels to help better inform the public and improve patient safety. FDA News 2005 Nov 2;P05-80.
http://www.fda.gov/bbs/topics/NEWS/2005/NEW01252.html

Probenecid to stretch the world Tamiflu® supply?? … A recent article published in *Nature* claims probenecid could stretch the world supply of Tamiflu® (oseltamivir). With the avian flu pandemic scare, countries are currently stock piling Tamiflu®, which is the WHO recommended antiflu medication.[1] The information is based on Roche's study that showed probenecid increased the Cmax and AUC of oseltamivir 2-fold and 2.5-fold, respectively.[3] According to an article in *Nature* the dose of Tamiflu® could be cut in half when given with probenecid. A problem is that Tamiflu® comes in a 75mg CAPSULE, and capsules cannot be cut in half. Tamiflu® also comes in a suspension, but countries have already stockpiled a large number of capsules. David Fedson, former director of Aventis Pasteur, commented that a capsule containing both Tamiflu® and probenecid should be developed, but that would take time.[1] At this time, adding probenecid to oseltamivir to stretch the supply is not practical.
Submitted by Audrey Davie, Pharm.D. Candidate
1. Butler D. Wartime tactic doubles power of scarce bird-flu drug, Use of common drug could stretch world stocks of Tamiflu. *Nature*. 2005; 438(7064): 6.
2. He G, Massarella J, Ward P. Clinical pharmacokinetics of the prodrug oseltamivir and its active metabolite Ro 64-0802. *Clin Pharmacokinet*. 1999; 37(6): 471- 84.

3. Hill G, Cihlar T, Oo C, Ho ES, Prior K, et al. The anti-influenza drug oseltamivir exhibits low potential to induce pharmacokinetic drug interactions via renal secretion—correlation of in vivo and in vitro studies. *Drug Metab Dispos*. 2002; 30(1): 13-9.

Diclofenac worsens osteoarthritis??... A recent study found that subjects who used diclofenac long term (>180 days) had a 2.4-fold increase in risk of progression of osteoarthritis (OA) of the hip, and a 3.2-fold increased risk of knee OA progression compared to subjects who took other NSAIDs and those who used diclofenac for less time. Standard radiographs were taken of the hip and knee at baseline and follow-up (mean interval = 6.6 years). Disease progression was defined as an increase in score on a standard assessment tool, or need for joint replacement. The authors concluded that diclofenac may induce accelerated radiographic progression of hip and knee OA. Whether this occurs due to an actual deleterious effect of diclofenac on joint cartilage or because pain relief leads to increased load on the affected joint(s) is unclear.
Reijman M, Bierma-Zeinstra SMA, Pols HAP, Koes BW, Stricker BHC, Hazes JMW. Is there an association between the use of different types of nonsteroidal antiinflammatory drugs and radiologic progression of osteoarthritis? The Rotterdam Study. *Arthritis Rheum*. 2005 Oct;52(10):3137-42.

Montelukast may be beneficial in cystic fibrosis… A small (N=26) randomized, placebo-controlled, double-blind crossover study compared montelukast to placebo in 6-18 year-old patients with cystic fibrosis (CF) to evaluate the anti-inflammatory effect, if any, of montelukast. Patients continued their regular treatment and were given montelukast or placebo in addition. Pulmonary function tests and serum and sputum inflammatory markers were significantly improved in the montelukast treatment compared to placebo. Montelukast may provide measurable anti-inflammatory effects in patients with cystic fibrosis.
Stelmach I, Korzeniewska A, Stelmach W, Maiak P, Grzelewski T, Jerzynska J. Effects of montelukast treatment on clinical and inflammatory variables in patients with cystic fibrosis. *Ann Allergy Asthma Immunol.* 2005;95:372-80.

Reviews of Note …

- McHughes M, Timmermann BN. A review of the use of CAM therapy and the sources of accurate and reliable information. *J Manag Care Pharm* 2005 Oct;11(8):695-703.
- Waosko PM, Solondz DK, Phillips RS, Schachter SC, Eisenberg DM. Lack of herbal supplement characterization in published randomized controlled trials. *Am J Med* 2005 Oct;118(10):1087-93.
- CDC. Controlling tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005 Nov 4;54(RR-12):1-81. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm

FROM THE LAY LITERATURE about medicine …

DEA driving the bus … A short article concerning legislation passed last year, and up for renewal this year that gives the Drug Enforcement Administration (DEA) the power to approve or deny a controlled substance for marketing. This in essence, overrides the FDA approval. Most healthcare professionals are skeptical at best and the DEA appears unapologetic.
Kaufman M. DEA is opposed on painkiller approval. *Washington Post.com* 2005 Nov 4; p. A10.

Medicare Part D, a new wrinkle … In addition to insurance, Medicare, etc, pharmaceutical companies have various programs which can supply drugs to patients for reduced

or no cost. Now, according to conflicting stories, these charity programs may be discontinued or be unavailable to patients choosing a Medicare Part D plan. There seems to be some discrepancy as to who will be eligible, with the government and the industry pointing fingers at each other. However, the federal government has followed up and issued a "special advisory bulletin" on how companies could legally continue to offer prescription assistance to certain Part D enrollees.

Saul S. Another choice for elderly: Charity or Medicare? *NY Times.com* 2005 Nov 7.
http://www.nytimes.com/2005/11/07/business/07drug.html (New York Times, free with registration)
http://www.oig.hhs.gov/fraud/docs/alertsandbulletins/2005/PAPAdvisoryBlletinFinal-Final.pdf (advisory bulletin)

Warning from maker of contraceptive patch … Ortho McNeil, manufacturer of the Ortho Evra birth control patch, announced on November 10, 2005 that women who use the patch are exposed to higher levels of estrogen than previously thought. The warning came four months after reports that women die and have blood clots three times more often with the patch than with oral contraceptives. Women using the patch are exposed to about 60% more estrogen than those who take oral contraceptives because although the patch contains the same amount of estrogen as "the pill", more estrogen is absorbed through the skin with the patch formulation. In addition, the patch delivers estrogen continuously, whereas the pill provides intermittent exposure to the hormone. Higher estrogen levels are linked to blood clots and other serious side effects. Lawsuits have been filed and the FDA is investigating the matter further.

Associated Press. Warning issued about birth control patch 2005 Nov 10.
http://www.cnn.com/2005/HEALTH/11/10/patch.warning.ap.ap/index.html (CNN)
http://www.orthoevra.com/ (OrthoEvra web site by Ortho McNeil)

The last "dose" …

National Diabetes Awareness Month November 2005

In 2005, an estimated 20.8 million persons in the United States, approximately 7% of the population, have diabetes; however, only 14.6 million are diagnosed.[1] Persons with diabetes have a risk for premature death approximately twice that of persons of similar ages without diabetes. In 2002, diabetes was the 6th leading cause of death in the U.S., with associated costs approximating $132 billion.

November is National Diabetes Awareness Month. Additional information about diabetes is available from CDC at http://www.cdc.gov/diabetes and from other organizations such as the American Diabetes Association http://www.diabetes.org/home.jsp .

1. CDC. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2005. Atlanta, GA: US Department of Health and Human Services, CDC; 2005. Available at http://www.cdc.gov/diabetes/pubs/factsheet05.htm.