

AU InforMed

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Key Inforbits

- New drug: etravirine (Intelence™)
- Heparins: 2 MedWatch reports
- ADA: Clinical Practice Recommendations
- New life expectancy estimates
- Fibromyalgia - rebuttal
- The mother of all virtues ...

NEW DRUGS, and other related stuff ...

New Drug ... (1/18/2008) The FDA has approved **etravirine (Intelence™)**, distributed by Tibotec Therapeutics, a division of Ortho Biotech Products, L.P.) tablets for the treatment of HIV infection in adults who have failed treatment with other antiretrovirals. Etravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that helps to block an enzyme which HIV needs to multiply. It received a priority review by the FDA. The most common adverse events reported were rash and nausea. In the overall development program for etravirine, rare cases of serious skin reactions such as Stevens-Johnson syndrome and erythema multiforme were reported. The long-term effects of etravirine are not known, and its safety and effectiveness in children ages 16 years and younger and in pregnant women, has not been studied.

[FDA and its work in HIV/AIDS](#)

<http://www.fda.gov/bbs/topics/NEWS/2008/NEW01783.html>

MedWatch ... (1/16/2008) The FDA notified healthcare professionals and patients about cases where children and adults have died when they were mistakenly given **Edetate Disodium instead of Edetate Calcium Disodium** (Calcium Disodium Versenate) or when Edetate Disodium was used for "chelation therapies" and other uses that are not approved by the FDA. Edetate Disodium was approved as an emergency treatment for certain patients with hypercalcemia or certain patients with heart rhythm problems as a result of digitalis toxicity. Edetate Calcium Disodium was approved to reduce dangerously high blood lead levels (severe lead poisoning). The two drugs have very similar names and are commonly referred to only as EDTA and therefore are easily mistaken for each other. Edetate Disodium and Edetate Calcium Disodium works by binding with heavy metals or minerals in the body allowing them to be passed out of the body through the urine. Read the FDA Public Health Advisory and Questions and Answers for important safety considerations.

Read the complete 2008 MedWatch Safety Summary including a link to the FDA Public Health Advisory and Questions and Answers at:

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

MedWatch ... (1/19/2008) The FDA modified the prescribing information for the **Ortho Evra Contraceptive Transdermal (Skin) Patch** to include the results of a new epidemiology study that found that users of the birth control patch were at **higher risk of developing serious blood clots**, also known as venous thromboembolism (VTE), than women using birth control pills. The label changes are based on a study conducted by the Boston Collaborative Drug Surveillance

Program on behalf of Johnson and Johnson. These findings support an earlier study that also said women in this group were at higher risk for VTE. The FDA believes that Ortho Evra is a safe and effective method of contraception when used according to the labeling, which recommends that women with concerns or risk factors for serious blood clots talk with their health care provider about using Ortho Evra versus other contraceptive options.

Read the complete 2008 MedWatch Safety Summary, including a link to the FDA News Release, at: <http://www.fda.gov/medwatch/safety/2008/safety08.htm#orthoevrapatch>

MedWatch ... (1/18/2008) AM2 PAT, Inc., announced a **nationwide recall** of all lots of both heparin and saline pre-filled flushes. These products are distributed under two brand names, Sierra Pre-Filled Inc and B. Braun. The products are sold in 3 ml and 5 ml sizes for heparin and 3 ml, 5 ml, and 10 ml sizes for normal saline. One lot of heparin IV flush syringes (1003-02, Lot 070926H) was contaminated with *Serratia marcescens* which has resulted in patient infections. This type of bacterial infection could present a serious adverse health consequence that could lead to life-threatening injuries and/or death. User facilities and consumers should stop using the product immediately, quarantine remaining inventory, and return the product to their distributor. Read the complete 2008 MedWatch Safety Summary including a link to the Manufacturer's Recall Notice regarding this issue at:

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

MedWatch ... (1/18/2008) Baxter Healthcare and the FDA announced a **voluntary recall of certain lots of Heparin** as a precaution due to an **increase in reports of adverse patient reactions** associated with these lots. Baxter is in the process of an in-depth investigation to determine the root cause of the reported reactions. Reported adverse events include abdominal pain, decreased blood pressure, burning sensation, chest pain, diarrhea, dizziness, drug ineffectiveness, dyspepsia, dyspnea, erythema, flushing, headache, hyperhidrosis, hypoesthesia, hypotension, increased lacrimation, loss of consciousness, malaise, nausea, pallor, palpitations, paresthesia, pharyngeal edema, restlessness, vomiting/retching, stomach discomfort, tachycardia, thirst, trismus, and unresponsiveness to stimuli. There have been no reports involving fatality. See the recall notice for a list of affected lots.

Read the complete 2008 MedWatch Safety Summary including a link to the firm's recall notice, at: <http://www.fda.gov/medwatch/safety/2008/safety08.htm#HeparinInj>

MedWatch ... (1/23/2008) Bayer and the FDA announced the market withdrawal of the current liquid formulation of Leukine. The product was withdrawn because of an upward trend in spontaneous reports of adverse reactions, including syncope, which are temporally correlated with a change in the formulation of liquid Leukine to include edetate disodium (EDTA). The same has not been observed with the use of lyophilized Leukine. Healthcare professionals should immediately stop using liquid Leukine and return unused vials to the manufacturer.

Read the complete MedWatch 2008 Safety Summary and Dear Healthcare Professional Letter at: <http://www.fda.gov/medwatch/safety/2008/safety08.htm#Leukine>

FROM THE MEDICAL LITERATURE ...

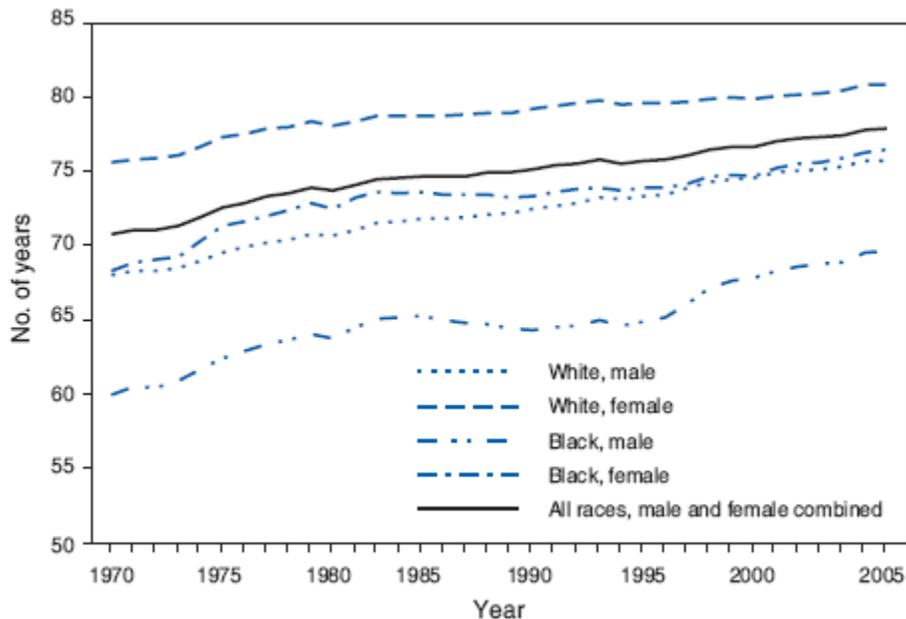
Clinical Practice Recommendations 2008 ... from the American Diabetes Association. There have been numerous revisions and additions to the “Standards of Medical Care in Diabetes. These are addressed under the broad topics of Diabetes Care, Prevention and Management of Diabetes Complications, Diabetes Care in Specific Populations, and



Diabetes Care in Specific Settings. The Clinical Practice Recommendations are issued annually in January.

Hirsch IR, Chair of the Professional Practice Committee. American Diabetes Association: Clinical Practice Recommendations 2008. *Diabetes Care*. 2008 Jan;31(Suppl 1):S1-S110.

Life Expectancy at Birth, by Race* and Sex - United States, 1970-2005



* Races include non-Hispanics and Hispanics.

Life expectancy at birth reached a record high of 77.9 years in 2005 for the total U.S. population. QuickStats: Life Expectancy at Birth, by Race and Sex - United States, 1970-2005. *MMWR*. 2008 Jan 4;56(51):1347. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5651a7.htm>

Reviews of Note ...

- Donahue KE, Gartlehner G, Jonas DE, Lux LJ, Thieda P, Jonas BL, et al. Systematic review: Comparative effectiveness and harms of disease-modifying medications for rheumatoid arthritis. *Ann Intern Med*. 2008 Jan 15;148(2):124-134.
- Gardiner P, Phillips R, Shaughnessy AF. Herbal and dietary supplement-drug interactions in patients with chronic illnesses. *Am Fam Physician*. 2008;77(1):73-78.
- Matchar DB, McCrory DC, Orlando LA, Patel MR, Patel UD, Patwardhan MB, et al. Systematic review: Comparative effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers for treating essential hypertension. *Ann Intern Med*. 2008 Jan 1;148(1):16-29.
- Gur S, Kadowitz PJ, Hellstrom WJG. Guide to drug therapy for lower urinary tract symptoms in patients with benign prostatic obstruction: Implications for sexual dysfunction. *Drugs*. 2008;68(2):209-229.
- Hatzimouratidis K, Hatzichristou DG. Looking to the future for erectile dysfunction therapies. *Drugs*. 2008;68(2):231-250.

Update ...

Opinion ... Fibromyalgia is a disease ... In response to: Fibromyalgia ... real or manufactured. *AU InforMed* 2008 Jan 17;6(2):8). Fibromyalgia (FM) is a chronic pain disorder affecting between 5% to 7% of people in the U.S.; it impacts both the patients' mental and physical health.¹ Although the exact pathology is not understood, most researchers believe that dysfunction within the central nervous system leads to abnormal processing of sensory function which is compounded by dysfunction in the autonomic nervous system. Simply stated, the disorder is a syndrome of pain magnification, "peripheral sensitization" in which normal stimuli like touch or temperature change may evoke a pain response. Several chemical changes may explain this increased sensitivity.² In FM, the central nervous system is also sensitized; this may result in a much smaller sensory input causing a severe pain response.³ Many patients with fibromyalgia experience neuroendocrine pathology as well that affect cortisol levels and alter ACTH response.⁴ Also, the serotonin system is poorly responsive contributing to less deep sleep and may promote pain transmissions in the descending cord.⁵

The article referenced in the previous *AU InforMed*, questions the legitimacy of FM. It is legitimate. The pathophysiology involves a very complex pain state with many neurochemical interactions. Monotherapy, based on one mechanism of action, will not significantly improve the patient's condition; combination therapies are needed. This leads to frustration for prescriber and patient. Patients should have realistic expectations; medications should be expected to improve pain and/or symptom scores by 2-3 points at most. Multidisciplinary care involving pain medications, physical/occupational therapy, exercise and other non pharmacologic interventions are also required to manage chronic pain states. These disorders should be approached in much the same manner that we would approach heart disease or diabetes with coordinated care to improve outcomes. *Karen F. Marlowe, Pharm.D., BCPS, DAAPM, Assistant Dean, Auburn University Harrison School of Pharmacy, Mobile, AL*

¹ Clayton AH, West SG. Combination therapy in Fibromyalgia. *Curr Pharmaceut Design*. 2006; 12:11-16.

² Staud R. Biology and therapy of fibromyalgia: pain in fibromyalgia syndrome. *Arth ResTher*. 2006; 8:208-215.

³ Ozgocmen S, Ozyurt H, Sogut S, Akyol O. Current concepts in the pathophysiology of fibromyalgia: the potential role of oxidative stress and nitric oxide. *Rheumatol Int*. 2006;26: 585-597.

⁴ Adler G, Kinsley K, Hurwitz S, Mossey C, Goldenberg D. Reduced hypothalamic-pituitary and sympathoadrenal responses to hypoglycemia in women with fibromyalgia syndrome. *Am J Med*. 1999; 106: 534-543.

⁵ Staud R and Rodriguez ME. Mechanisms of disease: pain in fibromyalgia syndrome. *Nature*. 2006; 2: 90-98.



The last "dose" ...

A thankful heart is not only the greatest virtue,
but the parent of all the other virtues.

~Marcus Tullius Cicero, Roman philosopher and orator [106 BC - 43 BC]



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