



NSU College of Pharmacy
Drug Information & Resources Center
N e w s l e t t e r

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Question of the Day

What is the generic name of the newly approved non-stimulant drug for Attention Deficit Disorder and why was its name switched from tomoxetine?

In the News

From the FDA

FDA PLACES TEMPORARY HALT ON GENE THERAPY TRIALS USING RETROVIRAL VECTORS IN BLOOD STEM CELLS

<http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01190.html>

In a precautionary measure, the Food and Drug Administration (FDA) has placed on "clinical hold" all active gene therapy trials using retroviral vectors to insert genes into blood stem cells. FDA took this action after it learned that a second child treated in a French gene therapy trial has developed a leukemia-like condition. Both this child, and another who had developed a similar condition last August, had been successfully treated by gene therapy for X-linked severe combined immunodeficiency disease (X-SCID), also known as "bubble baby syndrome." Infants with X-SCID have a gene defect that leads to a complete lack of white blood cells that can fight infection. Without treatment, they die from complications of infectious diseases during the first year of life. The only treatment for this condition is a bone marrow transplant. In early results of the French study in which a normal gene is inserted into blood stem cells of patients with X-SCID, nine of the 11 children had promising results and could leave the hospital and lead relatively normal lives. After notification of the first case last year, FDA identified the three U.S. gene therapy studies that most closely resembled the French trial and stopped enrollment of human subjects in those trials. They remain on clinical hold, a condition which FDA can impose when adverse events or other safety questions arise during a clinical

study. FDA's continuing review of adverse event reports from all U.S. studies involving retroviral vectors has to date found no evidence of leukemia caused by the gene therapy. Moreover, the agency has to consider the potential risks of any experimental therapy within the context of the disease it may treat - in this case a devastating disease in children. FDA's action includes a temporary hold on the enrollment of new patients in a subset of gene therapy trials that involve the use of retroviruses to insert new genes in blood stem cells, irrespective of the disease condition. The temporary hold reflects FDA's appreciation that some of these trials involve patient populations and gene therapy products that may be appropriate to continue after they are updated to reflect this new risk information. FDA will consider and evaluate specific requests for clinical indications for fatal or life-threatening disorders for which there are no viable alternative treatments. In all cases, sponsors will need to inform treated and new subjects of the two adverse events, and will need to have a plan to actively monitor subjects for leukemia like events. FDA continues to review the data from the adverse event in France, as well as the risks and potential benefits of all ongoing gene therapy trials, and will continue to work closely with the National Institute of Health's Office of Biotechnology Activities to oversee gene therapy studies in the U.S. The agency expects to hold an advisory committee meeting late next month to discuss the new adverse event in particular and retroviral gene therapy in general.

FDA PUBLISHES FINAL RULE TO REQUIRE LABELING ABOUT ANTIBIOTIC RESISTANCE

<http://www.fda.gov/bbs/topics/NEWS/2003/NEW00869.html>

FDA today announced that a final rule outlining new labeling regulations designed to help reduce the development of drug-resistant bacterial strains is on display at the Federal Register. This final rule is aimed at reducing the inappropriate prescription of antibiotics to children and adults for common ailments such as ear infections and chronic coughs. Antibiotics are often prescribed to young children who have symptoms of ear pain or pressure sometimes accompanied by a slight fever even when the cause of the symptoms may be viral opposed to bacterial. The danger associated with prescribing antibiotics to children with viral infections is that it can hasten the development of bacterial strains that are resistant to that antibiotic. Moreover, these children may pass these antibiotic resistant bacteria on to others, making treatment of their illnesses even more complicated. In older adults, the use of antibiotics to treat chronic coughs when sputum thickens is a common example of the over prescription of antibiotics. This thickening is commonly due to a viral infection, not a true bacterial infection such as bronchitis. Many of these patients would get better without antibiotic treatment. The new rule applies to all systemically absorbed human

antibacterial drugs and requires statements in several places in the physician labeling advising that these drugs should be used only to treat infections that are believed to be caused by bacteria. The rule also requires a statement in the labeling encouraging physicians to counsel their patients about the proper use of these drugs and the importance of taking them exactly as directed. This is part of ongoing efforts at FDA to encourage the development of new antimicrobials while preserving the usefulness of already existing ones.

"Antibacterial resistance is a serious and growing public health problem in the United States and worldwide," said FDA Commissioner, Mark McClellan, M.D., Ph.D. "Without effective antibiotic drugs, common infections, that were once easily treated, can create a serious health threat to children and adults alike." Many bacterial species, including the species that cause pneumonia and other respiratory tract infections, meningitis, and sexually transmitted diseases, are becoming increasingly resistant to the antibacterial drugs used to treat them. Several bacterial species have developed strains that are resistant to every approved antibiotic. Adoption of the rule represents the achievement of one of the objectives of the Public Health Action Plan To Combat Antimicrobial Resistance, a joint initiative of FDA, the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH). According to the CDC, half of the 100 million prescriptions a year written by office-based physicians in the United States are unnecessary because they are prescribed for the common cold and other viral infections, against which antibiotics are not active. Unnecessary use of antibiotics in hospitals is also reportedly common. An electronic version of the final rule can be found at <http://www.fda.gov/OHRMS/DOCKETS/98fr/00n-1463-nfr00001.pdf>. More information about antibiotic resistance can also be found on FDA's website at www.fda.gov/oc/opacom/hottopics/anti_resist.html.

FDA APPROVES FIRST BIOLOGIC THERAPY FOR PSORIASIS

<http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01194.html>

FDA today announced the approval of Amevive (alefacept), an injected medication that treats adults with moderate to severe plaque psoriasis. Plaque psoriasis is the most common form of psoriasis, a chronic relapsing disease of the skin that is characterized by scaling and inflammation. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, psoriasis affects between 1 and 2 percent of the United States population, or as many as 5.5 million people. Psoriasis primarily affects adults. People with psoriasis may suffer discomfort, including pain and itching, restricted motion in their joints, and emotional distress. Amevive treats plaque psoriasis through a unique immunosuppressive mechanism of action. Specifically, Amevive is believed to work by simultaneously blocking and reducing the cellular component of the immune system that is

thought to play a significant role in the disease process. FDA based its approval of Amevive on the results of two randomized, double-blind, placebo-controlled studies that enrolled a total of 1060 adults with chronic plaque psoriasis. Both of these studies showed that a significantly higher percentage of patients receiving Amevive responded to treatment compared to those receiving placebo based on pre- and post-treatment measurements of the percentage of affected skin surface area and severity of scaling and inflammation. In the approved labeling for Amevive, FDA is encouraging physicians to inform patients of the need for regular monitoring of white blood cell counts during therapy and that Amevive must be administered under the supervision of a physician. Moreover, the approved labeling states that patients should be informed that Amevive suppresses their immune system, which could increase their chances of developing an infection or malignancy. Therefore, patients should inform their physician promptly if they develop any signs of an infection or malignancy while undergoing a course of treatment with Amevive. Women of childbearing potential make up a considerable segment of the patient population affected by psoriasis. Because the effect of Amevive on pregnancy and fetal development, including immune system development, is not known, health care providers are encouraged to enroll patients taking Amevive who become pregnant into the manufacturer's pregnancy registry by calling 1-866-AMEVIVE (263-8483). Amevive is manufactured by Biogen, Inc., of Cambridge, Mass.

FDA APPROVES PYRIDOSTIGMINE BROMIDE AS PRETREATMENT AGAINST NERVE GAS

<http://www.fda.gov/bbs/topics/NEWS/2003/NEW00870.html>

The Food and Drug Administration (FDA) today announced approval of pyridostigmine bromide to increase survival after exposure to Soman "nerve gas" poisoning. The product is approved for combat use by United States military personnel. Pyridostigmine bromide is the first drug approved under a recently issued FDA rule (frequently referred to as the "animal efficacy rule") that allows use of animal data for evidence of the drug's effectiveness for certain conditions when the drug cannot be ethically or feasibly tested in humans. The "animal efficacy rule," which became effective on June 30, 2002, is an important component of FDA's efforts to make medical countermeasures available to treat or prevent the effects of biological and chemical agents. FDA Commissioner Mark B. McClellan, M.D., Ph.D., said, "Today's action will help protect American troops and others from nerve agent attacks." The "animal efficacy rule" enabled FDA to approve pyridostigmine bromide to increase survival from Soman poisoning despite the impossibility of ethically conducting human studies on the effectiveness of the drug. The nerve agent Soman causes loss of muscle control and death from respiratory failure. Evidence of the effectiveness of pyridostigmine bromide as a pretreatment for exposure to Soman was obtained

primarily from studies in monkeys and guinea pigs. This evidence shows that administration of the drug before exposure to Soman, together with atropine and pralidoxime given after exposure, increases survival. FDA believes that, based on the animal evidence of effectiveness, pyridostigmine bromide is likely to benefit humans exposed to Soman. The agency's safety assessment is based on long-term use of pyridostigmine bromide, first approved by FDA in 1955, to treat a neuromuscular disease called myasthenia gravis. The Department of the Army has submitted data from multiple controlled trials and uncontrolled clinical experience demonstrating pyridostigmine bromide is well-tolerated at the doses intended for military use. The dose used for myasthenia gravis is higher than the dose used for pretreatment to protect against Soman. To use this potentially lifesaving drug correctly, military personnel must carefully follow instructions and use the drug only under specific circumstances. For example, if U.S. troops faced the threat of exposure to Soman, they would be given instructions to take pyridostigmine bromide every 8 hours prior to the anticipated exposure. Soldiers will be warned that the drug is not effective and should not be taken at the time of, or after exposure to Soman. The troops are to use the drug in conjunction with other protective measures, including chemical protective masks and battle dress garments. Furthermore, effectiveness depends on the rapid use of the antidotes atropine and pralidoxime and discontinuation of pyridostigmine bromide at the first indication of nerve gas exposure. The Department of Defense plans to provide all military personnel with extensive training, prior to deployment, on the proper use of pyridostigmine bromide, as well as other methods used in the prevention and treatment of nerve agent poisoning.

A leaflet that explains the drug's use, benefits, and side effects will be provided to military personnel when the drug is distributed. The leaflet advises that pyridostigmine bromide should not be used by persons who have a history of bowel or bladder obstruction, or sensitivity to certain medicines used during surgery (like physostigmine). Side effects that may occur include stomach cramps, diarrhea, nausea, frequent urination, headaches, dizziness, shortness of breath, worsening of peptic ulcer, blurred vision, and watery eyes. The approved dose of pyridostigmine bromide for Soman pretreatment is one 30-mg. tablet every 8 hours. The leaflet states that pyridostigmine should be started at least several hours before exposure to Soman and emphasizes that it must be discontinued upon exposure to nerve gas, at which point the antidotes atropine and pralidoxime are given. During the Gulf War, FDA had allowed distribution of pyridostigmine bromide under its Investigational New Drug provisions because pretreatment with this drug had the potential to help save lives if nerve agents were used.

FDA Approves New Labels for Estrogen and Estrogen with Progestin Therapies for Postmenopausal Women Following Review of Women's Health Initiative Data
<http://www.fda.gov/bbs/topics/NEWS/2003/NEW00863.html>

FDA and Wyeth revised the prescribing information to include a boxed warning, which states that estrogens and estrogens plus progestin therapies should not be used for the prevention of cardiovascular disease. The boxed warning includes risk information from the Women's Health Initiative (WHI) study. The study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women during 5 years of treatment with conjugated equine estrogens (0.625 mg) combined with medroxyprogesterone acetate (2.5 mg) relative to placebo. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman. Read the MedWatch 2003 Safety Information Summary, including links to the "Dear healthcare Professional" letter, revised labels, and other supporting information, at:

<http://www.fda.gov/medwatch/SAFETY/2003/safety03.htm#prempr>

In the News

New Warning On Ephedra

<http://www.cbsnews.com/stories/2003/02/04/health/main539230.shtml>

Ephedra, an herb found in weight-loss and bodybuilding supplements, is unsafe even when taken in recommended doses and should be restricted, according to doctors who studied reports of bad reactions to the herb. U.S. poison control centers reported 1,178 adverse reactions to ephedra dietary supplements in 2001, said the study, which was to be posted on the Annals of Internal Medicine's Web site Tuesday and published in the journal next month. Ephedra accounted for 64 percent of all adverse reactions involving herbs, even though it is found in fewer than 1 percent of all herbal products sold. "It comes down to a risk-benefit ratio," said one of the report's authors, Dr. Stephen Bent of the San Francisco Veterans Affairs Medical Center. "The benefits for ephedra are not at all well established. It is a minimal benefit that goes away when you stop using the product. And the risks are really substantial." The study, based on data collected by the American Association of Poison Control Centers, is just the latest to question ephedra's safety. The Food and Drug Administration has reports of nearly 100 deaths of people who had taken the herb, a stimulant that can quicken a person's heart rate and cause their blood vessels to constrict. The American Medical Association has also advised people not to use ephedra, which has been banned by the International Olympic Committee, the National Football League and the National Collegiate Athletic Association. The Bush administration ordered a review of ephedra's safety in June. Wes Seigner, a lawyer for the Ephedra Education Council, a group funded by the supplement industry, insisted the herb can be used safely. He noted that the study compared ephedra only to other herbs, including such mild agents as ginseng

and St. John's wort, and not to medications used by people trying to lose weight. The study also didn't explore the seriousness of the reactions reported to poison centers, Seigner said. Some of the reported side effects could be as benign as a headache, he said. Seigner said that while the industry generally agrees that ephedra supplements should come with a mandatory warning label and shouldn't be marketed to children, banning them would be to ignore a potential treatment for obesity. Ephedra, also known by its Chinese name, Ma huang, was once widely used in the United States as a decongestant and asthma treatment. Doctors stopped prescribing it in the 1930s in favor of safer medications. Now it shows up most in "performance enhancing" dietary supplements marketed to athletes. An Alabama jury last year ordered supplement maker Metabolife International to pay \$4.1 million to four people who suffered strokes or heart attacks after taking an ephedra-based appetite suppressant. And the families of a dead 28-year-old bodybuilder in Las Vegas and a dead 27-year-old Marine Corps officer in Florida sued supplement-maker Twin Laboratories Inc. blaming the deaths on an ephedra supplement called "Ripped Fuel."

Safety concern as Cialis goes on sale over Internet

<http://news.moneycentral.msn.com/ticker/article.asp?Feed=RTR&Date=20030204&ID=2290077&Symbol=US:LLY>

Safety concerns were raised on Tuesday as Eli Lilly's new anti-impotence drug went on sale on the Internet, bypassing the usual European requirement for face-to-face consultation between patient and doctor. On the day the company launched its rival to Viagra in Britain, Internet sites were already advertising next-day deliveries of the drug Cialis for anyone prepared to pay up to 69 pounds (\$113) for four pills -- more than three times the price through the government-funded National Health Service. There has to be an element of danger involved when a patient can access prescription-only medicines without proper medical consultation," an Eli Lilly (LLY) spokesman said. Eli Lilly says the drug helps men get an erection when sexually stimulated, and is longer-lasting than Pfizer's (PFE) original breakthrough drug Viagra. The spokesman said Cialis should not be taken by men who have unstable angina or who have had a recent stroke or heart attack. Like other prescription-only medicines, Cialis should be prescribed only by doctors who see patients face-to-face and take a full medical history, he said. That appears to be a long way from the requirements of some Web sites. One British site proclaims: "No prior prescription is required, simply fill in our secure online order form! Your order will then be reviewed by a qualified UK doctor who will approve your medication if you are suitable!" All would-be buyers have to do is fill in an order form and a health questionnaire, which asks questions such as "Do you suffer from erectile failure? Are you a male? Do you have any cardiovascular disease problems? What medications do you take?" At the Cialis launch earlier on Tuesday, Eli

Lilly said it was restricting supplies to legitimate distributors. The spokesman did not explain how the Internet companies were already able to advertise the new product.

Dipentum (olsalazine sodium) Gets Relaunch

http://www.corporate-ir.net/ireye/ir_site.zhtml?ticker=CLL.uk&script=410&layout=0&item_id=369128

Celltech Pharmaceuticals, a leading biotechnology company and emerging leader in gastroenterology, announces the relaunch of Dipentum(R) (olsalazine sodium capsules) in the U.S. market. Dipentum is indicated for the maintenance of remission of ulcerative colitis (UC) in patients intolerant of sulfasalazine. "Ulcerative colitis is a chronic, debilitating condition that can be difficult to treat. Often, successful treatments in some patients may not be effective in others," said Dr. Dan Present, Clinical Professor of Gastroenterology, Mt. Sinai School of Medicine. "Patients need a drug that works for them and is easy to take. I've seen the benefit of taking a second look at effective therapies in the 5-ASA class that may have been overlooked in the past, and Dipentum may be such an example." Celltech licensed the U.S. marketing rights for Dipentum from Pharmacia Corporation in July 2002. The drug was approved by the United States Food and Drug Administration in 1990, although the product has not been actively supported or detailed to physicians since 1996. "We believe that Dipentum's benefits may have been ignored by physicians," said Simon Hatch, Director, Clinical Development, Celltech Group. "The 5-ASA class will remain a primary treatment for ulcerative colitis, yet the product may have been underutilized due to a lack of information. We believe that there may be a large population of ulcerative colitis patients who could benefit from its use." Dipentum combines proven efficacy with convenient dosing and tolerability. Clinical trials have proven that Dipentum (500 mg BID) is as effective as sulfasalazine (1000 mg BID) in maintaining remission of the disease (n= 164, n=322).(1,2) Dipentum targets the key action site of UC by delivering 98 to 99 percent of the drug's active ingredient directly to the colon to help reduce inflammation. Unlike some other drugs in the class, Dipentum's mechanism of action is not dependent on pH levels in the body. Patients find Dipentum convenient to take with a manageable side effect profile. Dipentum is taken in 2 capsules twice a day with meals, a patient-friendly lifestyle reminder that helps increase adherence. In two clinical trials (n=47, n=100), the tolerability of Dipentum (500 mg BID with meals) was similar to Asacol(R) (mesalamine) (1.2g per day in divided doses(3))(4,5). The most frequent adverse reaction to Dipentum is secretory diarrhea, which appears to be dose-related and may be reduced by administration with food. Dipentum does not contain sulfa, so there is no sulfa-related intolerance. Dipentum is contraindicated in patients with hypersensitivity to salicylates. In controlled clinical trials, the

incidence of adverse reactions with Dipentum therapy was comparable to placebo with the exception of diarrhea, abdominal pain, and rash/itching. The incidence of diarrhea in controlled studies was 11.1 percent with Dipentum vs. 6.7 percent with placebo. "Dipentum is a proven therapy that may benefit many ulcerative colitis patients," said Michael Yasick, Head, Gastroenterology Business Unit for Celltech. "With a new, dedicated gastroenterology sales force and proper marketing and educational support, our goal is to help healthcare professionals understand the true clinical profile of the drug, and help physicians and patients understand how to maximize its therapeutic benefits."

Lilly's Attention Deficit Strattera Drug Available

http://story.news.yahoo.com/news?tmpl=story2&cid=534&ncid=534&e=10&u=/ap/20030114/ap_on_he_me/lilly_new_drug

The first non-stimulant drug to treat attention deficit hyperactivity disorder has reached pharmacies nationwide, Eli Lilly and Co. said. Lilly, which won federal marketing approval for Strattera in November, said more than 46,000 pharmacies have stocked the drug and can begin filling prescriptions. Unlike Ritalin (news - web sites) and other drugs to treat ADHD, Strattera is not a stimulant - a factor Lilly hopes will make the medication more convenient to pick up from pharmacies. Because stimulants carry potential for abuse, pharmacies require written prescriptions and do not allow refills. Strattera, a capsule that can be taken once or twice a day, works by blocking reabsorption of a neurotransmitter that moves messages between brain cells. The U.S. Food and Drug Administration (news - web sites) approved Strattera for treatment of ADHD in children, adolescents and adults. ADHD is one of the most common behavioral disorders of childhood. Although not widely recognized in adults, experts estimate that 4 percent, or more than 8 million people, have the disorder, Lilly said. Symptoms include short attention span, impulsive behavior and difficulty focusing and sitting still. Industry analysts have said Strattera has strong growth potential and could offset recent setbacks for Lilly, including the 2001 loss of patent protection for the anti-depressant Prozac and manufacturing problems at Lilly plants in Indianapolis.

Asthmatics With Congestive Heart Failure Do Not Tolerate Carvedilol

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C960003FF3E?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

Patients with congestive heart failure combined with asthma tolerate carvedilol poorly, indicating that asthma is a contraindication to beta-blockade. In contrast, patients with congestive heart failure and chronic obstructive pulmonary disease tolerate carvedilol well with no

significant reversible airflow limitations. These were the findings of Dr E Kotlyar and colleagues of the cardiopulmonary Transplant Unit, St Vincent's Hospital, Sydney, New South Wales, Australia. The researchers enrolled 487 patients to receive open-label carvedilol. Thirty one patients had COPD and 12 had asthma. Sixty percent of the patients began carvedilol in the hospital, undergoing measurement of peak expiratory flow rates before and after dosing. Carvedilol was introduced safely in 84% of patients with COPD, with only one patient withdrawn from therapy for wheezing. In contrast, only 50% of patients with asthma tolerated carvedilol. Survival at 2.5 years was 72%. The researchers said, "Patients with CHF and COPD tolerated carvedilol well with no significant reversible airflow limitation, but patients with CHF and asthma tolerated carvedilol poorly." They added that the effect of carvedilol on left ventricular dimensions and function in patients with concomitant airway diseases was similar to that seen in the researchers' general group of patients. *J Heart Lung Transplant* 2002;21(12):1290-5. "Tolerability of carvedilol in patients with heart failure and concomitant chronic obstructive pulmonary disease or asthma."

N. Fla. Doctors Walk Out Over Insurance

<http://apnews1.iwon.com/article/20030206/D7P0ULH00.html>

Physicians in Florida closed their offices Wednesday to protest ballooning malpractice insurance rates, calling the situation a "ticking time bomb." The 300 doctors and health care workers who gathered outside Flagler Hospital in north Florida were the latest to protest skyrocketing premiums. In addition to Florida and New Jersey, Mississippi and West Virginia have also staged walkouts. Most are in favor of a \$250,000 cap on non-economic malpractice awards. President Bush and a Florida task force appointed by Gov. Jeb Bush have called for such a limit. "It's a ticking time bomb and if the Legislature doesn't act quickly, many people will be without health care because doctors won't be able to practice in this state, including me," said Dr. Miguel Machado, president of Flagler Hospital's medical staff. While some New Jersey doctors who have similarly protested will continue their job action. An American Medical Association study has identified 12 states in crises over medical malpractice: Florida, Georgia, Mississippi, Nevada, New Jersey, New York, Ohio, Oregon, Pennsylvania, Texas, Washington and West Virginia. The insurance companies blame rising premiums on excessive jury awards and meritless lawsuits.

Approvals From the FDA

FDA Approves Lamictal (Lamotrigine) For Children With Epilepsy

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CB4006858>

DE?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610

GlaxoSmithKline announced today that the U.S. Food and Drug Administration

(FDA) granted marketing clearance for Lamictal® (lamotrigine) Tablets as add-on therapy in partial seizures in children age two years old and up. This new indication expands the already-approved indications for adjunctive use in adults with partial seizures, and for the generalized seizures of Lennox-Gastaut Syndrome in children two years of age and older. Partial seizures are the most common type of epilepsy, affecting approximately 70% of all people with the illness. Partial seizures begin with abnormal electrical activity in a particular location in the brain. Specific effects of this kind of seizure depend on the part of the brain involved, and may include a dazed state, lip smacking, or jerking movements of certain body parts. According to the Epilepsy Foundation, epilepsy affects 2.3 million Americans of all ages, including approximately 300,000 American children under the age of 14. "FDA-approved therapies for children with epilepsy are limited, so any medication that can be clinically proven to effectively control seizures in this population with a favorable tolerability profile, provides an important new option to manage this condition," said Michael Duchowny, M.D., director of the Comprehensive Epilepsy Program at Miami Children's Hospital. "Lamictal is a welcome addition for children whose partial seizures are inadequately controlled on their existing therapy." Approval of Lamictal was based on a clinical study, published in the journal *Neurology*, demonstrating the efficacy of the drug as add-on therapy in pediatric patients who were still having frequent partial seizures (at least four per month) despite optimal doses of other antiepilepsy drugs (AEDs).

FDA Approves Finacea (Azelaic Acid) For Topical Treatment Of Rosacea
<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CA6006FAA-A1?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

Berlex Laboratories, Inc., the U.S. affiliate of Schering AG, Germany (NYSE: SHR), announced the U.S. Food and Drug Administration (FDA) has approved FinaceaT (azelaic acid) Gel 15 percent for the topical treatment of the inflammatory papules and pustules of mild to moderate rosacea. Finacea is the first new therapeutic option to be approved for the treatment of rosacea in more than a decade. Results of two multi-center, randomized, double blind, Phase III studies involving 664 patients showed that Finacea had a significantly greater efficacy than its vehicle in reducing the number of inflammatory papules and pustules associated with rosacea. Significant treatment effects were discernible as early as four weeks and progressive improvement continued to be shown week after week in the two 12-week studies. These findings were included in the New Drug Application (NDA) filed with the FDA in March 2002. Both protocols were identical. "Prior to the FDA approval of Finacea, Rosacea patients had waited more than a decade for a new treatment for this chronic condition. We now have the opportunity to address that unmet need" said Elise Klein, Vice President and General Manager, Dermatology, Berlex Laboratories, Inc. "The approval also is an

important milestone in Berlex Dermatology's commitment to building our product portfolio in the United States," she added

FDA Approves Lower Dose Flexeril (Cyclobenzaprine) For Treatment Of Muscle Spasm

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CC3005CC171?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

The U.S. Food and Drug Administration has approved Flexeril® (cyclobenzaprine HCl) 5 mg tablets, a new lower-dose, less-sedating version of the most frequently prescribed muscle relaxant, as an adjunct to rest and physical therapy for the relief of muscle spasm associated with acute, painful musculoskeletal conditions. McNeil Consumer & Specialty Pharmaceuticals will market the product in the United States. It is expected to be available in pharmacies in April. Until now, cyclobenzaprine HCl, the active ingredient in Flexeril 5 mg, has been available only in 10 mg tablets. Flexeril 10 mg is recognized as highly efficacious. In a clinical study versus placebo, each dosage strength of Flexeril demonstrated an ability to relieve muscle spasm pain, but patients taking Flexeril 5 mg reported significantly less drowsiness than patients taking the 10 mg tablet.

FDA Approves New Doses Of Immunosuppressant Azasan (Azathioprine)

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CC30055B557?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

aaiPharma Inc., (Nasdaq: AAIL) announced today that the U.S. Food and Drug Administration (FDA) has approved the Company's abbreviated new drug application (ANDA) for AzasanT (azathioprine) 75 mg and 100 mg tablets. Previously unavailable, these new 75 mg and 100 mg Azasan tablet strengths will provide physicians with more flexible dosage options and contribute to enhanced patient compliance. With this approval and the Company's currently marketed 50 mg dosage form, aaiPharma now offers the most comprehensive line of azathioprine dosage forms on the market today.

FDA Approves New Strength Of Mucinex (Guaifenesin) Tablet

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CB500592559?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

Adams Laboratories, Inc., a provider of specialty pharmaceuticals for respiratory care, today announced it has received approval from the U.S. Food and Drug Administration (FDA) for its new drug application (NDA) for the 1200 mg strength tablet of MucinexT , a single-entity, long-acting

guaifenesin product that will be available without a prescription. Mucinex provides the maximum therapeutic daily dosage of guaifenesin for adults by taking one 1200 mg tablet, or two 600 mg tablets, every 12 hours. It is indicated to help loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and make coughs more productive. The FDA approval of Mucinex 1200 mg is Adams Laboratories' second product approval in six months. In July of last year, the FDA approved the company's NDA for the Mucinex 600 mg tablet -- the first long-acting guaifenesin product to have an NDA approved by the FDA. As a result of the Durham-Humphrey Amendment of 1951 to the Federal Food, Drug, and Cosmetic Act which stipulates that a drug product cannot be marketed simultaneously both as a prescription and as a nonprescription product at the same strength and same dosage and for the same indication, the FDA issued warning letters on October 11, 2002, deeming all extended release guaifenesin tablets without an approved abbreviated new drug application (ANDA) or NDA illegal and misbranded.

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This Week in JAMA

Highlights of selected articles

<http://jama.ama-assn.org/issues/v289n5/ffull/jtw30001.html>

Original Contributions

Acetylcysteine for Prevention of Acute Deterioration of Renal Function

Following

Elective Coronary Angiography and Intervention: A Randomized Controlled Trial

<http://jama.ama-assn.org/issues/v289n5/abs/joc21724.html>

Health and Function of Patients With Untreated Idiopathic Scoliosis: A 50-Year

Natural History Study

<http://jama.ama-assn.org/issues/v289n5/abs/joc21444.html>

Evaluation of Safety Balls and Faceguards for Prevention of Injuries in Youth

Baseball

<http://jama.ama-assn.org/issues/v289n5/abs/joc10755.html>

Brief Report

Variation in Public and Private Supply of Pneumococcal Conjugate Vaccine During a Shortage

<http://jama.ama-assn.org/issues/v289n5/abs/jbr20398.html>

REVIEW

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FDA Orders Estrogen Safety Warnings: Agency Offers Guidance for HRT Use

<http://jama.ama-assn.org/issues/v289n5/ffull/jmn0205-3.html>

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<http://jama.ama-assn.org/issues/v289n5/rfull/jch30002-2.html>

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>From the Centers for Disease Control and Prevention

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Shell Eggs--United States, 1999-2001

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Blood Safety Monitoring Among Persons With Bleeding Disorders-- United States,

May 1998-June 2002

<http://jama.ama-assn.org/issues/v289n5/ffull/jwr0205-2.html>

Tobacco Use Among Middle and High School Students-- New Hampshire, 1995-2001

<http://jama.ama-assn.org/issues/v289n5/ffull/jwr0205-3.html>

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Peasant Spreading Manure

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<http://jama.ama-assn.org/issues/v289n5/ffull/jcs0205-1.html>

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MSJAMA

Full-text articles from the print version, plus Web specials.

<http://www.ama-assn.org/sci-pubs/msjama/index.htm>

Books, Journals, New Media

The Fever Trail: In Search of the Cure for Malaria (Honigsbaum)

<http://jama.ama-assn.org/issues/v289n5/ffull/jbk0205-1.html>

Evarts A. Graham: The Life, Lives, and Times of the Surgical Spirit of St. Louis

(Mueller)

The Academic Surgeon: An Autobiography (Hardy)

<http://jama.ama-assn.org/issues/v289n5/ffull/jbk0205-2.html>

The Health of Nations: Infectious Disease, Environmental Change, and Their Effects on National Security and Development (Price-Smith)

<http://jama.ama-assn.org/issues/v289n5/ffull/jbk0205-3.html>

Molecular Therapy: The Journal of the American Society of Gene Therapy (Verma, ed)

Gene Function and Disease (Doerfler, ed)

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Report says 100 Roma women have been forcibly sterilised in Slovakia

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Website of the Day

Sloan Kettering Integrated (Herbal) Medicine Website

<http://www.mskcc.org/mskcc/html/11570.cfm>

For evidence-based information on herbal products, including herbal-drug interactions, clinical efficacy (links to Pubmed), and references, Sloan Kettering has compiled a fairly complete and critical collection of monographs on 135 commonly used herbal products.

Answer of the Day

Atomoxetine (Strattera by Eli Lilly), a selective norepinephrine reuptake inhibitor used in the treatment of attention deficit hyperactivity disorder, was originally named tomoxetine, but changed to avoid potential confusion with tamoxifen. To confound the issue, both products are similarly dosed and are available in a similar dosage.
