



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 drug originates from the foxglove plant and was the topic of a published source in 1785 by William Withering?

## In the News

### **FDA Approves New Cholesterol Drug**

<http://apnews1.iwon.com/article/20021028/D7MURT400.html>

Merck & Co. and Schering-Plough Corp. said regulators have approved their new type of cholesterol-lowering drug called Zetia, a medicine expected to eventually reach blockbuster status because it significantly boosts the effectiveness of existing treatments. The news of Zetia's approval by the Food and Drug Administration on Friday sent shares of both companies higher on Monday. Zetia is viewed as life preserver for Schering-Plough, which is expected to lose crucial revenues when its top-selling allergy drug Claritin faces generic and over-the-counter competition later this year.

There are about 13 million patients taking statins, the most common class of drug used to treat cholesterol. Approximately, 60 percent of those patients don't reach their desired cholesterol level. When Zetia is added to patients' regimen, studies showed 72 percent of patients reached their goal. On average, Zetia added to an ongoing statin treatment provided a 25 percent additional reduction in cholesterol, compared with a 4 percent reduction for placebo. Zetia can be taken alone, but only reduces cholesterol by about 18 percent, while statins alone lower it by about 40 percent. "We are at the dawn of new treatment paradigm" for lowering cholesterol, said Dr. Enrico Veltri, vice president of clinical research at the Schering-Plough Research Institute. Zetia should hit the market in a few weeks, the companies said. Yet, analysts say Zetia won't be profitable for at least two years and will require an exceptionally aggressive marketing push to overcome concerns about its cost and change the prescribing patterns of doctors, who don't want to load patients up with too many pills. The fundamental question is whether adding Zetia is clinically and economically better than just increasing the dose of the statin, which doesn't increase the cost but can increase side effects. The wholesale cost for a 30-day supply of Zetia is \$57.90. That will be on top

of the statin's cost. Merck's statin, Zocor, has a wholesale price of \$105.81 for a 30-day supply regardless of the dose. Executives from the MerckSchering-Plough Pharmaceuticals LLC joint venture said doubling the dose of a statin will only reduce cholesterol by 6 percent. But Bernstein Research analyst Richard Evans said that 6 percent reduction will be enough to get 75 percent of patients who haven't met their goal to achieve it.

Robert A. McMahon, vice president and general manager of the joint venture, said Zetia's price represents a good value and the drug is a tremendous opportunity for patients who aren't achieving complete success on statins alone. The companies are testing a pill that combines Zetia and Zocor that they plan to file with the FDA next year. If approved, the drug will breathe new life into Zocor, which is expected to lose patent protection in 2006. Sales of such a drug combination could reach \$3.4 billion by 2006, said Prudential Financial analyst Tim Anderson, who said sales of Zetia alone could reach \$1.1 billion by then. But those sales won't come easy. Anderson said it will take a "paradigm shift" to convince doctors to prescribe two pills instead of one to treat cholesterol. "It is going to take a heck of a lot of marketing spending to get this drug prescribed," Anderson said. "They are going to be pushing up hill." Lehman Brothers analyst Tony Butler said Zetia provides an alternative for doctors who don't want to increase patients' statin dose for safety reasons.

Higher levels of statins have been linked to rhabdomyolysis, a life threatening condition which destroys muscle cells and releases them into the blood stream. Last year, Bayer AG withdrew its statin, Baycol, because it was linked more than 30 deaths. Clinical trials show that Zetia didn't increase the risk of rhabdomyolysis. Zetia works by inhibiting cholesterol absorption in the intestine. Statins prevent cholesterol production in the liver. Statins are the most widely prescribed drugs in the United States, with total sales increasing 18 percent to \$12.3 billion for the 12 months ended Aug 2, according to the research firm IMS Health. The number of prescriptions rose 8 percent to 115 million in the same period. In previous years, both numbers had been growing more than 20 percent. The slowdown comes even after federal guidelines widened the number of people who should be taking statins grew to 36 million. Evans attributes the muted growth to rising drug copayments which are causing some patients to rethink their medical choices. Cost-conscious consumers may be less willing to spring for another prescription, Evans said. Zetia was discovered by Schering-Plough and developed with Merck. Both will promote the drug. Initially, Schering will receive a slightly higher share of the profits but that will change as time progresses and the combination Zetia/Zocor pill is introduced. "Who is John Galt?" Schering shares jumped 78 cents, or nearly 4 percent, to close at \$21.13 on the New York Stock Exchange. Merck stock advanced \$1.32 a share, or 2.5 percent, to close at \$54.23.

### **Pfizer Agrees to Pay to Settle Suit**

<http://apnews1.iwon.com/article/20021028/D7MUR9GG0.html>

Pfizer Inc. said Monday it will pay \$49 million to settle Justice Department allegations that it overcharged the Medicaid program for its cholesterol-lowering drug Lipitor. The settlement will be split between the federal government and the states because Medicaid is a jointly funded program. The charges stemmed from a whistle-blower lawsuit alleging that educational grants by Parke-Davis to the Ochsner Health Plan in 1999 constituted a rebate that lowered the price of the drug for the Louisiana insurer. Federal law requires drug companies to offer the Medicaid program the lowest price paid by any purchaser. The suit was brought in 1999 by John David Foster, who worked for Parke-Davis at the time. Pfizer acquired Parke-Davis through its 2000 takeover of Warner-Lambert. The settlement represents more than double the \$21 million the Medicaid program was overcharged, according to Foster's lawyer, Joel Androphy. Foster will receive about \$6 million for his role in the settlement, Androphy said. As part of the settlement, the government will not pursue allegations made in the same lawsuit involving payments to five other health plans and two pharmacy benefits managers. Pfizer also said it had entered into a corporate integrity agreement with the Office of the Inspector General of the U.S. Department of Health and Human Services to make sure its policies comply with pricing regulations. Pfizer spokeswoman Mariann Caprino said the company already has a compliance program, but the new arrangement would require enhancing some procedures. She declined to elaborate. "The settlement was a legacy issue. We are pleased it is over," Caprino said. The settlement comes at a time when virtually all major pharmaceutical companies are the subject of government investigations and private lawsuits, most of which center on practices that allegedly led to higher prices. For example, attorneys general in 47 states are investigating whether Pfizer illegally marketed the epilepsy drug Neurontin to physicians. Pfizer shares fell 34 cents to close at \$31.56 on the New York Stock Exchange.

### **Drug Store Machines OK for Testing Blood Pressure**

[http://www.reuters.com/news\\_article.jhtml?type=search&StoryID=1650684](http://www.reuters.com/news_article.jhtml?type=search&StoryID=1650684)

Electronic blood pressure-monitoring machines found in drugstores, supermarkets and other locations are reasonably accurate, provided people take three readings about a minute apart, a researcher reported here at the medical meeting Canadian Cardiovascular Congress 2002. Patients typically insert their arm into the device for a quick update on their blood pressure, said Merle Wilson, a nurse in the Cardiovascular Risk Factor Reduction Unit at the University of Saskatchewan, Saskatoon. Wilson tested the devices in 16 pharmacies across the province, using four volunteers. Two of the four volunteers were being treated for high blood pressure while the other two had normal blood pressure. The researcher measured blood pressure in one arm with a traditional blood pressure cuff, and in the other arm with the electronic machines. The investigator found that the machines in drug stores tended to overestimate blood pressure by about 8

millimeters of mercury for systolic blood pressure (the top number in a blood pressure reading), and by about 4 millimeters of mercury for diastolic blood pressure (the lower number in a blood pressure reading).

The good news is that the devices did not underestimate blood pressure.

None of the drug store blood pressure monitoring machines "underestimated systolic blood pressure and only one underestimated diastolic blood pressure by more than 5 millimeters of mercury," she said. "We conclude that if a patient's blood pressure is at goal in the drug store, it is unlikely to be above goal in the physician's office." For people with high blood pressure without diabetes or kidney disease, blood pressure is considered to be "at goal" when it is less than 140/90 millimeters of mercury. Wilson also told Reuters Health that the accuracy of drug store blood pressure machines can be improved if people take three readings between 30 to 60 seconds apart, the last reading being the most accurate.

People should also try to sit quietly for a few moments before taking their blood pressure and refrain from drinking coffee or smoking for at least 30 minutes before using the machine, she said.

### **Regulatory Request Delays OTC Prilosec Till Q4/03**

<http://news.ft.com/servlet/ContentServer?pagename=FT.com/StoryFT/FullStory&c=StoryFT&cid=1035872840163>

A potential cheap version of Prilosec, the blockbuster heartburn medicine, is to be delayed after Procter & Gamble said it did not expect US regulatory approval of its over-the-counter product until late next year. Postponement of the final approval stems from the US Food and Drug Administration's request for a study to make sure consumers understood that the treatment was long-acting and once-per-day. That study will take eight more weeks and six months for regulatory review. The FDA has otherwise tentatively approved P&G's retail version. The US consumer products group owns the rights to over-the-counter sale of Prilosec, made and licensed by AstraZeneca, a UK pharmaceuticals company. Over-the-counter Prilosec would be the first available retail launch of the strong acid-blocking, proton-pump inhibitor drug class. The FDA move further delays the race to launch either an over-the-counter or prescription generic version of the one of the world's most prescribed medicines. AstraZeneca was hoping for a quick retail launch of Prilosec to gain as much revenue from the drug before generic rivals are launched. The damage to P&G is not great as it estimates sales of only \$200m-\$400m per year. An over-the-counter launch of Prilosec could damage generic competitors seeking to launch a cheaper prescription version, also delayed. A court ruling this month found Andrx, the generic group first in line to launch a version of Prilosec, in violation of AstraZeneca's patents. But that ruling could delay a generic launch until early 2004, as Andrx looks for options including a deal with Germany's Schwarz Pharmaceuticals, the only company found not to infringe Prilosec patents. AstraZeneca is focusing most of its attention on Nexium,

its new-generation ulcer treatment.

### **Heart Failure Drug Ups Death Risk in Women, Not Men**

[http://www.reuters.com/news\\_article.jhtml?type=search&StoryID=1658533](http://www.reuters.com/news_article.jhtml?type=search&StoryID=1658533)

Women with heart failure who take digoxin, a form of the drug digitalis, appear to have a higher risk of death than women who don't take the drug, according to a study released Wednesday. This does not appear to be true for men with heart failure. Women were found to have a 4.2% higher risk of dying during the study if they took digoxin, while the mortality risk for men was the same whether or not they took the drug, according to the study published in the October 31st issue of *The New England Journal of Medicine*. About 33% of women taking digoxin died compared with 28.9% of women taking an inactive placebo. After accounting for other factors that differed between men and women, Dr. Saif S. Rathore of the Yale University School of Medicine and colleagues found that digoxin increased a women's risk of death by about 23%. "Although digoxin appeared to have no clinically meaningful effect on mortality among men, we found that there was a suggestion of increased harm associated with digoxin use in women," said Rathore in a prepared statement. "This pattern persisted after we accounted for factors that differed between men and women taking digoxin and those who had been taking placebo," he added. Additional research should be done to confirm the findings, the authors say. For now, women with heart failure who are taking digoxin should talk with their doctor about whether they should continue the drug, they add. According to the report, women who took digoxin were less likely to be hospitalized than women taking a placebo, although "women may not consider the potential increased risk of death associated with digoxin therapy worth the small reduction in the risk of hospitalization," according to the report. The findings are based on a re-analysis of data previously collected as part of the Digitalis Investigation Group trial. Earlier findings showed that overall, patients who took digoxin spent less time in the hospital. The new analysis was not conducted in collaboration with those researchers. The study involved 302 clinics in the United States and Canada. It included 6,800 heart failure patients who came to the clinics between 1991 and 1993. The patients' average age was 64, and they were followed for about 3 years. All patients had heart failure, a seriously reduced ability to pump blood, often due to an underlying problem, such as heart disease. The patients, who had a normal heart rhythm and a wide range of heart-pumping capacities, were randomly assigned to receive either digoxin or an inactive placebo. Nearly all were also taking blood pressure drugs, including a diuretic (to reduce blood volume and the heart's workload) and angiotensin-converting enzyme (ACE) inhibitors, which help blood vessels relax. Digitalis is a drug extracted from the leaves of plants belonging to the foxglove family. Digoxin, a derivative of digitalis, is used widely for treating the heart's reduced pumping efficiency, which is the hallmark of heart failure. The

drug works by increasing the force of heart muscle contractions. With the aging of the population, heart failure has been on the rise in the United States, especially among older Americans. It currently affects about 4.8 million people, and causes more than 40,000 deaths annually. Of the 400,000 new cases diagnosed each year, about half die within five years. From The New England Journal of Medicine 2002;347:1403-1411.

### **New 'Zomig' Nasal Spray Provides Migraine Sufferers With Fastest Patient-Friendly Relief**

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/10-28-2002/0001829150&EDATE=>

A new, very fast acting formulation of the leading second-generation triptan, zolmitriptan, is now available allowing millions of European migraine sufferers to treat their debilitating and painful condition both rapidly and reliably. 'Zomig' Nasal Spray offers patients a highly effective, well-tolerated alternative to conventional tablets and sub-cutaneous injections according to migraine experts speaking at the European Federation of Neurological Societies (EFNS) meeting today. "The clinical trial data for Zomig Nasal Spray suggest that this new formulation offers patients and physicians a significant advance in migraine therapy", points out Professor Carl Dahlof from the Gothenburg Migraine Clinic in Sweden. "It is directly absorbed from the nasal passages and rapidly detected in the blood stream. This means that patients get their much-needed relief fast, starting 15 minutes after dosing. In addition, the data obtained in controlled clinical trials seems to penetrate into clinical practice." Oral triptan tablets may be effective and convenient for many migraine patients. However, a large number of migraineurs suffer from nausea and vomiting during attacks, making the oral route of administration less attractive. In addition, the onset of action with oral tablets is often too slow for those patients who require very fast pain relief. Subcutaneous injection is an alternative option, but many patients dislike injecting themselves or have a fear of needles. For the first time, 'Zomig' Nasal Spray offers a real alternative -- a patient-friendly (non-injection) triptan providing consistently effective relief within 15 minutes. "Migraine patients first and foremost want rapid, highly effective, reliable pain relief", says Dr Andrew Dowson, Director of King's Headache Services, King's College Hospital, London, UK. "The symptoms of migraine vary enormously and sufferers need a choice of treatment. Doctors need to take patients' needs and preferences into account when treating migraine and a range of formulations is required to ensure that patients get optimal therapy every time." Following administration of 'Zomig' Nasal Spray, uptake into the body begins at a high rate almost immediately.

Pharmacokinetic studies show that zolmitriptan is detectable in the plasma five minutes post-dose. At 10 minutes after intranasal dosing, 38% of the

maximum plasma concentration (C<sub>max</sub>) of zolmitriptan is already achieved. Such rapid absorption is predictive of a very fast onset of relief after administration of 'Zomig' Nasal Spray. Positron emission tomography (PET) data suggest that a large amount of the administered dose of 'Zomig' Nasal Spray is absorbed directly across the nasal mucosa, with the remainder passing down the oesophagus, being absorbed from the gastrointestinal tract. ZINC I, a multicentre, double-blind, double-dummy study, compared the efficacy and tolerability of 'Zomig' Nasal Spray to conventional 'Zomig' oral tablets (2.5 mg) and placebo for the treatment of moderate or severe migraine attacks in 1372 patients.<sup>(4)</sup> Headache response, defined as a reduction in headache intensity from severe or moderate at baseline to mild or none, was significantly greater with 'Zomig' Nasal Spray than with placebo as early as 15 minutes after dosing. A headache response was achieved two hours after taking 'Zomig' Nasal Spray in 70.3% of attacks with the 5 mg dose (p<0.001). Responses to 'Zomig' Nasal Spray were found to be consistent across multiple attacks. 'Zomig' Nasal Spray abolished migraine headache in significantly more attacks than placebo as early as 30 minutes after dosing. 'Zomig' Nasal Spray 5 mg was significantly more effective than the oral 2.5 mg 'Zomig' tablet 30 and 45 minutes after dosing. ZINC II, a double-blind, long-term extension of ZINC I involved 783 patients treating 10,507 migraine attacks over a year.<sup>(1,5)</sup> In addition to indicating that the nasal spray is remarkably well-tolerated, this follow-up study showed that the fast, high efficacy of 'Zomig' Nasal Spray 5mg was consistently maintained during the treatment of multiple migraine attacks over a long period.

### **Link Suggested in Hypertension and Painkillers**

<http://www.nytimes.com/2002/10/28/health/28PAIN.html?ex=1036811490&ei=1&en=5368157cad5b3dc7>

The pain relievers ibuprofen and acetaminophen, contained in scores of over-the-counter remedies, may increase the risk of high blood pressure, a study of women suggests. Skeptics say the connection needs more confirmation in better-designed studies, and the Harvard researchers who conducted the study do not recommend that people stop taking the medications. But the authors said their findings were plausible given what is known about how the drugs affect the body. The study, to be published in the Archives of Internal Medicine on Monday, involved 80,020 women ages 31 to 50 who participated in a nurses' health study and were not known to have high blood pressure at the outset. They were asked in 1995 about their use of painkillers. Information about high blood pressure was obtained from a survey two years later. In those two years, 1,650 participants developed high blood pressure. Women who reported taking acetaminophen 22 days a month or more were twice as likely to develop high blood pressure, or hypertension, as women who did not use the drug. Those who used nonsteroidal anti-inflammatory medicines, mostly ibuprofen, that frequently

were 86 percent more likely to develop hypertension than nonusers. Aspirin use did not appear to be associated with an increased risk. Acetaminophen is contained in Tylenol and ibuprofen is in Motrin, two of the most popular over-the-counter painkillers. While the relative risks sound high, the results suggest that the vast majority of women taking the medications will not develop high blood pressure, said Dr. William J. Elliott, an internal medicine and pharmacology specialist at Rush-Presbyterian-St. Luke's Medical Center in Chicago. Dr. Elliott, who was not involved in the research, also noted that the study lacked essential information on the doses participants used. Ibuprofen and similar drugs may raise blood pressure by blocking production of prostaglandins, hormone-like substances that can widen blood vessels and improve blood flow. The drugs also can increase sodium retention. Dr. Anthony Temple of McNeil Consumer and Specialty Products, the maker of Tylenol, Motrin and St. Joseph aspirin, said the study "does not show any cause and effect relationship." One author of the study, Dr. Gary Curhan of the School of Public Health at Harvard, said that because the drugs were so widely used, the possible connection merited further study.

### **First Long-Term Head to Head Study Shows Superiority of Reminyl(TM) Over Donepezil in Patients With Alzheimer's Disease**

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/10-29-2002/0001829771&EDATE=>

At the 6th Congress of the European Federation of Neurological Societies in Vienna, Shire Pharmaceuticals Group has today presented data with Janssen-Cilag Ltd which shows that over one year, Reminyl (galantamine) has a superior treatment profile compared to donepezil (Aricept (R)) when treating patients with Alzheimer's Disease (AD). This is the first one-year head to head study of the two drugs. Results of the long-term, rater-blinded, randomized study conducted in the UK show that in two assessments of AD patients, those treated with Reminyl had statistically superior scores on measures of cognition and attention compared to those treated with donepezil. Reminyl was shown to significantly improve a patient's attention within six weeks of commencing treatment, using a validated computerized test for assessing cognitive performance. These computerized assessments, by the independent company, Cognitive Drug Research (CDR), measure a patient's reaction times and showed that patients taking Reminyl significantly improved their choice reaction times (CRT) compared to donepezil patients after only six weeks of treatment. At 52 weeks, Reminyl patients' CRT had been maintained at baseline levels. Patients treated with donepezil had no significant changes in CRT throughout the study. The improvements in attention, as measured by the computerized tests for patients taking Reminyl, are thought to be due to its action on nicotinic receptors. "Reminyl is different to other acetylcholinesterase

inhibitors (AChEIs) because it increases the levels of acetylcholine by two separate mechanisms. As well as inhibiting acetylcholinesterase, it has also been shown to enhance activity of nicotinic receptors," says Dr Roger Bullock of the Kingshill Research Centre, Swindon. "Nicotinic receptors are known to be important in maintaining attention and concentration. These results demonstrate the importance of Reminyl's dual mode of action." Dr Bullock says: "Being able to improve a patient's ability to take part in family events by increasing their attention and concentration adds an important, but often neglected quality to the lives of both patients and their carers." Patients treated with Reminyl were also more likely to improve or maintain their level of dementia throughout the study compared with those patients taking donepezil, as measured by the MMSE (Mini Mental State Examination) assessment scale for AD. The MMSE, which measures cognition by testing functions such as memory, orientation and language, is the assessment scale recommended by the National Institute for Clinical Excellence (NICE) and the one that most clinicians use on a daily basis. At 13 and 26 weeks, the MMSE score for Reminyl was significantly improved compared with the baseline assessment. At 52 weeks, patients had been maintained at their baseline score. Patients treated with donepezil only saw significant improvement above baseline at the 13 week time point. At 26 weeks, their score had returned to baseline values, whilst after 52 weeks, patients treated with donepezil were statistically below their baseline scores. For those patients less severely affected by AD, (those who fitted the NICE criteria for treatment with AD drugs with a baseline MMSE score of 12-18 points), the results were even more favorable for Reminyl. Reminyl was significantly superior to donepezil at all time points measured throughout the 52 weeks study. Reminyl was comparable to donepezil in terms of safety and tolerability, with similar discontinuation rates during the study and similar numbers of patients continuing on therapy after the end of the study. The primary end point for the study was the Bristol Activities of Daily Living (BrADL) rating scale, which measures a patient's ability to function. Patients treated with Reminyl and donepezil performed equally well in this assessment. This study confirms that Reminyl treated patients demonstrate an early improvement in attention and sustained cognitive benefits.

### **Non Steroidal Anti-Inflammatories Decrease Risk Of Recurrent Myocardial Infarction In Patients Taking Aspirin**

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C6200>

6529FF?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249&abd=yes

Non steroidal anti-inflammatory drugs (NSAIDs) may reduce the risk of recurrent acute myocardial infarction (AMI), in patients taking low-dose aspirin, findings of a new study suggest. According to lead researcher, Dr. Marie Hudson, with McGill University Health Center, Montreal, Canada, NSAIDs might be expected to interfere with the effect of aspirin and

increase the risk of recurrent AMI. "But our overall data is reassuring especially for sporadic users," Dr. Hudson quoted. The researchers presented their findings here at the American College of Rheumatology 66th Annual meeting. To examine the interaction between low-dose aspirin and NSAIDs, the researchers conducted a population-based study of 28,881 patients aged 65 years of age and older., all of who were taking low dose aspirin (80 to 325 mg per day). The patients had had an AMI between January 1, 1992 and March 31, 1999, and they were followed for a period of one year after their index AMI. About 7 percent of participants had a recurrent AMI during follow-up. Overall, 21.7 percent were identified as non-aspirin NSAID users; the most commonly prescribed being diclofenac (6.98 percent), naproxen (6.09 percent), and ibuprofen (1.98 percent). Patients taking aspirin who were also taking NSAIDs were significantly less likely to experience recurrent AMI than those who took only aspirin, the researchers report. Overall, non-aspirin NSAID users were at a 23 percent decreased risk of having a recurrent AMI (95 percent CI 0.68-0.86). Individually, the adjusted odds ratio for naproxen was 0.84, diclofenac 0.75, ibuprofen 0.82, and acetaminophen 1.14. "The findings suggest no disadvantage in taking both aspirin and NSAIDs from the cardiac point of view," Dr. Hudson said," although she pointed out that the study did not look into other side effects, such as gastrointestinal complications. The researchers are now investigating the long-term effect of this combination as well as the effect of COX-2 inhibitors in low-dose aspirin users.

### **Linezolid Equivalent To Vancomycin In Treating Neonates, Children**

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C60006104CD?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249>

The antibiotic linezolid appears to be at least as effective as the gold standard treatment vancomycin treatment of various infections in children, according to a series of poster presentations. Reporting findings, doctors at the 40th annual meeting of the Infectious Diseases Society of America, said: ---Linezolid was better tolerated and as effective as vancomycin in the treatment of known or suspected resistant gram-positive infections in children from birth to 12 years of age. ---Linezolid proved as effective as vancomycin among neonates, including those children infected methicillin-resistant *Staphylococcus aureus* or methicillin resistant enterococci. ---Linezolid was at least as effective as vancomycin among children with nosocomial pneumonia caused by resistant bacteria -- and tended to alleviate symptoms faster than vancomycin. "It is important that we do these studies on children," said Sheldon Kaplan, MD, professor of pediatrics at the Baylor College of Medicine, Houston, Texas. "We feel very strongly that if you don't study a drug in pediatric settings you are not doing what is right for children. Children are not just little adults." He said the studies have shown that children metabolize linezolid more quickly than adults so they require a greater dose of the drug per kilogram than

adults. In his report, children whose parents completed a five-page informed consent document were randomized to receive either linezolid or vancomycin if the children had known or suspected nosocomial pneumonia, complicated skin or skin structure infections, bacteremia or other infections. Dr. Kaplan and colleagues from 59 institutions in the United States and Latin America randomized 215 patients to linezolid and 105 to vancomycin. Overall, the results were similar: in the intention to treat analysis 79.1 percent of linezolid patients versus 74.1 percent of vancomycin patients achieved a cure. Of those patients clinically evaluable, 89.3 percent of linezolid patients were clear of infection compared with 84.5 percent of the vancomycin patients; of the patients who underwent microbiological evaluation, 88.2 percent of linezolid patients and 87 percent of vancomycin patients were disease-free. Dr. Kaplan said those differences did not reach statistical significance. Drug-related discontinuations reached 6 percent among the vancomycin patients and was less than 1 percent among the linezolid patients, a difference that was significant, he said. In another study, Jaime Deville, MD, assistant clinical professor of pediatrics at the University of California and Los Angeles, said that among neonates, linezolid proved successful at clearing infections most related to line emplacement. He concurred that children are different in their reaction to drugs. With linezolid, he said, neonates are a lot like adults in metabolism of linezolid until their kidneys are developed, then they act like children. In some case dosing three times a day is necessary to maintain therapeutic levels of the medication. Dr. Deville enrolled 63 babies into his study -- 43 of whom were put on linezolid. In the intention to treat analysis, 77.5 percent of the linezolid babies were cures of their infections, compared with 61.1 percent of the vancomycin-treated children. Ma. Royo Morfin, MD, a pediatrician at Hospital Civil de Guadalajara in Mexico, enrolled 49 patients with nosocomial pneumonia to receive either linezolid or vancomycin. After three days on treatment one-third of the linezolid patients still had symptoms compared to 80 percent of vancomycin patients; after 10 days, 20 percent of linezolid patients still had symptoms compared with 33.3 percent of the vancomycin patients. Overall, Dr. Kaplan said, "Linezolid is an effective and well-tolerated empiric antibiotic therapy for known or suspected resistant gram-positive infections in children.

### **New Study Evaluates the Effectiveness of Valtrex? Caplets for Suppression of Genital Herpes in HIV-Infected Persons**

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C5D00739A34?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249>

Twice daily treatment with Valtrex? (valacyclovir HCl) caplets is effective in suppressing genital herpes recurrences in HIV-infected patients, according to data presented at the Infectious Diseases Society of America annual meeting. After six months, the proportion of patients

recurrence-free was 80 percent in those receiving Valtrex 500 mg twice daily, compared to only 38 percent of those receiving placebo. "Many people who are HIV-positive also suffer from genital herpes and will be pleased to know they can suppress their genital herpes outbreaks," said Timothy Schacker, M.D., Associate Professor of Medicine, University of Minnesota. "This is important information for people who have to deal with both genital herpes and HIV." In the study of 293 HIV-infected participants, those receiving Valtrex experienced a delay in the time to first genital herpes recurrence as well as a delay in the time to first oral herpes outbreak when compared to placebo. At the end of the six-month study period, researchers noted no change in HIV-1 RNA levels present in the blood for patients treated with either Valtrex or placebo. The randomized double-blind, placebo-controlled study evaluated 293 HIV-seropositive patients on anti-retroviral therapy for at least two months prior to randomization. 194 patients were randomized to Valtrex and 99 to placebo. Patients received either Valtrex 500 mg twice daily or placebo. The most common adverse events were headache, diarrhea, and respiratory tract infection, occurring with similar incidence in both groups when duration of follow-up was considered. There were no episodes of thrombotic microangiopathy. The study was sponsored by GlaxoSmithKline, maker of Valtrex<sup>®</sup> (valacyclovir HCl) caplets, one of the world's leading research-based pharmaceutical and health care companies.

### **FDA tells Biogen to stop misleading drug promotion**

<http://www.forbes.com/home/newswire/2002/10/30/rtr772413.html>

The U.S. Food and Drug Administration has told Biogen Inc. to stop publishing misleading promotions for its multiple sclerosis drug Avonex. In a letter dated Oct. 24 and posted on its Web site Wednesday the regulatory agency listed several examples of promotions to physicians and patients that it said violate federal regulations. Examples of the violations include a headline in a promotional brochure to doctors and patients stating that "Avonex delivers the highest rate of satisfaction -- 95 percent among patients," followed by a bar graph which the FDA says misrepresents the results of the survey. That's because of the 75 patients surveyed, only 60 percent said they were "very satisfied" with Avonex while 35 percent said they were "only somewhat satisfied." "The omission of these details is misleading to the reader," the FDA's letter said. "You should immediately cease any further dissemination of all advertising and promotional materials that contain these claims and similar presentations." Multiple sclerosis affects about 350,000 people in the United States. The company said it had responded to the agency. "We're in conversation with the FDA on this," said Tim Hunt, a Biogen spokesman. "We'll work with the FDA to ensure they're happy." The FDA admonition comes amid an increasingly fierce battle for dominance in the \$1.3 billion U.S. market for multiple sclerosis treatments. Avonex, which is Biogen's only marketed product, was

once by far the biggest-selling drug for the disease. Now its market share has slipped to just over 50 percent. In March, Europe's Serono SA launched a rival product, Rebif, which is making steady inroads into Biogen's territory. In response, Biogen, based in Cambridge, Massachusetts, has increased its marketing budget and become more aggressive in defending Avonex. Shortly after Rebif's launch, Biogen appealed to the FDA to prevent Serono from claiming Rebif is superior to Avonex. Biogen said the FDA had agreed to "take enforcement action" if Serono made broad claims of superiority. But the FDA denied Biogen's statement. Dan Troy, the agency's legal counsel, said through a spokeswoman that he was "not happy" about Biogen's public exploitation of a private phone conversation with the company. In its latest complaint, the FDA also took issue with the company's promotional statements that "Cognitive dysfunction is significantly correlated with brain atrophy," something that Biogen's clinical trials of the drug did not evaluate. The agency also criticized, among other statements, the company's exhortation to doctors to "Prescribe Therapy That is Strong Over The Long Term" with the subsequent statements "2 years, 4 years, and 5 years" implies efficacy beyond that approved in the drug's label. Multiple sclerosis begins with individual symptoms, such as numbness in limbs, and progresses until muscle spasms become constant and often disabling.

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## **Up the Pipeline**

TAP Pharmaceutical Products Inc. Submits New Drug Application for UPRIMA(R) (Apomorphine HCL Tablets) Sublingual for Treatment of Erectile Dysfunction

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/10-29-2002/0001830071&EDATE=>

TAP Pharmaceutical Products Inc. announced today that it has submitted a New Drug Application (NDA) with the U.S. Food and Drug Administration for UPRIMA(R) (apomorphine HCl tablets) sublingual for the treatment of erectile dysfunction (ED). The NDA includes data for 2 mg and 3 mg doses. UPRIMA is a tablet that is placed under the tongue and rapidly dissolves prior to intercourse. UPRIMA is the first in a new class of ED treatment with a mechanism that is thought to be centrally-acting, originating in the brain to help stimulate an erection. "When approved, we believe that UPRIMA will offer doctors and their patients an important new option for treating ED," says Xavier Frapaise, M.D., vice president of Research and Development at TAP. Erectile dysfunction is defined as the inability to attain and maintain an erection sufficient for intercourse. ED is a common condition estimated to affect about 30 million men in the U.S. including those with partial ED. "UPRIMA has been studied extensively in men and, when approved, will provide an alternative for men affected by ED," says John Mulhall, M.D., director of Sexual Medicine, Department of Urology, Weill Medical

College of Cornell University and UPRIMA clinical investigator. In clinical studies, UPRIMA was administered to men with organic (physical cause), psychogenic (psychological cause) or mixed etiology (combination of physical and psychological causes) erectile dysfunction. UPRIMA was evaluated for its ability to produce an erection firm enough for intercourse in men with mild, moderate or severe ED. The most common side effects of UPRIMA were nausea, headache and dizziness, which were mild to moderate in most cases. TAP's parent companies, Abbott Laboratories and Takeda Chemical Industries, Ltd., currently market apomorphine (as UPRIMA and IXENSE(R), respectively) in ex-U.S. markets.

Bayer Corporation Submits Additional New Drug Application For Once-Daily Cipro(R) XR

[http://biz.yahoo.com/prnews/021030/nyw036\\_1.html](http://biz.yahoo.com/prnews/021030/nyw036_1.html)

Bayer Corporation, Pharmaceutical Division today announced it has submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) to market Cipro XR (ciprofloxacin extended-release) in a once-daily modified release tablet formulation for the treatment of complicated urinary tract infections (UTIs). This new formulation of ciprofloxacin has been submitted for once-daily dosing for a course of 7-14 days. Cipro XR was developed using a bilayer matrix of the active ingredient ciprofloxacin. This new formulation enables an initial rapid release of ciprofloxacin, which distributes to the serum and tissues within hours. This is followed by a second extended release of the active ingredient over 24 hours. In March 2002, Bayer submitted an NDA to the Food and Drug Administration to market Cipro XR (ciprofloxacin extended-release tablets) as a once-daily, three-day treatment for uncomplicated urinary tract infections. "This NDA submission for Cipro XR in complicated urinary tract infections represents Bayer's commitment to developing and bringing to market innovative therapies," said Dr. Lawrence Posner, Senior Vice President and Worldwide Head, Regulatory Affairs, Bayer Corporation. "We asked physicians what was most important to their UTI patients and once-a-day dosing was a common response," he added.

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Website of the Day

Pharma Lexicon

<http://www.pharma-lexicon.com/>

This site provides has the world's largest online database of pharmaceutical and medical abbreviations - over 56,000 and growing with links to PubMed. It also provides a searchable database for accessing Pharmaceutical Companies, lists of hospitals, schools of pharmacy, journals, health ministries and more. For those of you who don't know what DUMB stands for...

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Answer of the Day

Digoxin.