



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 antipsychotic was discovered in 1958 in the research institute of Dr. Wander of Switzerland and first marketed in Europe in 1972?

hint...think agranulocytosis

In the News

US Voters Send Mixed Messages on Health Initiatives

http://story.news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=16&u=/nm/20021106/hl_nm/election_initiatives_dc

Voters in three US states approved ballot measures aimed at cracking down on tobacco use, but three other measures to lower penalties for marijuana use were defeated. And voters in Oregon overwhelmingly rejected a proposal to create the nation's first "universal coverage" plan for all state residents, after opponents spent more than \$1 million to defeat it. Probably the most sweeping health initiative passed was in Florida, where voters amended the state constitution to ban smoking in most workplaces, including restaurants. The only exemptions would be for stand-alone bars, tobacco shops and designated hotel guest rooms. The measure garnered more than 70% support. "This is a huge public health victory for every Floridian and everyone who visits Florida," said John L. Kirkwood, president of the American Lung Association. Voters in Arizona approved an initiative to raise the tobacco tax to \$1.18 per pack, making it one of the nation's highest. Funds raised would help underwrite the state's trauma system. And in Montana, voters ordered the state to spend at least 32% of funds from the 1998 settlement with tobacco makers on smoking cessation and control programs. In Michigan, however, voters defeated an effort to direct 90% of the state's settlement funds to research and healthcare, while in Missouri, an effort to raise tobacco taxes was trailing narrowly as of Wednesday morning. Voters were more of one mind when it came to weakening penalties for possession of marijuana, even for medical use. Ballot questions in Nevada, Arizona and Ohio all failed, after opponents, including the White House, argued they would undermine the war on illegal drugs. And voters in

Oregon defeated two high-profile ballot questions. One would have created a "universal healthcare system" within the state to be run by a government-appointed board. It went down after opponents, including the health insurance industry, raised and spent a reported \$1.2 million to defeat it. "Who is John Galt?" Voters also rejected a proposal that would have required explicit labeling of genetically modified food.

Drug Co., Fla. Make Pact to Thwart OxyContin Abuse

http://www.reuters.com/news_article.jhtml?type=search&StoryID=1670082

Florida's top consumer watchdog on Friday announced an unusual agreement with Purdue Pharma LP aimed at preventing abuse of the prescription painkiller OxyContin. The pact--the first of its kind in the nation--ends an investigation launched by the Florida Attorney General's Office in 2001 into Purdue Pharma's marketing of the oft-abused narcotic. No charges were ever filed as a result of the probe, a state spokeswoman said. Under the agreement, Purdue Pharma will provide up to \$2 million in funding to the state for development of a software program capable of tracking a patient's prescribing history in real time. The program would be designed to monitor prescriptions for all controlled substances. Florida's state legislature must authorize the system's implementation. The Stamford, Connecticut-based drugmaker also agreed to provide \$150,000 for a series of programs around the state to help train Florida law enforcement officials on prescription drug abuse and diversion. Attorney General Bob Butterworth said the agreement represents a novel partnership among members of the medical community, state law enforcement and the pharmaceutical company. "It was not lawyer-driven," he told reporters attending a Friday afternoon briefing in Fort Lauderdale. "We've not been compelled to do this," added Howard Udell, Purdue Pharma's executive vice president and general counsel. "We're doing this because we care about our patients," he said. "The abuse of that drug is hurting patients, and doctors are afraid to prescribe it because they're afraid they'll be scammed." Udell noted that states have been hampered in their efforts to rid the streets of illegal drug traffic "simply because they don't have the money" to develop and implement sophisticated computed technology. Florida has agreed to make the system it develops available, at no cost, to any other state that requests it. "The state of Florida will be first, the state of Florida will be the leader, but it will be available to all states," he said. Purdue Pharma has been the target of more than a dozen lawsuits charging that it failed to adequately warn consumers about OxyContin's potential for abuse or take other action to prevent its illegal use. The company has maintained its innocence and remains resolved to defend against the charges.

"Over-prescribing and also under-prescribing has been a major problem in Florida," said Dr. Zachariah P. Zachariah, chairman of the Florida Board of Medicine. Giving doctors access to a real-time software program will allow them to check whether a patient has had another prescription for OxyContin,

even if the prescription was written by another doctor just "moments before," he said. It's the "best way we can avoid over-prescribing and also under-prescribing." Broward County (Florida) Sheriff Ken Jenne added that Purdue Pharma's investment in the state would help doctors identify abusers and help law enforcement officials fight illegal street sales of prescription narcotics. "What Purdue Pharma is going to do for us is to give us the training to enforce the law," he said.

Drug [ReoPro] doesn't cut heart patient risk

http://abcnews.go.com/wire/Living/ap20021106_848.html

A promising anti-clotting drug does not improve hospitalized heart attack patients' chances of surviving a year when it is added to the standard treatment, a study found. The disappointing results came in a follow-up international study of 16,588 patients who received intravenous doses of a standard clot-busting medicine with or without the newer drug, abciximab, or ReoPro. ReoPro, known as a "super aspirin," helps keep blood particles called platelets from sticking together and forming a clot that can cause a heart attack. The older drug, reteplase, attacks different substances in blood clots. ReoPro's primary use is for patients undergoing angioplasty, a technique that opens clogged blood vessels. In a study reported last year and funded by ReoPro's U.S. marketers Centocor and Eli Lilly, researchers tried using it in a different way, combining it with a reduced dose of reteplase in patients who had just suffered a heart attack. The combination treatment lowered patients' 30-day risk of a repeat heart attack by 30 percent. But in the follow-up study, the death rates after a year were identical nearly 700 patients in both groups died, or about 8 percent in each. The findings were published in Wednesday's Journal of the American Medical Association. The researchers said the reasons for the findings are unclear. Dr. A. Michael Lincoff of Cleveland Clinic, who helped conduct the study, said ReoPro may still be a useful drug because it can reduce the short-term risk of repeat heart attacks and has other heart benefits.

Statin Drugs Show M.S. Promise

<http://apnews1.iwon.com/article/20021106/D7N4ME102.html>

California scientists say a statin drug already used by millions of heart patients to lower harmful cholesterol levels has improved and even reversed some of the debilitating symptoms of multiple sclerosis in mice. And while that does not prove the drug would work for humans, another study using a second statin drug on a small number of MS patients is showing early positive signs. "The animal data is quite striking," said the senior author of the mouse study, neurologist Scott S. Zamvil of the University of California-San Francisco. "We didn't have any conflicting data." Other researchers said the California results, if they can be repeated in humans, could help launch statins into the exceptional class of drugs like aspirin

that were developed to treat one type of illness but turn out to offer a range of medical benefits. They said the drugs' anti-inflammatory effects might also be effective in treating rheumatoid arthritis, juvenile diabetes and other autoimmune diseases in which the body mistakenly turns its biochemical guns on healthy tissue. Other trials suggest statins might protect against Alzheimer's, too. But scientists urged physicians and their patients not to rush to use statins to treat MS until the mice study finding is safely evaluated in humans, which could take several years. "Anyone who looks at an animal model as a suggestion for a drug's use in humans is mistaken," said Stephen Reingold, vice president for research at the National Multiple Sclerosis Society. Currently, the small clinical trial is evaluating simvastatin - sold as Zocor - on 32 MS patients in three states. Those results could be published next spring, researchers said. "There is accumulating data that would strongly suggest that statins should have a positive effect," said neurologist William R. Tyor of the Medical University of South Carolina in Charleston who is coordinating part of the human trial. "There may be unforeseen problems with administering statins to patients with MS, although admittedly this is unlikely," he said. MS is a degenerative disease of the central nervous system. High levels of one of the body's immune chemicals - gamma interferon - wrongly activate T-helper cells to mount an inflammatory attack on the myelin sheath that insulates nerve fibers. Accumulating scar tissue slows the transmission of nerve impulses and interrupts cell communication, leading to episodes of paralysis, tremors and blurry vision. The California study published in the current issue of the journal Nature was limited to high doses of atorvastatin, which is sold under the brand-name Lipitor. At UCSF and Stanford University, mice were bred to develop experimental autoimmune encephalomyelitis, or EAE, which mimics MS in lab animals. The mice were given doses of atorvastatin equal to 80 milligrams, the highest dosage approved for humans. Heart patients typically receive lower doses to reduce cholesterol. Among mice experiencing their first MS-like attack, Zamvil said high doses prevented the animals from developing permanent symptoms. Among animals that were suffering a relapse, the drug reversed emerging paralysis and restored mobility. Zamvil said statin therapy also reduced paralysis among a third group of animals that had developed chronic symptoms associated with late-stage MS. He said all of the mice treated with atorvastatin suffered less brain and spinal damage than expected. Zamvil said the drug appeared to reprogram the immune cells that attack myelin so they instead would produce anti-inflammatory agents and protect the nerve coatings. Current MS therapies include regular injections of synthetic beta interferon after an MS attack to counterbalance the gamma interferon overload. Beta interferon carries strong side effects and fails to work about half the time. In contrast, statins are oral medications with few side effects - at least at lower doses. Federal regulators are considering Zamvil's proposal for a nationwide human clinical trial in 2003. In October, MS researchers in Germany reported that a third statin -

lovastatin - reduced autoimmune activity in blood samples, especially when combined with beta interferon. Hartmut Wekerle of the Max Planck Institute of Neurobiology said statins are an "attractive candidate" for MS therapies, but more experiments must determine which statin might work best. MS affects about 1 out of 1,000 people. Women are affected more commonly than men. Attacks typically begin when patients are in their 30s.

No Evidence Vaccine Causes Autism

http://story.news.yahoo.com/news?tmpl=story2&cid=534&ncid=534&e=2&u=/ap/20021107/ap_on_he_me/vaccine_autism

A large study from Denmark offers reassuring evidence that the widely used measles, mumps and rubella vaccine does not cause autism, as some fear. Some have speculated that the measles portion of the vaccine might trigger autism, in part because autism often becomes apparent during the second or third year of life, around the same time the shots are given. However, several large careful studies have turned up no proof of this, and the latest of these was published in Thursday's issue of the New England Journal of Medicine. Dr. Kreesten Meldgaard Madsen and others from the Danish Epidemiology Science Center in Aarhus reviewed the records of 537,303 children born in Denmark during the 1990s. The risk of autism was the same for those who got the vaccine and those who did not. Autism cases have risen substantially during the past 20 years, although some speculate this is a result of better recognition of the disorder, not a true increase. A review by Dr. Edward Campion, the journal's senior deputy editor, said the latest study is unlikely to put an end to the controversy, although "the association of autism with MMR vaccination appears to be only a predictable coincidence."

Study Looks at Heart Drug, Color Blindness Link

http://story.news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=5&u=/nm/20021105/hl_nm/heart_blindness_dc

Up to 30% of elderly patients who take digoxin, a form of the drug digitalis used to treat heart failure and other heart problems, may experience at least some degree of red-green color confusion as a side effect, new study findings from the UK show. The effect seems to occur even in patients with normal levels of the drug in their blood, suggesting that doctors cannot test for the color deficiency to help determine if a patient is experiencing digoxin toxicity. According to the report published in the British Journal of Ophthalmology, digoxin toxicity remains a "common medical problem, particularly in the elderly, where it is often difficult to diagnose." The condition is most often associated with headache, nausea, fatigue and confusion. Previously, experts had speculated that color blindness in these patients could be an indication that their dosage of digoxin was too high. To investigate, Dr. J. G. Lawrenson of City

University in London, UK, and colleagues evaluated the theory among a group of 30 elderly patients who were receiving digoxin treatment. "Slight to moderate red-green (visual) impairment was found in approximately 20% to 30% of patients (taking digoxin)," the authors write. About 20% of patients also had difficulty distinguishing between shades of blue. None of the patients noticed any impairment in their vision prior to the tests. "There was no correlation between color vision impairment and (blood) digoxin level," the authors note. 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. "In summary, elderly patients receiving maintenance digoxin therapy showed a high incidence of color vision impairment," Lawrenson and colleagues write. "As a result, color vision testing in this population would have limited value for the detection of drug toxicity," they conclude. SOURCE: British Journal of Ophthalmology 2002;86:1259-1261.

Treatment-Related Cardiovascular Risks For Rofecoxib And Non-Steroidal Anti-Inflammatories Re-Examined

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C62006D6E57?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249>

Rofecoxib does not have more treatment-associated cardiovascular events (CV) than do placebo or other non-steroidal anti-inflammatory drugs without potent and sustained anti-platelet profiles (diclofenac, ibuprofen, or nabumetone). There is also a lower risk of CV events among subjects treated with naproxen when compared to rofecoxib, researchers report. This research was presented here at the annual meeting of the American College of Rheumatology. The investigators, from the New England Medical Center in Boston, Massachusetts, United States, made a retrospective analysis of CV thrombotic events from 27 phase IIb-V rofecoxib studies. A previous analysis of over 23,000 patients (more than 14,000 patient-years) had indicated no evidence that rofecoxib, a selective COX-2 inhibitor, was associated with excess CV events compared with either placebo or non-naproxen NSAIDs. This new analysis was done to address the possibility of treatment associated CV risks and to study the possible CV benefits of selective COX-2 inhibition. The purpose was, "to update the pooled estimates comparing the risk for CV thrombotic events among patients receiving rofecoxib, non-selective NSAIDs, and placebo," wrote the authors. The investigators compared data on rofecoxib subjects to data on those taking either placebo, naproxen (an NSAID with near complete inhibition of platelet function throughout its dosing interval), or the other studied non-selective NSAIDs (diclofenac, ibuprofen, or nabumetone). They analyzed over 30,500 patients, representing approximately 18,500 patient-years of risk. The combined endpoint used by the Antiplatelet Trialists

Collaboration (APTC) was used as the primary outcome measure. This measure includes CV, hemorrhagic, and unknown deaths, non-fatal myocardial infarctions, and non-fatal strokes. They found that the relative risk (with a 95 percent confidence interval) for an APTC endpoint was 0.94, (0.62, 1.42) for rofecoxib compared to placebo. The relative risk was 0.87, (0.48, 1.58) for rofecoxib compared to non-naproxen NSAIDs, and 1.61 (1.04, 2.50) for rofecoxib compared to naproxen. "These results support the conclusions from the original analysis: (1) There is no evidence that rofecoxib was associated with excess CV events compared with either placebo or the non-naproxen NSAIDs evaluated without potent sustained anti-platelet effects. (2) There was a decreased risk of CV events in patients treated with naproxen relative to rofecoxib which is consistent with the hypothesis that naproxen provided cardioprotective effects in these studies." the authors concluded. The research was supported by Merck.

U.S. to Audit Tenet Healthcare

<http://apnews1.iwon.com/article/20021106/D7N4NQP01.html>

The federal government is investigating whether Tenet Healthcare Corp. hospitals overbilled Medicare millions of dollars for costly procedures, the company announced Wednesday. The U.S. Department of Health and Human Services will audit Tenet's accounts at several hospitals. The probe was triggered by an insurance company reporting concerns over billings for a higher-than-average number of procedures, such as heart surgeries, that qualify for special payments. The so-called "outlier" payments are meant to reimburse hospitals for expenses over and above the flat fee Medicare pays for certain conditions. "We're seeing indications of a problem there and want to see how extensive it is," said Katherine Harris, a spokeswoman for the inspector general's office of the health department. The payments in question were made over a period of months this year, Harris said. "We're going to visit hospitals to be sure Medicare claims complied with Medicare regulations and were based on usual and customary charges for private pay patients," Harris said. We are pleased to cooperate with this audit, as we are confident that it will demonstrate that our hospitals did, in fact, obey the rules," said Jeffrey Barbakow, chairman and chief executive of the Santa Barbara-based company. Last week, federal agents searched the office of two doctors who practice at a Tenet hospital in Redding, Calif. Tenet also is investigating allegations that the two performed unnecessary heart surgeries. The Medicare audit is not connected to the Redding investigation, Harris said. That development came the same week as a Wall Street analyst questioned the growth prospects of the company based on the high amount of outlier payments it received in 2002. The news sent Tenet's stock tumbling 37 percent last week. Shares of Tenet were off 19 cents at \$26.03 in afternoon trading Wednesday on the New York Stock Exchange.

U.S. Food and Drug Administration Approves Effective New Tool to Help Smokers Quit

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/10-31-2002/0001832492&EDATE=>

The nearly 50 million smokers now have an effective new treatment to help them quit. The U.S. Food and Drug Administration (FDA) today approved the Commit(TM) Lozenge -- the first and only nicotine lozenge -- for over-the-counter (OTC) sale. The Commit Lozenge, from the marketers of Nicorette(R), helps control cravings by delivering craving-fighting medicine fast. Additionally, its groundbreaking new dosage-selection tool, "Time to First Cigarette" (TTFC), enables smokers to get the right strength of nicotine based on how quickly they need to smoke after waking. The Commit Lozenge has been shown to be effective in helping people quit, including smokers who have tried quitting before. The benefits of the Commit Lozenge were even greater when quitters used the minimum recommended number of lozenges per day in the early part of their quit attempts (i.e., nine lozenges per day for the first six weeks of therapy). "As the marketers of Nicorette nicotine gum and NicoDerm(R) CQ(R) nicotine patch, we have provided increased access to safe and effective tools that have helped millions of smokers quit successfully," said Steve Burton, vice president of Smoking Control, Strategic Development and Switch at GlaxoSmithKline Consumer Healthcare. "We understand, however, that when trying to quit, smokers have different needs. Our newest option, the Commit Lozenge, provides smokers with a new treatment option to help them manage their quit attempts while also offering a unique dosage-selection tool to ensure that they are receiving the right amount of medicine." The Commit Lozenge Features Unique Dosage Selection Tool: "Time to First Cigarette" The Commit Lozenge uses a unique method for smokers to determine their degree of physical dependence on nicotine. This groundbreaking new indicator is called Time To First Cigarette (TTFC) and is available only with the Commit Lozenge. With TTFC, those who smoke their first cigarette within 30 minutes of waking are directed to use the 4mg strength of the Commit Lozenge, whereas those who smoke their first cigarette after 30 minutes of waking are directed to use the 2mg strength. Leading experts regard TTFC as one of the best indicators of dependence because all smokers wake up in a state of nicotine deprivation, and the drive to quickly self-administer is a strong indicator of nicotine dependence. Using TTFC means that smokers get the most appropriate strength for their needs, which can help improve their chances of quitting. "Currently, smokers who use nicotine replacement therapy are instructed to self-select the appropriate strength based on the number of cigarettes they smoke per day. This marker of nicotine dependence may not be suitable for everyone, especially as smoking restrictions force smokers to smoke fewer cigarettes -- and with variation across cultural and ethnic groups," said Saul Shiffman, Ph.D.,

professor of psychology at University of Pittsburgh. "The groundbreaking 'Time to First Cigarette' dosage selector ensures the user gets the appropriate level of nicotine to help the user quit." Similar to Nicorette nicotine gum and NicoDerm CQ nicotine patch, the Commit Lozenge helps relieve craving and nicotine withdrawal symptoms by providing a temporary alternative source of nicotine, without exposing the quitter to the harmful tars and carbon monoxide from cigarette smoke. The Commit Lozenge goes to work after you place it in your mouth, releasing nicotine as it dissolves to effectively reduce cravings. The quitter uses fewer and fewer lozenges during the 12-week program until he/she is completely nicotine-free. The 72-count Commit Lozenge packs will include a comprehensive user's guide that explains the process of quitting, how the Commit Lozenge works, the TTFC dosage method, specific tips for quitting and advice about staying smoke-free. Purchasers of the Commit Lozenge also receive free enrollment in Committed Quitters(R), a personalized behavioral support program that, when compared to NRT alone, has been clinically proven (among participants who read or reviewed the CQP materials) to increase a smoker's chance of quitting successfully by up to 26 percent when paired with NicoDerm CQ and by up to 50 percent when paired with Nicorette. Participants in the Committed Quitters program submit a detailed "smoking history" online or via telephone and receive a tailored profile and quitting program. A series of customized self-help materials is sent throughout the 12-week course of therapy to help users successfully cope with their specific triggers and issues in quitting. Additional information about Commit Lozenge, is available at: <<http://www.commitlozenge.com>>. The new Commit Lozenge will be available in 2mg and 4mg strengths by the end of November at many drug stores, mass merchandisers and supermarkets that carry a large selection of non-prescription health products. GlaxoSmithKline Consumer Healthcare, marketer of the Commit Lozenge, plans to communicate the availability of the new product through extensive advertising, consumer and event promotion, as well as public relations initiatives.

Auxilium Receives U.S. FDA Approval to Market Testim? Testosterone Replacement Gel

http://biz.yahoo.com/rc/021101/health_bentley_approval_3.html

Bentley Pharmaceuticals Inc. on Friday said U.S. regulators approved a testosterone replacement gel to be sold by Auxilium Pharmaceuticals in combination with Bentley's patented drug delivery technology. The companies announced that the U.S. Food and Drug Administration approved Testim, a topical gel formulation for use in treating men with low testosterone levels. Abnormally low levels of testosterone have been linked to a decline in energy, decreased muscle mass, reduced bone density, decreased libido and sexual function, fatigue and depression. "We're very pleased and somewhat shocked that approval went through so quickly," Bentley Chairman and Chief Executive James Murphy said. "We thought approval would be at the

end of this year or early next year." Bentley said it had licensed its CPE-215 technology for use with testosterone to Auxilium, a privately held company based in Norristown, Pennsylvania. CPE-215 enhances absorption by the body's membranes, Murphy explained. Under the licensing agreement, Auxilium conducted the clinical trials and applied for and received the FDA approval to market the drug under the Testim name. Testim will be Auxilium's first commercial product. It hopes to launch Testim in the first quarter of 2003, Chief Executive Gerri Henwood said. The gel is designed to be rubbed into the upper arm or shoulder once a day. Auxilium said the assumption is that Testim would be long-term -- in many cases permanent -- therapy for most patients. Shares of Bentley Pharmaceuticals rose \$1.77, or 23 percent, in trade on the American Stock Exchange on Friday to close at \$9.47.

FDA Committee Recommends Approval for Clozaril to Treat Suicidal Behavior -- Drug Could Be First Ever With Indication

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C680056EE80?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249>

Novartis Pharmaceuticals Corporation announced that the US Food and Drug Administration (FDA) Psychopharmacologic Drugs Advisory Committee voted to recommend that the FDA approve the use of Clozaril? (clozapine) for the treatment of emergent suicidal behavior in patients with schizophrenia or schizoaffective disorder. FDA reviewers will consider the panel's suggestion before making a final decision. If the new indication is granted, it will mark the first time that any medication has been approved for use in treating suicidal behavior. Novartis filed a supplemental New Drug Application (sNDA) in March 2002, for the indication based upon data from the International Suicide Prevention Trial (InterSePT(TM)), the first study ever to prospectively evaluate a medication in reducing the risk of suicidal behavior. Dr. Daniel Vasella, Chairman and Chief Executive Officer of Novartis AG commented, "Current estimates suggest that at least two million Americans suffer from schizophrenia, about ten percent of whom will actually die as a result of suicide. The data from our InterSePT(TM) study demonstrated that Clozaril reduced the risk of suicide attempts and hospitalizations to prevent suicide among individuals suffering from schizophrenia or schizoaffective disorder by 26% compared to Zyprexa?*(olanzapine). I am most gratified that our drug Clozaril, has the potential to provide a life saving benefit to those schizophrenia patients who are most in need." Suicidal behavior embodies symptoms ranging from suicidal thoughts, to suicidal plans and actual suicide attempts. InterSePT(TM) was a multi-center, randomized study initiated in 1998 to compare the efficacy of two antipsychotic compounds, Clozaril and Zyprexa* one of the world's most widely prescribed antipsychotic medications, in reducing the risk of suicidal behavior among patients with schizophrenia or schizoaffective disorder. In addition to reduced suicide attempts and

hospitalizations to prevent suicide, patients treated with Clozaril also required fewer concomitant psychotropic medications. The safety profile observed in the study was consistent with the well-known characteristics of Clozaril. "Today's FDA Advisory Committee recommendation is an important milestone because the risk of suicide and suicidal behavior in schizophrenia is enormous," said Dr. John M. Kane, Vice President for Behavioral Health Services at the North Shore Long Island Jewish Health System, and a lead investigator in the study. "Approximately half of all patients with schizophrenia will attempt suicide during their lifetime. The consequences of that are staggering. When the data suggested that Clozaril might offer hope to these most vulnerable of patients, it was heartening that Novartis moved quickly to conduct this study despite the fact that many other companies would have considered Clozaril a mature product."

According to the National Institute of Mental Health (NIMH), 29,199 Americans committed suicide during 1999. While no reliable data exists on the number of attempted suicides each year, researchers believe that there are between 8 and 25 attempts for each completed suicide. A study by Palmer et al, published in *Clinical Neuropharmacology* in 1995 estimated that each suicide attempt results in at least \$33,000 in direct and indirect costs.

"Overall, this study demonstrated that Clozaril is superior to Zyprexa?* for the prevention of suicide attempts in patients with schizophrenia and schizoaffective disorder who are at high risk for suicide," Dr. Kane said.

"Wider use of Clozaril in this population could very well help to save many lives each year. I think that InterSePT? will fundamentally change the care that suicidal patients with psychosis receive in the future." James McNulty, president of the Board of Directors of the National Alliance for the Mentally Ill (NAMI), welcomed the news about the panel vote, "The human toll of suicide in schizophrenia is unacceptable," he notes. "Very often the caregivers for people with schizophrenia are parents or other family members who expend tremendous emotional and financial resources on their care. To lose a beloved family member to suicide creates a void in the fabric of family life that can never be repaired."

Xigris Sustains Survival Long Term in Severe Sepsis Patients

<http://newsroom.lilly.com/news/story.cfm?id=1129>

Xigris? (drotrecogin alfa [activated]) sustains survival of severe sepsis patients long term, according to study results presented at the 68th annual International Scientific Assembly of the American College of Chest Physicians (ACCP) in San Diego. In one of four abstracts on Xigris presented today, the analysis indicates that the drug also saves lives without lengthening hospital stays compared with the use of standard care alone. Xigris already had proved effective in decreasing the short-term risk of death (28 days) in adults with life-threatening severe sepsis in the landmark PROWESS Phase III clinical trial. Eli Lilly and Company received FDA approval for Xigris in November 2001 to reduce mortality in

adult severe sepsis patients at high risk of death (e.g., as determined by APACHE III) and was recently approved by the European Commission for use in the 15 countries it represents. Results of a long-term follow-up analysis of PROWESS (n=1,690), conducted from September 2001 until April 2002, showed that reduction in mortality in Xigris-treated patients was sustained over the duration of the study, which followed patients up through two and a half years.² "Xigris has already proven that it dramatically improves patients' chances of making it through the most dangerous stage of life-threatening severe sepsis - those first 28 days," said study researcher Derek C. Angus, M.D., M.P.H., associate professor of anesthesiology and critical care medicine, University of Pittsburgh. "Our new data show that the survival benefit of Xigris is sustained over the long term. These findings are wonderful news - and offer much-needed hope - for thousands of patients with severe sepsis and their families." Additional data presented today demonstrate that the survival rate in Xigris-treated patients from all clinical trials to date has remained consistent with the PROWESS clinical trial results. In five clinical trials and two compassionate use studies of Xigris, the 28-day mortality rate for all patients receiving active treatment was 25.3 percent, comparable to the 24.7 percent Xigris mortality and less than the 30.8 percent placebo mortality demonstrated in the PROWESS trial. A comprehensive review of cumulative safety data from both clinical trials and postapproval experience in the United States shows that the only significant adverse event associated with Xigris is bleeding, and the data suggest risk of bleeding is generally manageable. Importantly, this analysis indicates that such events were frequently associated with other hemorrhage-causing factors, such as invasive procedures and thrombocytopenia (platelets < 30,000 per milliliter).

Nosocomial Pneumonia Indication Approved For LEVAQUIN?

http://www.jnj.com/news/jnj_news/20021105_111257.htm

The U.S. Food and Drug Administration (FDA) has approved LEVAQUIN? (levofloxacin) Tablets/Injection and LEVAQUIN? (levofloxacin in 5% dextrose) Injection 750mg for the treatment of nosocomial (hospital-acquired) pneumonia. With this indication, LEVAQUIN?, a fluoroquinolone anti-infective, is now approved by the FDA to treat a form of pneumonia that affects approximately 300,000 patients in the United States annually. LEVAQUIN? is marketed by Ortho-McNeil Pharmaceutical, Inc. "This indication further adds to the clinical utility of LEVAQUIN?," said Joseph Lynch, III, M.D., professor of medicine, Division of Pulmonary and Critical Care Medicine, University of Michigan School of Medicine, Ann Arbor. "The ability to increase the dose of LEVAQUIN? to 750 mg from 500 mg without a major change in safety or side effects is a benefit when treating the more serious pathogens associated with nosocomial pneumonia, like *Pseudomonas aeruginosa*." The new indication is based on data from a

pivotal, multi-center, randomized, open-label study with 438 patients comparing intravenous LEVAQUIN[®] (750mg once daily) followed by oral LEVAQUIN (750 mg once daily) for a total of seven-15 days to intravenous Primaxin[®]1 (imipenem/cilastatin) (500-1000 mg dosed every six-eight hours) followed by oral Cipro[®]2 (ciprofloxacin) (750 mg dosed every 12 hours daily) for a total of seven-15 days. Data provided to the FDA demonstrated that LEVAQUIN[®] was as effective as the comparator treatment used in this study. LEVAQUIN[®] is indicated for nosocomial pneumonia due to methicillin-susceptible *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, or *Streptococcus pneumoniae*. Adjunctive therapy should be used as clinically indicated. Where *Pseudomonas aeruginosa* is a confirmed or suspected pathogen, combination therapy with an anti-pseudomonal beta-lactam anti-infective is recommended.

Glucosamine Sulfate Delays Progression of Knee Osteoarthritis

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C6300>

59B880?OpenDocument&c=&count=10&id=48DDE4A73E09A969852568880078C249

Long-term treatment with glucosamine sulfate delays the progression of knee osteoarthritis, according to Czech and Italian researchers. In a randomised, placebo-controlled, double-blind study led by Karel Pavelka, M.D., PhD, from the Department of Medicine and Rheumatology, Charles University, and the Institute of Rheumatology, Prague, Czech Republic, the researchers randomized 202 patients with knee osteoarthritis to receive either oral glucosamine sulfate, 1500 mg once a day, or placebo. Disease progression in osteoarthritis is not retarded by conventional symptomatic treatments. The aim of this trial was to determine whether long-term treatment spanning three years with glucosamine sulfate can alter the progression of joint structure and symptom changes in knee osteoarthritis. Patients were enrolled using the American College of Rheumatology criteria. The status and progression of osteoarthritis were measured by changes in radiographic minimum joint space width in the medial compartment of the tibiofemoral joint. Also, symptoms of osteoarthritis were assessed using the Lequesne and Western Ontario and McMaster Universities (WOMAC) indexes. At enrollment, osteoarthritis was mildly to moderately severe with average joint space widths less than four mm and a Lequesne index score of less than nine points. The researchers found that after three years of placebo use, progressive joint narrowing was -0.19 mm. In the glucosamine sulfate group, the researchers found no average change in joint space width. The difference between the two groups was significant ($p=0.001$). Five percent of patients treated with glucosamine sulfate experienced predefined severe narrowings (>0.5 mm), versus 14 percent of patients who were administered a placebo ($p=0.05$). While symptoms improved slightly with placebo use, they improved significantly by 20 to 25 percent with the use of glucosamine sulfate. There were significant final

differences between both groups on the Lequesne index and the WOMAC total index, as well as on the pain, function, and stiffness subscales. The authors found that safety was good and the same in both groups. This study was funded by the Rotta Research/Rottapharm Group, Monza, Italy. Archives of Internal Medicine 2002;Vol. 162 No. 18, October 14.

Application Submitted to FDA for Topamax(R) Monotherapy Treatment of Epilepsy

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-01-2002/0001832775&EDATE=>

Ortho-McNeil Pharmaceutical, Inc., today announced it has submitted data to the U.S. Food and Drug Administration to support use of TOPAMAX(R) (topiramate) as stand- alone treatment (monotherapy) in adults and children age six and older with newly diagnosed epilepsy. If the FDA application is approved, Topamax would be the first of the newer anti-epileptic drugs to be approved for the monotherapy treatment of both partial-onset and generalized seizures in adults and children. Currently, Topamax is approved in the United States for use in combination with other anti-epileptic medications to treat partial onset and generalized "tonic-clonic" seizures, as well as Lennox-Gastaut syndrome. Outside the United States, more than 30 countries already have approved its use as stand- alone treatment for epilepsy.

Extra-Strength Tylenol: An Extra Headache?

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-05-2002/0001834779&EDATE=>

True or false? Extra-strength Tylenol (acetaminophen) gives greater relief from pain and headache than regular strength Tylenol. More like not proven. According to a report in the October 28 issue of The Medical Letter(R) on Drugs and Therapeutics, there are no published data showing that 1000 mg of Tylenol (two extra-strength tablets) is more effective than 650 mg (two regular-strength tablets) in treating everyday causes of pain such as headache or osteoarthritis. The Federal Food and Drug Administration has recommended that a stronger warning about potential serious liver injury at higher-than-recommended doses be added to the labeling for acetaminophen products. The Medical Letter says that usual doses of acetaminophen are not likely to cause hepatotoxicity even in people who drink moderate amounts of alcohol. Recommended doses can be dangerous, however, when people take Tylenol with one or more of the many "combination products" containing acetaminophen, or take any two of these products simultaneously. Some common over-the-counter acetaminophen combinations include various products of brands such as Alka-Seltzer, Benadryl, Comtrex, Contac, Coricidin, Dimetapp, Drixoral, Excedrin, Goody's, Midol, Percogesic, Robitussin, Singlet, Sinutab, Sudafed, Tavist, TheraFlu, Triaminic, Vanquish and Vicks.

Since acetaminophen turns up in so many of these products, why take extra-strength Tylenol when regular strength may do just as well?

Are Drugs Taken After Their Expiration Date Dangerous? Is it ever safe to take prescription drugs after the expiration date on the label?

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-05-2002/0001834779&EDATE=>

According to a report in the October 28 issue of The Medical Letter(R) On Drugs and Therapeutics, the expiration date doesn't mean that the drug will go bad after that date, but only that it will still be good on that date. In the last 40 years, surprisingly, there has only been one report of toxicity due to a breakdown of the products in outdated drugs. Even that drug (tetracycline) has been reformulated and would not have that effect today. The amount of potency a drug retains depends on the drug and the storage conditions, especially humidity. The Medical Letter reports that many drugs stored under reasonable conditions retain 90% of their potency for at least five years after the expiration date found on the label. And some drugs have been found to retain potency for 25 or 30 years! Liquid medication is not as stable as solid forms. Solutions that become cloudy or discolored should be discarded. Specifically, The Medical Letter reports that epinephrine in EpiPen injections, used to treat serious allergic reactions, loses potency after its expiration date.

In the Pipeline

Coviracil(R) NDA for the Treatment of HIV Disease Accepted by the Food and Drug Administration

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-04-2002/0001833785&EDATE=>

Triangle Pharmaceuticals, Inc. announced today that the U.S. Food and Drug Administration (FDA) has notified the Company that its New Drug Application (NDA) for marketing approval of Coviracil for the treatment of HIV disease has been accepted for filing. Filing of the NDA is recognition by the FDA that the application is sufficiently complete for review. "We are very pleased with this notification," commented Daniel G. Welch, Chairman and Chief Executive Officer of Triangle. He continued, "Consistent with our previous guidance when we submitted our NDA, the FDA granted Coviracil a standard review. This means that as early as the third quarter of 2003, we hope to have our first NDA approved. We believe, once approved, Coviracil will offer patients and physicians an important new medicine for the management of HIV disease. We will now turn our efforts to completion of the review process with the FDA to work towards the timely approval of Coviracil." Coviracil is a potent, once-a-day Nucleoside Reverse Transcriptase Inhibitor (NRTI). The NDA includes data from over 2,000 patients and is supported by two pivotal trials, FTC-303 and FTC-301.

Triangle expects to file a European Marketing Authorisation Application (MAA) by December 31, 2002.

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Website of the Day

The Medical Letter on Drugs and Therapeutics

<http://www.medletter.com/>

The Medical Letter, a nonprofit organization founded in 1958, through its newsletters, The Medical Letter on Drugs and Therapeutics and Treatment Guidelines from The Medical Letter, publishes critical appraisals of new drugs as well as comparative reviews of older drugs. Although access to the newsletter requires a subscription, there is a "free reading room" with some key articles (eg. Generic Drugs), treatment guidelines (eg. Drugs for Diabetes), and other articles of interest (eg. Sunscreens: Are they Safe and Effective?) available via adobe acrobat. We've all read the articles, now bookmark the page.

Answer of the Day

Clozaril (Clozapine) is a dibenzodiazepine derivative atypical anti-psychotic whose therapeutic effects are mediated by dopaminergic and serotonergic activity. Although the drug is one of the most effective antipsychotic drug for treatment-resistant schizophrenia, its general use is limited because of a risk of agranulocytosis.

The drug was first marketed in 1972 in Europe, but withdrawn in 1975

following the deaths of eight Finnish patients who developed agranulocytosis. Subsequently, the drug was re-introduced when it was realized that the agranulocytosis was reversible and by keeping a close watch through weekly WBC counts, one could avoid fatal incidents. These findings, together with a proposal for a national mandatory haematological monitoring service for all patients, enabled clozapine to be given a product licence in the the US in September 1989, the UK in January 1990, and in Ireland in August 1993. Did you hear that?