



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 were the top 10 selling drugs in the US in 2002?

In the News

FDA Approves Prilosec OTC to Treat Frequent Heartburn

<http://www.fda.gov/bbs/topics/news/2003/NEW00916.html>

The Food and Drug Administration (FDA) has announced the approval of Prilosec OTC (omeprazole), the first over-the-counter treatment for frequent heartburn. "Today's approval of over-the-counter Prilosec is yet another example of the important role FDA serves in improving access to safe and effective treatments for conditions that people can treat themselves," said Mark B. McClellan, M.D., Ph.D., Commissioner of Food and Drugs. "As has been the case for many other over-the-counter switches, the availability of Prilosec OTC will help reduce costs and expand the availability of treatment options for millions of Americans." Unlike the two classes of currently marketed over-the-counter heartburn treatments, antacids and acid reducers, Prilosec OTC is indicated for the treatment of heartburn that occurs two or more days per week (frequent heartburn). It stops acid production at its source in the stomach. Prescription Prilosec is currently widely prescribed for frequent heartburn and other related, but more serious, problems that need the care of a physician. Antacids and acid reducers, which have long been available over-the-counter, are used for the relief of acute heartburn symptoms. Acid reducers are additionally used for the prevention of meal-induced heartburn. According to the American College of Gastroenterology, over 60 million Americans experience heartburn at least once a month and some studies have suggested 15 million Americans experience heartburn daily. Heartburn occurs when stomach contents containing acid back up and out of the stomach into the esophagus causing a burning sensation in the chest or throat. Prilosec OTC is a delayed-release 20mg tablet that must be taken before eating once a day, every day for 14 days. Prilosec OTC may take one to four days for full effect, although some consumers may get complete relief of symptoms within 24 hours. Prilosec OTC is not for people

who have heartburn infrequently, one episode of heartburn a week or less, or for those who want immediate relief of heartburn. If frequent heartburn returns soon after 14 days of Prilosec OTC treatment, consumers should contact their healthcare providers. Consumers should not take a 14-day course of Prilosec OTC more often than every four months for frequent heartburn unless directed by a doctor. FDA based its approval of Prilosec OTC on the results of various studies, including two clinical studies. These two clinical studies demonstrated that Prilosec OTC was effective in increasing the proportion of patients with no heartburn over 24 hours and that the effectiveness of Prilosec OTC increases from Day 1 to Day 14. Before using Prilosec OTC or any medicine, FDA advises consumers to read the package label for complete information about the product's uses, warnings, and directions. Although side effects from Prilosec OTC are not common, they can occur and may include: headache, diarrhea, constipation, upset stomach, vomiting, stomach pain, cough, cold symptoms, dizziness and rash. Prescription Prilosec (omeprazole), first approved by FDA in 1989, will remain available as a prescription treatment for diseases that require diagnosis and supervision by a doctor, such as Gastroesophageal Reflux Disease (GERD), inflammation of the esophagus (esophagitis) and ulcers. Because of the safety studies performed by the manufacturer of Prilosec OTC, this product will have three years of over-the-counter exclusivity. Generic versions of the prescription product will not be able to market an OTC version until the marketing exclusivity has expired.

First Once-Daily Protease Inhibitor Approved; Reyataz

<http://news.moneycentral.msn.com/ticker/article.asp?Feed=RTR&Date=20030620&ID=2650748&Symbol=US:BMV+>

The U.S. Food and Drug Administration has approved Bristol-Myers Squibb Co.'s (BMV) new once-daily drug meant to help control the virus that causes AIDS, the drug maker said. In addition to its convenient less-frequent dosing, Bristol-Myers said the drug, Reyataz, did not raise cholesterol levels in clinical trials, as other drugs in the same class tend to do. The drug is a protease inhibitor, one of the main classes of medicine used in special drug cocktails to treat HIV. "If Reyataz has a better lipid (cholesterol) profile than other protease inhibitors, that will be a good selling point," said Shaojing Tong, an analyst for New York research firm Mehta Partners. Protease inhibitors are often used in combination with reverse transcriptase inhibitors, another kind of HIV medicine that blocks replication of the virus. Many patients become quickly resistant to HIV drugs so the availability of a new medicine will provide doctors a new treatment option. Like many other HIV drugs, Reyataz is not expected to be a blockbuster, although analysts believe it could generate annual sales between \$200 million and \$600 million by 2007. The drug is part of a pipeline of new medicines that could provide a much-needed lift for Bristol-Myers, the New York drug maker suffering from slow earnings and

tainted by recent scandals. The company earlier this year restated its earnings downward dating back to 1997 after artificially propping them up by coaxing wholesalers to buy far more of their drugs than they could sell, a practice now under investigation by U.S. authorities. It also reached a \$670 million deal to settle charges it unfairly delayed cheaper generic competition for its Taxol cancer drug and BuSpar anxiety medicine. Moreover, Bristol-Myers has been criticized for agreeing in 2001 to invest nearly \$2 billion in a cancer drug partnership with ImClone Systems Inc. (IMCLE), the company at the center of an insider trading scandal that involves Martha Stewart, the domestic and culinary trendsetter. Bristol-Myers this year and next year faces patent expirations on several drugs whose sales could then be badly hurt by cheaper generics. But some industry analysts believe Reyataz and the company's recently launched schizophrenia drug Abilify could help keep the company's earnings growth on track.

Genentech/Novartis' Xolair wins FDA nod

<http://main.pslgroup.com/news/industrynews.nsf/FWStoriesFrameSet?OpenForm&id=&newsid=9E3D63705F61599C85256D4D00533F5E&ref=&u=http://www.smartmoney.com/news/ON/index.cfm?story=ON-20030620-000948-2024>

Genentech Inc. (DNA) won government approval late Friday to sell its new type of asthma medication Xolair, a drug that stops the inflammation and airway tightening before it starts.

Specifically for allergic asthma, Xolair is the first targeted treatment for the ailment that strikes some five million Americans. Xolair attacks the root cause of the life-threatening ailment by blocking a protein called immunoglobulin E from attaching to inflammatory cells. If those two don't hook up, they can't produce the chemicals that lead to the asthmatic reaction. The Food and Drug Administration will allow the genetically engineered Xolair on the market as a treatment for people 12 years and older with allergic asthma whose current medications haven't controlled their symptoms. "Xolair is the only thing that gets to the root of the problem with allergy," said Dr. Bob Lanier, who was the head investigator on several Xolair trials. The average yearly wholesale cost of Xolair will range from \$10,000 to \$12,000. Depending on the patient's size and level of the protein immunoglobulin E, some patients will need more or may need fewer injections which cost \$433 each wholesale. Although with more-frequent injections Xolair will be pricey, the drug's overall value will outweigh the dollars spent, said Dr. Lanier, who is also a clinical professor of pediatrics at the University of North Texas. He noted one shot of Xolair may cut out the need to take a handful of medicines to control asthma. Genentech expects to have Xolair, the first biotech product for asthma, available by mid-July. "This is a big deal for people who have allergic asthma who are not well controlled by existing medications," said Ira Loss, a pharmaceutical analyst

with Washington Analysis. But patients won't be the only beneficiaries. Mr. Loss said, "The biotech industry needed a positive development to keep the investment momentum going." Although some 17 million Americans have asthma, not all are triggered by allergy. Of the five million with allergic asthma, Genentech said about 500,000 will fit Xolair's target group, those who have tried and failed other treatments. Genentech plans to conduct long-term studies to see if there is a relationship between Xolair and cancer. In the trials there were very few cases of cancer, but there were more in the patients treated with Xolair than those given an inactive placebo. Genentech will jointly market and share the profits from Xolair with Novartis Pharmaceuticals (NVS). Tanox Inc. (TNOX) partnered with the two companies in the drug's development.

U.S. approves Glaxo's Lamictal in bipolar disorder

<http://www.reuters.com/newsArticle.jhtml?type=topNews&storyID=2972766>

GlaxoSmithKline, Europe's biggest drugmaker, has said the U.S. Food and Drug Administration had approved its Lamictal anti-seizure pill as a long-term treatment for bipolar disorder. Lamictal, which was cleared for use in patients already receiving treatment for acute mood episodes, is the first new maintenance therapy for the disorder since the introduction of lithium in the 1970s. Bipolar disorder, also known as manic depression, is a brain condition characterised by mood swings of extreme highs and intense lows. The FDA approval follows two clinical studies showing Lamictal, an established treatment for epilepsy, was effective in delaying episodes of depression and mania in patients suffering from bipolar disorder, although the finding was more robust for depression.

FDA Approves First Co-Packaged Treatments for Heart Disease

<http://www.fda.gov/bbs/topics/nEWS/2003/NEW00917.html>

The Food and Drug Administration (FDA) is announcing the approval of Pravigard PAC (co-packaged pravastatin sodium and buffered aspirin tablets) for use when treatment with both Pravachol (pravastatin) and buffered aspirin is appropriate. This co-packaged product may be more convenient for some patients. Pravachol and buffered aspirin are both indicated to reduce the occurrence of cardiovascular events, including death, myocardial infarction or stroke, in patients who have clinical evidence of cardiovascular and/or cerebrovascular disease. Patients receiving treatment with Pravigard should also be placed on a standard cholesterol-lowering diet. Pravachol is a prescription medication that both lowers the amount of "bad" (or LDL) cholesterol and raises the amount of "good" (or HDL) cholesterol. High cholesterol levels can lead to plugs or clots in blood vessels. Buffered aspirin stops the normal blood clotting process and keeps clots from forming in blood vessels that can lead to myocardial infarctions or strokes. Buffered aspirin has aspirin in it along with other ingredients

that may lower patients' chances of getting an upset stomach. Pravigard PAC should not be taken by patients who have certain liver or kidney problems, women who are pregnant or planning to become pregnant, individuals less than 18 years of age or by individuals who are allergic to non-steroidal anti-inflammatory (NSAID) medicines or any of the ingredients in Pravigard PAC. Possible serious side effects associated with the use of Pravigard PAC include muscle damage, liver damage, bleeding and stomach problems. It is therefore important for patients taking Pravigard PAC to tell their doctors if they experience any of the following: unexplained muscle pain or weakness, unusual bleeding, heartburn, nausea or vomiting, stomach pain or bowel movements or stools that look like black tar. Liver function tests may be performed prior to the initiation of Pravigard PAC. The usual dose of Pravigard PAC is 1 aspirin tablet with 1 Pravachol tablet once a day. Pravigard PAC is available in cartons containing either 30 buffered aspirin 81mg or 325mg tablets packed with either 30 Pravachol 20mg, 40mg or 80mg tablets.

FDA Panel Backs New Indication for Amgen Arthritis Drug

<http://www.reuters.com/newsArticle.jhtml?type=topNews&storyID=2981858>

Amgen Inc. on Tuesday won a U.S. panel's backing for its bid to market rheumatoid arthritis drug Enbrel to treat a painful and sometimes disabling stiffness of the spine. The panel's unanimous endorsement moves Amgen closer to winning Food and Drug Administration approval to promote Enbrel for reducing signs and symptoms of a type of spinal arthritis called ankylosing spondylitis. The FDA usually follows its panels' advice. Amgen and Wyeth co-market Enbrel, which was approved in 1998 for treating rheumatoid arthritis. Enbrel sales hit \$274 million in the first quarter. Competitors include Johnson & Johnson's drug Remicade. Mike King, an analyst with Banc of America Securities, said ankylosing spondylitis could add an incremental \$200 million to Enbrel sales. He estimates 2003 Enbrel sales of \$1.33 billion, rising to \$1.66 billion in 2004. About 350,000 Americans suffer from ankylosing spondylitis, which makes the spine more rigid and causes back pain. The disease usually starts afflicting patients in their 20s and 30s and may progress over decades to become disabling. The condition strikes men more often than women. Current treatments, including non-steroidal anti-inflammatory drugs, give only limited symptom relief, Amgen officials told the panel. Studies showed Enbrel "provides rapid and dramatic improvement in pain, stiffness, function and mobility to people who have had no meaningful alternatives," said Dr. Daniel Burge, Amgen's vice president for clinical development. FDA staff members who reviewed clinical data said 25 milligrams of Enbrel injected under the skin twice weekly demonstrated an improvement in increasing mobility and reducing pain and inflammation in studies of patients after 12, 16 and 24 weeks of treatment compared with those taking a placebo. Side effects, including injection site reactions and infections, were similar to what has been seen with Enbrel when used to

treat rheumatoid arthritis, FDA reviewers and Amgen officials said. Enbrel works by inhibiting tumor necrosis factor, a protein linked to inflammation. Amgen shares gained 93 cents, or 1.45 percent, to \$65.05 in afternoon trading on Nasdaq.

FDA Approves Multiple Generics of Remeron [Mirtazapine Tablets]

http://biz.yahoo.com/djus/030619/1559001088_2.html

Eon Labs Inc. and Mylan Laboratories Inc. received final Food and Drug Administration (News - Websites) approval to make and sell three dosages of Mirtazapine, the generic equivalent of the antidepressant Remeron. Eon, a generic pharmaceutical company, said in a press release Thursday that it has been cleared by the regulator to sell Mirtazapine in 15-, 30- and 45-milligram dosages. In a separate release, Mylan said it has been cleared to sell Mirtazapine in the same dosages. Both companies said they plan to launch or ship their respective products immediately. Earlier Thursday, Teva Pharmaceutical Industries Ltd. (TEVA), an Israeli concern, said it has been approved by the FDA to sell Mirtazapine in 45mg dosages. Teva was cleared to sell 15mg and 30 mg dosages in January. Watson Pharmaceuticals Inc. also received clearance to sell the drug in 15mg, 30mg and 45mg doses. Remeron is the property of Organon Inc. (NasdaqNM:AKZOY - News), a unit of Akzo Nobel NV. Eon said the drug generated \$270 million in sales over the last 12 months. Mylan's shares recently traded down \$1.42, or 4.1%, at \$32.85 on composite volume of 1.3 million shares. Average daily volume was about 1.6 million.

More Bad News for Hormone Drugs in U.S. Study

<http://www.reuters.com/newsArticle.jhtml?type=topNews&storyID=2982206>

The most common hormone replacement drug therapy not only increases the risk of breast cancer in post-menopausal women but also makes cancer harder to detect with mammography, a report said on Tuesday. The finding is the latest in a continuing stream of bad news for preparations that combine estrogen and progestin. The hormones have been shown to halt or reverse osteoporosis, lessen the risk of hip fractures and prevent uterine cancer. But a major government study on long-term use was halted in the summer of 2002 after it showed the estrogen-progestin combination sold as Wyeth's Prempro carried an increased risk of ovarian cancer, heart attack and stroke.

Wyeth has won government approval to market lower dose versions of its drug which it says address the risk problems. Tuesday's study was a closer analysis of findings in the study halted a year ago. Published in the Journal of the American Medical Association, the new research affirmed the breast cancer problem, finding a 26 percent increase in the risk of that cancer for women taking estrogen plus progestin. But the report, from Harbor-UCLA Research and Education Institute, Torrance, California, also

found that the cancers tend to be diagnosed at more advanced stages and result in substantial increases in abnormal mammograms. In an editorial in the same issue commenting on the study Peter Gann and Monica Morrow, physicians at the Feinberg School of Medicine at Northwestern University in Chicago, said: "The ability of combined hormone therapy to decrease mammographic sensitivity creates an almost unique situation in which an agent increases the risk of developing a disease while simultaneously delaying its detection. "It strongly suggests that the breast cancers related to estrogen plus progestin use are not 'good' (easily treatable) ones, that they occur earlier than expected based on some previous studies, that there are no easily identified subgroups at higher risk and that, to top it off, women using estrogen plus progestin experience a much higher rate of mammographic abnormalities leading to anxiety and further costly work-ups." The study findings came from the now-halted Women's Health Initiative, which involved 16,608 post-menopausal women some of whom received combination hormone treatment, others an inert placebo. It said that there was "an absolute increase in abnormal mammograms of about 4 percent per year in women receiving estrogen plus progestin" that translates into "approximately 120,000 otherwise avoidable abnormal mammograms annually for the estimated 3 million U.S. post-menopausal women currently using this hormone regimen." The study was paid for by the National Heart, Lung, and Blood Institute, part of the National Institutes of Health. In a second study published in the same journal, researchers at the Fred Hutchinson Cancer Research Center in Seattle said they found there was a breast cancer risk even when progestin is not taken every day in combination with estrogen -- so-called sequential treatment. The conclusion came from a look at 51 other previously published studies.

Carvedilol Has Significant Mortality Benefit Over Metoprolol

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256D4E005544C9?OpenDocument&id=9F874D6C503400D485256AFD0071B610&c=Congestive%20Heart%20Failure&count=10>

Carvedilol, a drug used in the treatment of heart failure, results in a significantly lower mortality rate compared to another beta-blocker, metoprolol. Professor Phillip A. Poole-Wilson, London, United Kingdom, presented the primary results of the Carvedilol or Metoprolol European Trial (COMET) here June 23rd during the late breaking trials session at the 2003 Heart Failure conference sponsored by the European Society of Cardiology and the International Society for Heart Research. In COMET, 3,029 patients with New York Heart Association class II and III were randomized to receive carvedilol 25 mg twice daily or metoprolol tartrate 50 mg twice daily. The mean dose achieved was 42 mg and 85 mg daily, respectively. Both agents lowered heart rate and blood pressure to a similar degree. Peanut. The follow-up period was nearly 5 years, making it the longest heart failure

trial conducted thus far. The primary end point -- all-cause mortality -- showed that carvedilol-treated patients had a 17% lower mortality rate ($P=.0017$) than metoprolol-treated patients. The annualized mortality rates were 8.3% for the carvedilol group compared to 10% for the metoprolol group. Overall, there were 512 deaths in the carvedilol group compared with 600 in the metoprolol group. Carvedilol use prolonged the median survival time by 1.4 years. There was no discernable difference in the mode of death between the groups. The analyzed co-primary end point, the combination of all-cause mortality and cardiovascular hospitalization, failed to show a significant difference between the two groups. After the 5-year follow-up period, 73.9% of 1,511 carvedilol-treated patients met the end point, compared with 76.4% of 1,518 metoprolol-treated patients. Professor Poole-Wilson said, "These results are significant, and show that the preferred beta-blocker in the treatment of heart failure should be carvedilol." The number of patients needed to treat to save one life in 1 year with carvedilol instead of metoprolol is 59, he said. The percentage of patients with adverse events and the withdrawal rate was lower with carvedilol. Metoprolol tartrate is a beta1- selective agent, while carvedilol blocks beta1, beta2, and alpha1 adrenergic receptors. Both agents have been used to treat heart failure, usually in combination with angiotensin-converting enzyme inhibitors, diuretics, and digoxin. COMET was the first head-to-head trial comparing mortality with two beta blocking agents in patients with chronic heart failure.

FDA: Kids Should Not Take Paxil; GSK Reassures Public

<http://news.moneycentral.msn.com/ticker/article.asp?Feed=RTR&Date=20030619&ID=2647555&Symbol=US:GSK>

The U.S. Food and Drug Administration on Thursday warned that patients under age 18 should not take GlaxoSmithKline's antidepressant Paxil because of a possible increased risk of suicidal impulses associated with the drug. The statement from the FDA comes nine days after British regulators issued similar precautions for children and adolescents. The drug, one of Glaxo's top sellers, is known as Seroxat in the UK. The drug generated global sales of about \$3.4 billion last year, but it is facing the prospect of generic competition in the United States within the next 18 months. The medicine has been the subject of increased public concern because of reports of adverse reactions, prompting Britain to set up an expert panel to investigate. Although only officially approved for adults, doctors have had discretion to prescribe Paxil/Seroxat to young people on a so-called "off-label" basis. Although companies are allowed to promote and market drugs only for approved uses, doctors are free to prescribe drugs to patients at their discretion. Children account for a small portion of patients taking the antidepressant. For instance, a total of 4 million prescriptions were written for Seroxat in Britain last year, with around 8,000 patients under 18 receiving treatment. New data from various clinical

trials showed episodes of self-harm and potentially suicidal behavior were between 1.5 and 3.2 times higher in patients under 18 taking the drug than in those receiving a placebo.

Merck's Proscar may have role in preventing prostate cancer

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/840A452E4DCA243285256D50004D1A3F?opendocument&id=>

A National Cancer Institute study suggests that Merck's Proscar may reduce prostate cancer risk by 25 percent, news sources report citing research reported on the NEJM Web site. The lead researchers of the study say that men with a high risk of prostate cancer might consider taking the drug as a preventative measure. However, the study results are not without controversy.

"This is the first intervention that has proved to reduce a man's risk of prostate cancer," lead researcher of the study Dr. Ian Thompson is quoted as saying. The seven-year study, which included nearly 19,000 participants, found that 24 percent of the men given a placebo developed prostate cancer compared to just 18 percent of those taking Proscar. However, of those in the Proscar group that did develop prostate cancer, the disease appeared to be an aggressive form -- occurring in 6.4 percent of the Proscar group compared to 5.1 percent taking the placebo. The study results are likely to provoke debate among medical experts. Dr. Peter T. Scardino, a urologist from Memorial Sloan-Kettering Cancer Center, in an accompanying editorial, said that he wouldn't advise using the drug to prevent prostate cancer. Other medical experts echoed his scepticism over the positive study results and added that there are still important unanswered questions about the drug in this role. Proscar, which was approved in 1992 as a treatment for benign prostatic hyperplasia, is also sold in a lower-dose form as Propecia, an alopecia treatment. The combined sales of the two versions of the drug were \$550 million last year. According to news sources, Merck might use the study results to seek expanded regulatory approval for the drug's use in the prevention of prostate cancer. Increasing the market for Proscar could provide a boost Merck needs as it faces declining sales of Vioxx and Zocor, a news source reports.

Malpractice Woes Frustrate Fla. Doctors

<http://apnews1.iwon.com/article/20030626/D7RTCPA00.html>

With the Legislature having quit a special session this week unable to agree on how to make malpractice insurance more affordable for doctors, many lawmakers and physicians are in the same frustrated frame of mind. Doctors say they can't continue to practice - and with the Legislature so far unable to help lower their insurance rates, they are renewing warnings that many may simply close their offices and move out of state. While critics say it's a veiled threat meant to intimidate legislators, doctors say they're weary

of legislative inaction and can't promise they'll all still be here at the end of the year. "Doctors are very exasperated and what's going to happen I have no idea," Florida Medical Association CEO Sandra Mortham said Wednesday.

Patrick Hinton, executive director of a much smaller group, the Jacksonville Orthopedic Institute, also doesn't know what will happen if the 22 doctors there don't get relief on their rates, which are scheduled to go up by more than half in September. "We know we can't tolerate those kinds of increases," said Hinton. "What we will do ultimately if we don't get anything done, I have no idea, but I will tell you it's not an issue we can continue to deal with." "Who is John Galt?" The Legislature gave up Tuesday after a week in special session trying to fix the crisis. Both the Senate and House propose to try to lower rates in part by limiting lawsuit damages, which the insurance industry blames for high premiums. But they can't agree on how to cap damages. Two physicians at the Jacksonville Orthopedic Institute are talking about leaving, Hinton said, echoing a refrain heard around the state for nearly a year now: If something isn't done, access to health care is in jeopardy for many patients. State Sen. Dennis Jones said he isn't buying the threat. Jones is a chiropractor in St. Petersburg, and just down the street a new ophthalmology practice has opened with several doctors. Jones said it seems to him that there are lots of new doctors looking for patients, and he said the numbers bear that out. "Last year 1,249 medical doctors passed the state board," said Jones. "These new people aren't coming to Florida to take the Florida board and then go practice in Wyoming." There aren't any firm estimates of how many doctors have left Florida because of higher insurance rates. "The doctors are not taking out a full page ad saying, 'I'm leaving the state,'" said Mortham. "They're very quietly closing their offices." Florida Hospital Association lobbyist Bill Bell said hospitals are having a hard time keeping doctors too. Most are trying to hold out as long as possible, he said. "(To leave) goes against their natural grain," Bell said. "They're trying to do the best they can and provide the community with as much care as they can give."

Aventis reveals generic threat to Lovenox

<http://main.pslgroup.com/news/industrynews.nsf/IndNFrameSet?OpenForm&id=&new sid=86F8EC0CE35475C785256D51004A6BC2&ref=&u=http://news.ft.com/servlet/ContentServer?pagename=FT.com/StoryFT/FullStory&c=StoryFT&cid=1054966447028&p=1012571727117>

Aventis, the French pharmaceuticals group, said on Thursday it was facing a generic challenge to a US patent for Lovenox, its blood-thinning drug used to treat deep-vein thrombosis, which had sales of ?1.56bn (\$1.8bn) last year. Shares in the company fell 6.7 per cent to ?47.46 after it said Amphastar Pharmaceuticals of the US had filed an application with the Food and Drug Administration to develop and market a generic version of Lovenox - its second-biggest selling drug. However, Aventis said the move was "not

unexpected" since the five-year non-patent data exclusivity over the drug's enoxaparin sodium compound expired in 1998. France's largest drugs maker also sought to play down the threat to Lovenox, claiming that "generic competition is neither certain nor imminent". It said a second patent for the drug did not expire until December 2004, preventing Amphastar from launching a generic competitor before then. It has also applied for a modification of the challenged patent, which it said could be completed by the end of 2004.

Fears about a generic threat to Lovenox were heightened in April, when Aventis said a generic application challenging the drug had been published in error on the FDA's website and was later withdrawn. Analysts said the latest challenge would damage sentiment over Aventis, but they were sceptical about the chances of a successful generic threat to Lovenox, because the complexity of the drug's molecular structure was difficult to replicate. Aventis said: "Some products claiming to be enoxaparin sodium have been removed from the market by regulatory authorities in some countries due to lack of equivalency." For investors, the growing uncertainty over patent disputes has become almost as big a concern as the large number of drugs approaching the end of their patent life. Aventis is already facing a generic challenge to Allegra, its blockbuster allergy drug with sales of \$2bn last year, after Dr Reddy's Laboratories of India said this year it planned to launch a copycat version in the US. Lovenox suffered a disappointing year in 2002, due to overstocking, but Aventis has forecast sales growth of 15 per cent this year, and analysts forecast the drug could reach sales of \$2.5bn by 2007.

FDA to post company responses to warning letters on Web site

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/A0DA6E59C819CF7185256D4E00683AAA?opendocument&id=>

The FDA has announced that it will begin posting company responses to warning letters on its Web site on a trial basis beginning in three months, a news source reports. After six months, the agency will evaluate the programme and determine whether to continue it. The programme is part of the FDA's response to a 1999 citizens' petition that asked it to post records relating to warning letters. The agency retains the right not to post a response if it feels that the public would be misled about the product's safety or efficacy, the news source reports. "If during the pilot programme the agency determines that the public is being misled, experiences undue burden in dealing with the process or finds that the process is too resource-intensive, FDA may discontinue the program," the agency is quoted as saying in a statement.

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Hypereosinophilic Syndrome

Chronic Neuropathic Pain

Correction: Diffuse Cerebral Infarction after Cardiac Arrest

Interstitial Pneumonitis Related to Rituximab Therapy

Neutropenia in Patients Treated with Rituximab

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Journal of the American Medical Association

JAMA 2003;289 3207

<http://jama.ama-assn.org/cgi/content/full/289/24/3207?etoc>

Original Contributions

Influence of Estrogen Plus Progestin on Breast Cancer and Mammography in Healthy Postmenopausal Women: The Women's Health Initiative Randomized Trial

JAMA 2003;289 3243-3253

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3243?etoc>

Relationship Between Long Durations and Different Regimens of Hormone Therapy and Risk of Breast Cancer

JAMA 2003;289 3254-3263

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3254?etoc>

Neurobehavioral Outcomes of School-age Children Born Extremely Low Birth Weight or Very Preterm in the 1990s

JAMA 2003;289 3264-3272

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3264?etoc>

Renal Insufficiency in the Absence of Albuminuria and Retinopathy Among Adults With Type 2 Diabetes Mellitus

JAMA 2003;289 3273-3277

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3273?etoc>

US Military Smallpox Vaccination Program Experience

JAMA 2003;289 3278-3282

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3278?etoc>

Myopericarditis Following Smallpox Vaccination Among Vaccinia-Naive US Military Personnel

JAMA 2003;289 3283-3289

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3283?etoc>

Focal and Generalized Folliculitis Following Smallpox Vaccination Among

Vaccinia-Naive Recipients

JAMA 2003;289 3290-3294

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3290?etoc>

Response to Smallpox Vaccine in Persons Immunized in the Distant Past

JAMA 2003;289 3295-3299

<http://jama.ama-assn.org/cgi/content/abstract/289/24/3295?etoc>

Contempo Updates

Sarcoidosis

JAMA 2003;289 3300-3303

<http://jama.ama-assn.org/cgi/content/full/289/24/3300?etoc>

Editorials

Combined Hormone Therapy and Breast Cancer: A Single-Edged Sword

JAMA 2003;289 3304-3306

<http://jama.ama-assn.org/cgi/content/full/289/24/3304?etoc>

Smallpox Immunization in the 21st Century: The Old and the New

JAMA 2003;289 3306-3308

<http://jama.ama-assn.org/cgi/content/full/289/24/3306?etoc>

Letters

Adverse Drug Effects in Ambulatory Elderly Patients

JAMA 2003;289 3238

<http://jama.ama-assn.org/cgi/content/full/289/24/3238?etoc>

Adverse Drug Effects in Ambulatory Elderly Patients--Reply

JAMA 2003;289 3238

<http://jama.ama-assn.org/cgi/content/full/289/24/3238-a?etoc>

Adverse Drug Effects in Ambulatory Elderly Patients--Reply

JAMA 2003;289 3238-3239

<http://jama.ama-assn.org/cgi/content/full/289/24/3238-b?etoc>

Measuring Functional Status and Disability in Older Adults

JAMA 2003;289 3239

<http://jama.ama-assn.org/cgi/content/full/289/24/3239?etoc>

Measuring Functional Status and Disability in Older Adults--Reply

JAMA 2003;289 3239-3240

<http://jama.ama-assn.org/cgi/content/full/289/24/3239-a?etoc>

Handling Conflicts of Interest Between Industry and Academia

JAMA 2003;289 3240

<http://jama.ama-assn.org/cgi/content/full/289/24/3240?etoc>

Handling Conflicts of Interest Between Industry and Academia--Reply

JAMA 2003;289 3240-3241

<http://jama.ama-assn.org/cgi/content/full/289/24/3240-a?etoc>

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Prescriptions for Estrogen Replacement Therapy in Ontario Before and After
Publication of the Women's Health Initiative Study

JAMA 2003;289 3241-3242

<http://jama.ama-assn.org/cgi/content/full/289/24/3241?etoc>

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Accelerated Approval Scrutinized: Confirmatory Phase 4 Studies on New Drugs
Languish

JAMA 2003;289 3227-3229

<http://jama.ama-assn.org/cgi/content/full/289/24/3227?etoc>

Use of Biologics for Rheumatoid Arthritis Tempered by Concerns Over Safety,
Cost

JAMA 2003;289 3229-3230

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The Cover

Mountain Fire

JAMA 2003;289 3211

<http://jama.ama-assn.org/cgi/content/full/289/24/3211?etoc>

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Case History: Persephone

JAMA 2003;289 3215

<http://jama.ama-assn.org/cgi/content/full/289/24/3215?etoc>

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THEORY AND PRACTICE.

JAMA 2003;289 3358

<http://jama.ama-assn.org/cgi/content/full/289/24/3358?etoc>

JAMA Patient Page

Diabetes and the Kidney

Sharon Parmet, Cassio Lynm, and Richard M. Glass

JAMA 2003;289 3372

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Website of the Day

RxPatrol (Pattern Analysis Tracking Robberies and Other Losses)

rxpatrol.org

RxPATROLT is a collaborative effort between industry and law enforcement designed to collect, collate, analyze and disseminate pharmacy theft information. Theft report forms are available for completion, which then allow appropriate investigation. RxPATROLT analyzes all available data and provide it to the respective law enforcement agencies for action as they deem appropriate. Run by Purdue Pharma (yeah of OxyContin Fame) this website is innovative and important but not clinically useful. FYI

Answer of the Day

In decreasing order of 2002 Sales, the Top 10 Drugs....drum roll please

1. Lipitor- 6.1 billion
2. Zocor- 4.2 billion

3. Prevacid- 3.7 billion
4. Prilosec- 3.5 billion
5. Procrit- 3.1 billion
6. Zyprexa- 2.9 billion
7. Epogen- 2.8 billion
8. Celebrex- 2.6 billion
9. Zoloft- 2.5 billion
10. Paxil- 2.3 billion