NEW DRUGS

Influenza Vaccine (Afluria)
The U.S. Food and Drug Administration (FDA) has approved Afluria, a seasonal influenza vaccine for immunizing people 18 years of age and older against influenza type A and type B flu viruses.

Manufactured by CSL Ltd. of Australia, the vaccine received accelerated approval. In this case, the company demonstrated that the vaccine induced levels of antibodies in the blood likely to be effective in preventing seasonal influenza.

Afluria contains inactivated influenza viruses grown in chicken eggs. People who are allergic to eggs or any other component of the vaccine should not receive this vaccine.

Administered as a single injection in the upper arm, Afluria is available in a single-dose, preservative-free, prefilled syringe or in a multidose vial with thimerosal, a mercury derivative, as a preservative.

(Source: FDA, October 1, 2007.)

Raltegravir (Isentress) For HIV Infection
Raltegravir tablets (Isentress, Merck) have been approved for the treatment of human immunodeficiency virus (HIV)-1 infection, in combination with other antiretroviral agents, in patients who have received other therapies and who have evidence of viral replication and HIV-1 strains that are resistant to multiple antiretroviral agents.

Raltegravir is the first agent of the pharmacological class known as HIV integrase strand transfer inhibitors, which are designed to interfere with the enzyme needed by HIV-1 in order to multiply. When raltegravir is used with other anti-HIV medications, it may reduce the amount of HIV in the blood and may increase the number of white blood cells that help fight off other infections.

(Source: FDA, October 17, 2007.)

Sevelamer Carbonate (Renvela) For Dialysis Patients
The FDA has granted marketing approval of Genzyme’s sevelamer carbonate (Renvela) for the control of serum phosphorus in patients with chronic kidney disease on dialysis.

Renvela is considered to be an improved version of Renagel (sevelamer HCl), a common phosphate binder. Like Renagel, Renvela is free of calcium and metals, and it has the added benefit of a carbonate buffer. It will initially be available as an 800-mg tablet.

Genzyme expects to launch Renvela for dialysis patients in the U.S. in early 2008. Renagel will continue to be available, with the long-term goal of switching patients to Renvela.

(Source: Genzyme, October 22, 2007; www.renvela.com.)

Generic Trileptal for Seizures
The first generic versions of oxcarbazepine (Trileptal, Novartis), an anticonvulsant drug, have been approved. Oxcarbazepine is indicated for use alone or in combination with other medications to treat partial seizures in adults and children four years of age and older.

The tablets will be available in three strengths (150 mg, 300 mg, and 600 mg) and are manufactured by Roxane Laboratories, Glenmark Pharmaceuticals Ltd., and Sun Pharmaceutical Industries Ltd. (Source: FDA, October 10, 2007.)

Doripenem (Doribax) For Complicated Infections
The FDA has approved doripenem for injection (Doribax, Ortho-McNeil) as a new treatment for complicated intra-abdominal and complicated urinary tract infections, including pyelonephritis. Doripenem is active against a wide range of gram-positive and gram-negative bacteria, including Pseudomonas.

As an antibacterial carbapenem, doripenem is indicated as a single agent for the treatment of complicated intra-abdominal infections caused by susceptible strains of Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides caccae, Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Staphylococcus intermedius, Streptococcus constellatus, or Peptostreptococcus micro. It is also used to treat complicated urinary tract infections, caused by susceptible strains of E. coli, including cases with concurrent bacteremia, K. pneumoniae, Proteus mirabilis, P. aeruginosa, or Acinetobacter baumannii.

The approval of doripenem was based on results of two multicenter, prospective, randomized, double-blind clinical trials. (Source: Ortho-McNeil, October 15, 2007.)

Ixabepilone (Ixempra) For Advanced Breast Cancer
Patients with advanced breast cancer that has not responded to other anticancer drugs may soon have a new treatment option. Ixabepilone (Ixempra, Bristol-Myers Squibb) has been approved for use in combination with another cancer agent, capecitabine (Xeloda, Roche), in patients who no longer benefit from treatment with an anthracycline (such as doxorubicin [Adriamycin, Bedford]) and a taxane (such as paclitaxel [Taxol, Bristol-Myers Squibb] or docetaxel [Taxotere, Sanofi-Aventis]). Ixabepilone is also approved for use alone in patients who no longer benefit from an anthracycline, a taxane, and capecitabine.

In one phase 2 study, ixabepilone was...
evaluated alone in 126 patients, of whom 88% had received at least two lines of prior chemotherapy. Researchers found clinically significant tumor shrinkage in 12%. The responses, they report, were “durable and notable;” median durations of response and progression-free survival were 5.7 and 3.1 months, respectively. Median overall survival was 8.6 months.

In another trial involving 752 patients, a combination of ixabepilone and capetitabine was compared with capetitabine alone. The combination treatment was better at delaying cancer progression or death.

The drug binds to cancer cell microtubules, which play a role in cell division. Patients taking ixabepilone should not take drugs that are strong inhibitors of cytochrome CYP 3A4, one of the enzymes that metabolizes ixabepilone. Other women who should not take this drug are those who have had severe allergic reactions to drugs that contain Cremophor (a stabilizer) or its derivatives or women with baseline bone marrow suppression.

Side effects include peripheral neuropathy, bone marrow suppression, constipation, nausea, vomiting, muscle pain, joint pain, fatigue, and general weakness.

(Source: FDA, October 22, 2007.)

NEW INDICATIONS

Docetaxel (Taxotere) plus 5-FU For Head and Neck Cancer

Docetaxel (Taxotere Injection Concentrate, Sanofi-Aventis), combined with cisplatin and 5-fluorouracil (5-FU), is now approved for induction therapy for locally advanced squamous cell carcinoma of the head and neck before patients undergo chemoradiotherapy and surgery.

The FDA based its approval on the results of a phase 3 randomized, open-label, international trial (TAX 324) that established the efficacy and safety of the docetaxel-based regimen in significantly improving survival.

Docetaxel is also indicated for patients with breast cancer, non–small cell lung cancer, and prostate cancer.

(Source: Sanofi-Aventis, October 1, 2007.)

Bortezomib (Velcade) For Impaired Kidney Function In Multiple Myeloma

Millennium Pharmaceuticals has announced the FDA’s approval of bortezomib (Velcade), without dose adjustments, for use in patients with impaired kidney function, including patients who need dialysis. Impaired kidney function is a common complication related to multiple myeloma.

The label expansion is based on data from a prospective phase 1 trial. Bortezomib was approved in 2003.

The drug is being co-developed with Johnson & Johnson. For a limited period of time, Millennium and Ortho Biotech are co-promoting bortezomib in the U.S.

In the U.S., this product is indicated for patients with multiple myeloma who have received at least one prior therapy and for patients with mantle cell lymphoma who have received at least one prior therapy.

(Source: Millennium, October 15, 2007.)

Bacterial Meningitis Vaccine (Menactra) for More Ages

The FDA has expanded the approved age range for Menactra (Sanofi-Pasteur), a bacterial meningitis vaccine, to include children two to 10 years of age.

Menactra was first approved in January 2005 for children and adults from 11 to 55 years of age. Previously, Menumune was the only meningococcal vaccine available in the U.S. for use in children two years of age and older. Both vaccines offer protection against four groups of Neisseria meningitidis, the bacterium that can cause meningitis.

In clinical trials, Menactra produced an immune response one month after vaccination in people ages 2 to 55 years of years.

Although Guillain-Barré syndrome (GBS) was not observed in these trials, a possible but unproven risk was noted in some adolescents after they received Menactra, occurring in an estimated one person in one million vaccine recipients. As a precaution, people who have had GBS should not receive this vaccine.

The FDA and CDC will continue to monitor the safety of Menactra through their joint Vaccine Adverse Event Reporting System.

(Source: FDA, October 19, 2007.)

NEW FORMULATIONS

Oral Terbinafine (Lamisil) For Scalp Ringworm

Terbinafine HCl (Lamisil Oral Granules, Novartis) has been approved for the treatment of tinea capitis, a fungal infection of the scalp, in children four years of age and older. Tinea capitis most commonly affects children and is often characterized by severe itching, dryness, and bald patches. This contagious infection does not usually respond to topical treatment.

The granules can be sprinkled on food and are administered once a day for six weeks. The actual dosage is based on the child’s weight.

(Source: FDA, October 1, 2007.)

Oral Topotecan (Hycamtin) For Relapsing Small Cell Lung Cancer

The FDA has approved oral topotecan (Hycamtin) capsules for patients with relapsed small cell lung cancer (SCLC). This agent is indicated for patients who have had a complete or partial response to first-line chemotherapy and who are at...
least 45 days from the end of that treatment.

The capsules, to be available in 2008, are the only oral single-agent chemotherapy agent approved for SCLC after frontline therapy has been unsuccessful.

Hycamtin is a topoisomerase I (topo-I) inhibitor. Topo-I is a naturally produced protein essential for cell division in both normal and cancer cells. Interaction between topo-I and Hycamtin results in permanent damage to the cell’s genetic material and in the death of dividing cells. The capsules have a mild-to-moderate nonhematological toxicity profile.

(Source: GlaxoSmithKline, October 15, 2007.)

Diclofenac Topical Gel (Voltaren)

Diclofenac sodium topical gel 1% (Voltaren, Novartis) has been approved as the first topical prescription treatment that patients can apply directly to sites of pain associated with osteoarthritis, a condition in which the cartilage in the joint breaks down.

Voltaren Gel is a nonsteroidal anti-inflammatory drug (NSAID) that can be used to treat pain associated with osteoarthritis in joints amenable to topical treatment (e.g., the knees and hands).

The gel has a favorable safety profile. Its systemic absorption is 94% less than the comparable oral diclofenac treatment. However, it should not be administered to asthmatic patients or to those with urticaria or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.

This product is contraindicated for treating perioperative pain in the setting of coronary artery bypass graft surgery, and it should not be used in combination with other oral NSAIDs or aspirin.

The combined use of the gel with other topical products, such as sunscreens and cosmetics, on the same skin area has not been tested and should be avoided because of the potential to alter local tolerability and absorption.

Voltaren is also available as 25-, 50-, and 75-mg tablets.

(Source: Novartis, October 22, 2007; www.voltarengel.com.)

New Dosage: Clopidogrel Bisulfate (Plavix)

Sanofi-Aventis and Bristol-Myers Squibb have announced the approval of a supplemental New Drug Application (sNDA) for a 300-mg tablet of clopidogrel bisulfate (Plavix) for acute coronary syndrome (ACS) patients as soon as possible after hospital admission. Currently available as a 75-mg tablet taken once a day, clopidogrel helps to prevent platelets from sticking together and forming clots. It was initially approved in 1997.

Acute ST-segment elevation myocardial infarction (STEMI), along with unstable angina and non-ST segment elevation myocardial infarction (NSTEMI), are the three conditions classified as ACS, a major cause of emergency medical care and hospitalization in the U.S.

The 300-mg tablet will be available in the U.S. later this year. It is also under review in Europe.

(Source: Sanofi-Aventis, September 27, 2007.)

Cetuximab (Erbitux) Label Adds Survival Data For Colorectal Cancer

The FDA has approved updated labeling for cetuximab (Erbitux, ImClone/Bristol-Myers Squibb) to include overall survival data. Cetuximab is indicated for the treatment of EGFR-expressing, metastatic colorectal carcinoma after unsuccessful regimens of both irinotecan (Camptosar, Pfizer) and oxaliplatin (Eloxatin, Sanofi-Synthelabo). As a single agent, cetuximab is also indicated for the treatment of EGFR-expressing metastatic colorectal cancer in patients intolerant to irinotecan-based regimens.

The approval of the sBLA is based on

DRUG NEWS

MRSA Infections Increasing

The Centers for Disease Control and Prevention (CDC) reports that nearly 19,000 people died in the U.S. in 2005 after being infected a virulent drug-resistant bacterium, methicillin-resistant Staphylococcus aureus (MRSA). The number of deaths associated with MRSA exceeds those attributed to AIDS, Parkinson’s disease, emphysema, and homicide each year.

Most invasive MRSA infections were associated with health care treatment. In hospitals, the bacteria can be transported from patient to patient by doctors, nurses, and unsterilized equipment. In addition, busy hospital workers often disregard basic standards of hand-washing. Some hospitals have reduced infection rates by isolating infected patients and requiring workers to wear gloves and gowns for every contact.

First isolated in the U.S. in 1968, MRSA causes 10% to 20% of all infections acquired in health care settings. The bacteria are resistant to several front-line antibiotics and can cause infections of a surgical site, in the urinary tract, and in the lungs. These opportunistic bacteria can be brought unknowingly into hospitals and nursing homes by asymptomatic patients, and they can enter the bloodstream through incisions and wounds. They can then overwhelm a weakened immune system.

The new study found higher prevalence and death rates for the elderly, African-Americans, and men.

prolonged overall survival from a randomized, multicenter, phase 3 trial comparing cetuximab plus best supportive care with best supportive care alone in 572 patients after unsuccessful irinotecan-based and oxaliplatin-based regimens.

(Sources: Bristol-Myers Squibb and ImClone, October 2, 2007; www.erbitux.com.)

**Retaining Potency Of Thyroid Drugs**

The FDA is tightening standards for levothyroxine sodium (e.g., Synthroid, Abbott), to ensure that the drug’s potency is retained over its entire shelf life. More than 13 million patients use levothyroxine to treat underactive thyroid glands and other thyroid conditions. Currently, these thyroid products are allowed a potency range of 90% to 110%. The FDA is mandating a stricter range of 95% to 105%. Manufacturers and marketers have two years to comply with the revised specification.

The FDA received data from manufacturers of all approved, marketed levothyroxine products made between July 2003 and June 2005. The data revealed a trend toward a loss of potency: some preparations showed a potency approaching 90% of labeled potency by the expiration date; some rapidly degraded over their labeled shelf life; some package types (blister packs) degraded more rapidly than others; and expiration dating periods varied among products from different manufacturers.

Some tablets remain stable, losing less than 5% of their labeled potency within 24 months, but other products lose almost 10% of their labeled potency in nine months. The agency hopes to reduce this variability, which could have clinical consequences in achieving target thyroid levels, especially for the patients with thyroid cancer.

(Source: FDA, October 4, 2007.)

**FDA in the News**

**New Drug Safety Law**

Under a bill that President Bush has signed into law, the FDA will have broader responsibilities to ensure the safety of prescription drugs. For example, the agency’s focus would shift from experimental drugs pending approval to those already on the market. The FDA would have more power to require drug companies to perform additional studies, to fine companies for not completing follow-up studies, and to require fees from drug companies and medical device makers to cover the costs of hiring, updating technology, and expanding safety monitoring. At the same time, the FDA would be required to become more active in its surveillance of new safety problems with drugs.

(Source: Associated Press, September 27, 2007.)

**Faster Reviews for Generics**

Generic drugs may soon get speedier FDA reviews. New policies have been
designed to reduce the backlog of more than 1,300 drugs awaiting approval.

A lack of resources has prevented the FDA’s Office of Generic Drugs from keeping pace with the growing number of applications for copies of medications whose patents expired or were challenged.

The agency approved or tentatively cleared 682 generic drugs in the fiscal year ending September 30, 2007, up by more than 30% from the previous year. The FDA currently takes 16 to 17 months to review an application.

The new policies include priority reviews for drugs that are the first of their type and that are not subject to litigation. Previously, the agency reviewed applications in the order in which they were submitted. The FDA is also shifting to electronic data submission and communications.

(Source: Bloomberg News, October 4, 2007.)

New Drug Research Center: Problems in Store?
The FDA is planning to launch a drug research center to be paid for by the companies it regulates. The goal is to improve the development of drugs and medical devices.

However, some consumer advocates suggest that the new partnership might increase the FDA’s vulnerability to industry influence. Some critics worry that drugs might be developed more cheaply, thus improving pharmaceutical manufacturers’ profits, but might not necessarily result in safer and less expensive drugs for consumers. Some also say the FDA is too accommodating to drug companies.

It remains to be seen whether one problem might be resolved: the imbalance between how much companies spend on drug research and the number of drugs that make it to market. Companies spend on average almost 15 years and $1 billion to bring a new drug to market, and the drug-development process can involve tracking up to 15,000 patients for as long as five years.

(Source: Associated Press, October 15, 2007.)

Sudden Hearing Loss: Labels For Erectile Dysfunction Drugs Revised
Labeling changes have been approved for erectile dysfunction drugs such as Cialis, Levitra, and Viagra, to display the potential risk of sudden hearing loss in a more prominent fashion. The FDA plans to require the same changes for Revatio, which is used to treat pulmonary arterial hypertension (PAH).

The FDA asked for the label revisions after a small number of patients taking these drugs reported sudden hearing loss, sometimes accompanied by ringing in the ears and dizziness.

Patients taking Cialis, Levitra, or Viagra who experience sudden hearing loss should immediately stop taking the drug and should seek prompt medical attention.

Those using Revatio should contact their health care providers if they experience sudden hearing problems. Because Revatio is used to treat a potentially life-threatening condition, the FDA recommends that patients do not stop taking it abruptly.

The FDA found a total of 29 postmarketing reports of sudden hearing loss, both with and without accompanying tinnitus, vertigo, or dizziness. In most cases, the hearing loss involved one ear. In one third of cases, the event was temporary.

Although no causal link has been confirmed, the strong relationship between the use of these drugs and sudden hearing loss warrants revisions to the product labeling for this drug class.

(Source: J Laryngol Otol April 2007; FDA, October 19, 2007.)

Myocardial Infarction Redefined
A long-awaited universal definition of myocardial infarction (MI) has been released. A global task force with expertise in biomarkers, electrocardiographic (ECG) criteria, imaging, interventions, clinical trials, and public policy has updated the consensus document from the year 2000. The revised definition is being published simultaneously in European Heart Journal, Journal of American College of Cardiology, and Circulation.

The new definition is important for several reasons. Defining a disease enables clinicians to label patients (make a diagnosis); labeling has implications for patients with respect to their relationships to the medical community and to the rest of society. For example, receiving a diagnosis of MI may change a person’s ability to perform certain jobs.

Unfortunately, clinicians and clinical scientists often define the same disease in different ways. Characteristics that define a disease in one country might be interpreted differently by physicians in another country. This makes it difficult to compare the results of various studies of patients with a particular disease.

Such is the case with MI. Past attempts to arrive at a standard definition failed, often because of evolving diagnostic technology and confusion surrounding the suggested definition. The first consensus committee recommended that MI be qualified by referring to the amount of heart muscle loss, to the circumstances leading to the infarct, and to the timing of the heart muscle cell death in relation to the time of the observation.

How to label small elevations in blood troponin that occur following percutaneous coronary intervention (PCI) is still controversial. Most delegates favored calling these tiny procedure-related
episodes of myocardial injury “true” in-farcts because they occurred in the setting of recognizable coronary arterial ischemic interventions. However, it was felt that these PCI-related events should be distinguished from spontaneous (“wild-type”) MI, which usually presents with the traditional clinical scenario of substernal chest discomfort, accompanied by ischemic electrocardiographic changes and resulting from rupture of an atherosclerotic coronary arterial lesion.

The changes in the definition of an MI have serious consequences for less developed and developing countries. The definition should be used by developed countries immediately and by developing countries as quickly as resources become available.

(Sources: European Society of Cardiology, American College of Cardiology, American Heart Association, and World Heart Federation, October 19, 2007.)

**Future Blood Test For Alzheimer’s Disease?**

Researchers at Stanford University School of Medicine have identified some distinctive proteins in the blood of patients with Alzheimer’s disease (AD) that could be used to diagnose the condition more effectively.

Doctors generally diagnose AD only by eliminating other possible causes of mental decline. Only after a patient dies can surgeons examine brain tissue to look for the protein plaques and tangles that are the hallmark of the disease.

Researchers are trying to change that situation by finding biomarkers. The Stanford team reported the discovery of 18 proteins that together seemed fairly diagnostic of AD. If the biomarkers are confirmed by more rigorous testing, they could result in a simple blood test to diagnose the disease. Patients could then take medications to delay the effects of AD.

Scientists are using spinal taps or high-powered imaging studies on living patients, although examining the blood is easier and may be less expensive than those methods.


**Reducing Cardiac Events Before Surgery**

People with heart disease should take special precautions before undergoing all operations, even noncardiac surgery, to reduce their risk of a cardiac event, according to new joint guidelines issued by the American College of Cardiology and the American Heart Association. The guidelines update those from 2002. Some of the new recommendations are as follows:

- Patients should not stop taking cholesterol-lowering drugs before surgery.
- Many heart patients can safely have noncardiac surgery without first correcting their heart disease with an artery-opening procedure or coronary bypass grafting.
- For non-emergency procedures, bypass surgery or angioplasty is rarely necessary to lower the risk of surgery unless the patient needs the intervention anyway.
- If the noncardiac surgery is an emergency, heart testing should be forgone and patients should be taken straight to the operating room.

Patients should be evaluated and treated before noncardiac surgery only for active cardiac conditions such as severe angina, decompensated heart failure, significant arrhythmias, and severe heart valve disease.

- Patients needing elective noncardiac surgery and an artery-opening procedure beforehand should receive angioplasty with a bare metal stent, followed by four to six weeks of anticoagulation therapy.
- For patients with a drug-eluting coronary stent who need urgent noncardiac surgery that requires stopping the prescription anticoagulation drug, aspirin therapy should continue, if feasible; prescription medication should be restarted as soon as possible.
- Patients with two or more blocked blood vessels, unstable angina, or heart attack symptoms should have coronary artery bypass grafting or angioplasty before undergoing noncardiac surgery.
- Preoperative testing should be limited to circumstances in which test results would affect treatment.

(Source: Circulation, September 27 and October 23, 2007.)

**Antibiotics for Pneumonia: What’s the Best Length Of Time?**

What’s the best duration of treatment for community-acquired pneumonia?

Current guidelines suggest five to 14 days, but a study by San Francisco Veterans Affairs researchers suggests that adults with mild-to-moderate pneumonia can be treated safely and effectively in seven days or less.

The researchers examined 15 randomized, controlled trials involving almost 2,800 inpatients and outpatients. Four of the antibiotic classes most commonly used for community-acquired pneumonia (macrolides, fluoroquinolones, beta-lactams, and ketolides) were represented; most of the studies examined short-course macrolide antibiotics.

No significant differences were noted between short-course and extended-course regimens in terms of clinical success, mortality, bacteriological success, or adverse drug events. The results were
consistent across a wide range of analyses, including individual antibiotic classes. The researchers add a caveat: most of the trials had included only mild-to-moderate pneumonia, and elderly patients were generally underrepresented. Even in the inpatient studies, respiratory failure and septic shock were common exclusion criteria. Therefore, although the results of this meta-analysis should be generalizable to most adults, they cannot be extrapolated to patients with severe community-acquired pneumonia. (Source: Am J Med 2007;120:783–790.)

No Reason To Stint on Stents For Older Patients

A patient’s age isn’t necessarily a good reason to not try a sirolimus-eluting stent, according to a German study of 6,755 patients.

The sirolimus stents resulted in “an impressive relief of angina,” the researchers reported. In-hospital (1%) and six-month (4%) mortality rates, as expected, were higher in patients older than 75 years of age. Older patients had a higher risk of renal failure, diabetes, hypertension, and triple-vessel disease; they also had a higher incidence of smaller vessels, left main disease, and vein graft interventions. However, the main finding of the study—representing a real-world scenario—was that six months after stent implantation, the rate of nonfatal complications such as myocardial infarction and the need for another target vessel revascularization, was equal or even lower in patients over 80 years of age, compared with the rate in younger patients.

More information about sirolimus stents appears on page 599. (Source: Am Heart J 2007;154:682–687.)

Beta Blockers and New-Onset Diabetes

Treating patients with beta blockers for hypertension may heighten their risk of diabetes, say researchers from New York and Israel. Findings from their analysis of 12 studies involving 94,492 patients suggest that beta-blocker therapy leads to a 22% higher risk.

Atenolol and metoprolol raised the risk by as much as 34%, compared with other agents. The studies evaluating propranolol (Inderal, Wyeth), by contrast, showed a trend toward lowering the risk by 23%, although the studies were heavily weighted by comparison with diuretics, the researchers add.

Elderly patients and those with higher baseline fasting glucose levels and higher baseline body mass indexes were most vulnerable. The researchers also found that risk increased “exponentially” with a longer duration of beta-blocker therapy.

Beta blockers also raised the risk of stroke by 15%.

Given that 65 million Americans have hypertension, the researchers concluded that beta-blocker treatment could lead to 910,000 cases of diabetes, 195,000 deaths, and 305,500 excess strokes—“hardly an acceptable risk–benefit ratio,” they note. (Source: Am J Cardiol 2007;100:1254–1262.)

Inappropriate Prescribing In the Emergency Room

One-third of older emergency department (ED) patients may be taking a potentially inappropriate medication, according to a retrospective analysis from Cleveland Clinic and MetroHealth Medical Center.

The average number of medications taken per patient was 8.4. Of the 352 patients, 111 (32%) were taking at least one potentially inappropriate drug when they arrived at the ED. Propoxyphene/acetaminophen (Darvocet, Xanodyne), muscle relaxants, and antihistamines were the most common ones.

Among 101 patients discharged home with a new prescription, 13% received potentially inappropriate prescriptions, most commonly propoxyphene/acetaminophen, diazepam (Valium, Roche), cyclobenzaprine (Flerexil, McNeil), and diphenhydramine (Benadryl, Johnson & Johnson).

In contrast to earlier studies, this study focused on drugs reported in the usual medication lists of older ED patients, who may be at a higher risk for future adverse drug events. Unlike medications prescribed from the ED, which are often intended for short-term use, many of the drugs in this study are likely to be taken for a longer time. Patients with painful musculoskeletal problems may be at even higher risk: Darvocet and muscle relaxants accounted for 11% of all inappropriate prescriptions in outpatient medication lists.

The medications on the list have been associated with increased morbidity and mortality in older patients. Education to enhance awareness of medication risks in older patients is needed for all health care groups, the researchers suggest; they say that the physician–patient interaction in the ED provides a good opportunity for improving care.

Even if emergency physicians in the study had focused only on the three most common inappropriate drugs (Darvocet, muscle relaxants, and routine outpatient use of antihistamines), they could have reduced the number of potentially inappropriate prescriptions by nearly 15%. (Source: Am J Emerg Med 2007;25:804–807.)

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**NEW DRUGS**

**Drug News**

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**Antibiotic Resistance Impedes Therapy for *H. pylori* Infection**

These days, first-line therapy for *Helicobacter pylori* infection consists of a proton pump inhibitor (PPI) plus an antibiotic, such as clarithromycin (Biaxin, Abbott) and amoxicillin (Amoxil, GlaxoSmithKline) or a nitroimidazole. However, recent studies have suggested that eradication rates might be dropping because of antibiotic resistance.

Researchers from Turkey compared one-week and two-week treatments in 80 patients with dyspepsia. The one-week group (PAC-1) received 40 mg of pantoprazole (Protonix, Wyeth), 1,000 mg of amoxicillin, and 500 mg of clarithromycin twice daily. The second group (PAC-2) received the same treatment for two weeks.

One month after the end of therapy, the patients underwent another endoscopy.

All 34 patients in each group who completed the study took the drugs as prescribed. Fifteen PAC-1 patients and 20 PAC-2 patients were found to be resistant to clarithromycin.

*H. pylori* was eradicated in four of the 15 patients and in 12 of the 20. Among the clarithromycin-sensitive patients, *H. pylori* infection was eradicated in 12 of the PAC-1 group and 13 of the PAC-2 group.

All 17 duodenal ulcers in both groups were healed. None of the patients discontinued the treatment as a result of adverse events.

Approximately one-third of patients in both groups reported mild side effects such as taste perversion, emesis, and diarrhea.

There was no consensus on how long PPI-based triple therapies should be maintained. The two-week treatment was associated with a 92.8% success rate in clarithromycin-sensitive patients; however, the rates of successful eradication of infection (26.7% for one week and 60% for two weeks) were disappointing in the clarithromycin-resistant patients.


**Prophylactic Norfloxacin (Noroxin) Improves Survival in Cirrhosis**

Spontaneous bacterial peritonitis, an infection of ascites, is a common cause of death in patients with cirrhosis. This infection can be cured with antibiotics, but hepatorenal syndrome may develop and patients sometimes die of severe hepatic and renal insufficiency. Therefore, it was thought that preventing spontaneous bacterial peritonitis might increase survival. In fact, primary prophylaxis with norfloxacin (Noroxin, Merck) did have a great impact in patients with advanced cirrhosis, according to researchers from Spain. They say that the drug can help significantly prolong survival—especially good news to a patient waiting for a liver transplant.

The investigators compared norfloxacin 400 mg/day with placebo in 68 patients with cirrhosis and ascites. The patients received follow-up visits every two months.

The main endpoints were survival at three months and at one year. The secondary endpoints included a one-year probability of developing spontaneous bacterial peritonitis and hepatorenal syndrome.

Spontaneous bacterial peritonitis developed in two patients in the norfloxacin group and in 10 patients in the placebo group. Spontaneous bacteremia occurred in none of the norfloxacin patients and in four of the placebo patients.

Similarly, renal failure was significantly less common with treatment: it affected seven patients receiving norfloxacin and 16 receiving placebo.

Hepatorenal syndrome developed within the first three months of follow-up in nine placebo patients but in only one norfloxacin patient. Ten norfloxacin patients and three placebo patients died. The cause of death was hepatorenal syndrome in five of the norfloxacin patients and in eight of the placebo patients.

Norfloxacin dramatically reduced the one-year probability of developing spontaneous bacterial peritonitis (7% vs. 61%) and the risk of hepatorenal syndrome (28% vs. 41%).

Treatment also improved the three-month (94% versus 62%) and the one-year (60% vs. 48%) probability of survival, compared with placebo.

Patients who developed spontaneous bacterial peritonitis received IV albumin to prevent hepatorenal syndrome, and this therapy was very effective. Hepatorenal syndrome associated with the infection affected only one of 12 patients with spontaneous bacterial peritonitis.

(Source: *Gastroenterology* 2007;133: 818–824.)

**Oral Polio Vaccine Spreads Disease in Nigeria**

A polio vaccine has been associated with a polio outbreak in Nigeria, leaving at least 69 children paralyzed. The outbreak was caused by the live poliovirus used in vaccines that are taken orally.

The oral route is preferred in developing countries, because it is cheaper and medical training is not necessary to dispense the vaccine. In the West, an inactivated virus is used.

The oral polio vaccine contains a weakened version of poliovirus. Children who have been vaccinated excrete the virus. Where unsanitary conditions exist, the virus can find its way into the water supply; it can also pass through children who have not been immunized.

More than 10 billion polio doses have been given to children worldwide, and the vaccine has reduced the incidence of...
polio incidence by more than 99% since 1988.

Many more children are paralyzed by the wild poliovirus than the virus spread by the vaccine.

(Source: The Associated Press, 2007.)

**Children Using More PPIs: Is Obesity the Cause?**

The number of young children taking prescription drugs for heartburn and other digestive problems has increased by more than 50% in recent years. A report by Medco Health Solutions suggests that more than two million children 18 years of age and younger used drugs for digestive or gastrointestinal complaints in 2006.

Acid-reducing drugs, or proton pump inhibitors (PPIs), are the most common medications prescribed for acid reflux associated with heartburn and gastroesophageal reflux disease. Heartburn is a common complication of being overweight. More than 10% of preschoolers and 30% of older children are considered overweight.

Heartburn and acid reflux are common in infants and young children. Some children need prescription drugs, but many recover with no treatment or by eating smaller, more frequent meals or fewer fatty foods.

More parents are asking doctors to prescribe medications for reflux in their children, partly because of direct-to-consumer marketing and also because they prefer a quick fix for symptoms that can include frequent regurgitation and irritability.

(Source: Associated Press, October 5, 2007.)

**Pramlintide (Symlin) Pen Injector for Diabetes**

Amylin Pharmaceuticals, Inc., has announced the approval of the Symlin Pen 120 and the Symlin Pen 60 devices for administering pramlintide acetate (Symlin) injection. The pre-filled pen injectors feature simple, fixed dosing to improve mealtime glucose control. For diabetic patients who use mealtime insulin, the addition of Symlin is thought to enhance glucose control with the potential for weight loss.

Symlin Pen 60 delivers 15, 30, 45, or 60 mcg of Symlin per dose. Symlin Pen 120 delivers 60 or 120 mcg per dose.

Both devices can be stored at room temperature not to exceed 86°F (30°C) after the first use. The devices should be available to patients by December 2007.

(Source: Amylin, October 1, 2007.)

**NEW MEDICAL DEVICES**

**Marvin M. Goldenberg, PhD, RPh, MS**

**Name:** ProLipo Laser Module  
**Manufacturer:** Sciton, Palo Alto, CA  
**Approval Date:** July 12, 2007  
**Use Classification:** The module is indicated for laser-assisted lipolysis, and its broadband-pulsed light was approved for the treatment of wrinkles.

**Description:** The ProLipo laser module provides a minimally invasive treatment that ablates and liquefies fat deposits in treated areas.

**Purpose:** Ideally, the device should be used in combination therapy with other proprietary treatments developed by Sciton. The result is skin that appears more firm, toned, and smooth. As a stand-alone procedure or in combination with liposuction, ProLipo can be performed comfortably with local anesthesia with less recovery time than traditional lipolysis.

**Benefit:** Broadband-pulsed light is the first intense pulsed light system to receive clearance for wrinkle treatment. The SkinTyte accessory is suited for use in combination with ProLipo and provides physicians with a new modality for facial rejuvenation.

**Sources:** www.pharmacyonesource.com; www.lifesciencesworld.com
help guide the decision to excise additional lymph nodes and can aid in patient staging. The assay is used on fresh lymph node tissue intraoperatively excised during sentinel lymph node biopsy.

**Benefit**: The assay offers a new approach to sentinel node testing. Results are available while patients are on the operating table; rapid access to results can provide a way for some women to avoid a second operation. The assay can detect the spread of cancer into the lymph nodes more accurately than other rapid methods and thus has the potential to reduce the need for stressful and costly second surgical procedures.

**Source**: www.fda.gov/ohrms/dockets/AC/06/briefing/2006-4249b1_04.pdf

**Name**: Demipulse Generator and Demipulse Duo Generator
**Manufacturer**: Cyberonics, Inc., Houston, TX
**Approval Date**: July 16, 2007

**Use Classification**: The generators are used for vagus nerve stimulation (VNS) therapy in patients with depression.

**Description**: The devices are the next generation of VNS Therapy technology. They are 43% smaller in volume than the Model 102 generators, and they include improved diagnostics (e.g., direct lead impedance measurement), faster communication with a programming system, and a platform for introducing additional features in the future.

**Purpose**: VNS Therapy is indicated for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and who have not responded adequately to four or more antidepressant treatments. Vagus nerve stimulation affects serotonin and norepinephrine neurotransmitters and brain structures that are thought to be involved in regulating mood. Preliminary imaging studies suggest that VNS Therapy affects many areas of the brain implicated in mood regulation.

**Benefit**: The device delivers very mild, intermittent brief electrical pulses to the left vagus nerve. These pulses are transmitted to the central nervous system, and they go to specific areas that control mood, motivation, sleep, appetite, and other symptoms that are relevant to depression.

**Sources**: www.leaddiscovery.co.uk; www.vnstherapy.com

### Devices in the News

#### Stent Study

Overall, drug-eluting and bare-metal stents carry similar mortality risks, but sirolimus-eluting stents may confer the least risk for revascularization or myocardial infarction (MI).

Researchers examined data from 38 randomized controlled trials comparing sirolimus- and paclitaxel-eluting stents with each other or with bare-metal stents. Follow-up ranged from six months to four years.

The three stents did not differ in all-cause mortality, cardiac mortality, or overall stent thrombosis. The risk for late stent thrombosis, however, was about twice as high with paclitaxel-eluting stents than with the other types. In addition, although both drug-eluting stents decreased the risk for target-lesion revascularization, sirolimus-eluting stents were more protective than paclitaxel-eluting stents. Sirolimus stents were also associated with the lowest risk for MI.

The authors suggested that sirolimus-eluting stents were clinically superior to bare-metal and paclitaxel-eluting stents.


#### Defibrillator Alert

Medtronic is voluntarily suspending distribution of its Sprint Fidelis defibrillator leads because a small number of fractures have been detected and the defect might have contributed to five deaths. As a result, these leads will no longer be sold or manufactured. Any remaining product should be pulled from inventory and returned to the company.

The company first notified physicians about the fracture rate in March 2007 and about the proper method of implantation.

Defibrillators are surgically implanted in patients who are at high risk of their hearts racing uncontrollably toward cardiac arrest. Implantable cardioverter defibrillators shock the heart back into normal rhythm by sending a pulse of energy through an electronic wire or lead that is connected to the heart. In the infrequent circumstance in which a lead breaks, the lead may send false signals that cause inappropriate defibrillator shocks, or therapies such as pacing or shocks might not be delivered.

Although fractures have affected fewer than 1% of the 268,000 leads implanted worldwide, it is unclear whether this rate of adverse events will remain constant or will increase over the life of these leads.

Medtronic says that if a Sprint Fidelis lead is fractured, it will pay for a new lead free of charge plus up to $800 for non-reimbursed medical expenses. The company also recommends that leads be removed from patients only if an actual fracture exists. Cardiologists agree, because surgical removal of a lead is potentially deadly itself.

The cardiologist can reprogram the defibrillator to increase its ability to sense a defect so it can send out a warning beep if a problem is detected.

Patients can also sign up for Medtronic’s monitoring system, which can alert them to possible fractures in the lead.

**Sources**: FDA; *The Wall Street Journal*, October 16, 2007.)