

**NEW DRUGS**

**Low-Dose, 365-Day Contraceptive (Lybrel)**

Wyeth’s new oral contraceptive, consisting of levonorgestrel 90 mcg/ethinyl estradiol 20 mcg (Lybrel), is now available by prescription in pharmacies. This is the first low-dose combination tablet that can be taken 365 days a year, without a placebo phase or a pill-free interval.

Lybrel provides women with more hormonal exposure (13 additional weeks per year) than conventional cyclic oral contraceptives containing the same strength of synthetic estrogens and a similar strength of progestins.

Unscheduled bleeding or spotting may occur, but the convenience of having no regular menstrual periods should be weighed against this inconvenience. Because monthly bleeding does not occur with Lybrel, it might be difficult for women to tell whether they are pregnant.

Adverse effects include headache, menstrual cramps, upper respiratory infection, vaginal bleeding, and nausea.

(Source: Wyeth, July 30, 2007.)

**Generic Doxorubicin (Adriamycin)**

Abraxis BioScience, Inc., has announced the launch of doxorubicin HCl injection, USP 2 mg/mL, the generic equivalent of Adriamycin PFS (Bedford Labs/Boehringer Ingelheim). The product is preservative-free and latex-free.

Doxorubicin is used to produce regression of lymphoblastic and myeloblastic leukemias; Wilms’ tumor; neuroblastoma; sarcomas, breast, ovarian, thyroid, gastric, bronchogenic, and transitional cell bladder carcinomas; Hodgkin’s disease; and malignant lymphoma.

It is also indicated as part of adjuvant therapy in women with auxiliary lymph node involvement following resection of primary breast cancer.

(Source: Abraxis, August 9, 2007.)

**Maraviroc (Selzentry) For HIV Infection**

The Food and Drug Administration (FDA) has approved maraviroc (Selzentry, Pfizer), an antiretroviral drug for adults with human immunodeficiency virus (HIV) infection. It is the first in a new class of drugs designed to slow the advancement of the infection.

Maraviroc is approved for use in combination with other antiretrovirals for the treatment of adults with CCR5-tropic HIV-1 with elevated viral levels and who have been treated with other HIV medications. Instead of fighting HIV inside white blood cells, maraviroc prevents the virus from entering uninfected cells by blocking the predominant route of entry, the CCR5 co-receptor.

The labeling includes a boxed warning about liver toxicity and a statement in the Warnings/Precautions section about the possibility of heart attacks. The FDA recommends that HIV-positive women not breast-feed, whether or not they are taking antiretroviral medications.

Pfizer plans to make the treatment available for patients with no insurance or with limited financial resources.

(Source: FDA; AIDS Healthcare Foundation, August 7, 2007.)

**Lidocaine (Zingo) Pre-treatment**

The FDA has approved lidocaine HCl monohydrate powder intradermal injection system (Zingo, Anesiva) to provide local topical analgesia to reduce the pain associated with venous access procedures, such as intravenous (IV) insertions or blood draws, in children three to 18 years of age.

Zingo is a needle-free system containing 0.5 mg of sterile lidocaine powder. It provides a rapid onset of action, allowing line placement or venipuncture to begin one to three minutes after administration. Currently available local anesthetics often take 20 minutes or longer to act.

(Source: Anesiva, August 17, 2007.)

**NEW INDICATIONS**

**Once-Yearly Zoledronic Acid (Reclast) for Osteoporosis**

Zoledronic acid injection (Reclast) Injection has been approved by the FDA as the first once-yearly medication for postmenopausal osteoporosis.

Unlike oral bisphosphonate therapies taken daily, weekly, or monthly, Reclast is given as a 15-minute IV infusion once a year, with the potential of improving compliance.

Three-year data from the Pivotal Fracture Trial showed that Reclast increased bone strength and reduced fractures in the hip, spine, wrist, arm, leg, and rib.

Zoledronic acid is also available as Zometa in a different dosage for use in oncology.


**Risperidone (Risperdal) Approved for Two Conditions in Children and Adolescents**

The FDA has approved risperidone (Risperdal, Janssen) for the treatment of schizophrenia in adolescents 13 to 17 years of age and for the short-term treatment of manic or mixed episodes of bipolar I disorder in children and adolescents ages 10 to 17. This is the first
FDA approval of an atypical antipsychotic drug to treat either disorder in these age groups. Until now, there had been no FDA-approved drug for the treatment of schizophrenia for pediatric use, and only lithium is indicated for bipolar disorder in adolescents ages 12 and older.

Risperidone was approved in 1993 for adults with schizophrenia and was later approved for the short-term treatment of acute manic or mixed episodes associated with bipolar I disorder in adults and for the treatment of irritability associated with autistic disorder in children and adolescents 5 to 16 years of age.

(Source: FDA Office of Pediatric Therapeutics, August 22, 2007.)

**DRUG NEWS**

**Some Restrictions Lifted For Tegaserod (Zelnorm)**

The FDA is permitting the restricted use of tegaserod maleate (Zelnorm, Novartis) for women younger than 55 years of age who meet specific guidelines. This agent is used to treat irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation.

The protocol allows the use of tegaserod in patients with these two illnesses if the physician determines that the drug is medically necessary. Patients must sign a consent form to ensure that they have been informed about potential risks and benefits.

On March 30, 2007, the FDA asked Novartis to suspend its marketing and sales in the U.S. because of a higher chance of heart attack, stroke, and unstable angina in patients taking tegaserod, compared with patients taking a placebo.

Patients must have no known or pre-existing heart problems, and they must have a critical need for this drug. Tegaserod remains off the market for general use.

(Source: FDA, July 27, 2007.)

**New Warnings and Guidelines**

**Diabetes Drugs And Heart Failure**

Manufacurers of some drugs approved to treat type-2 diabetes have agreed to add a boxed warning about the risk of heart failure.

After a review of postmarketing adverse event reports, the FDA determined that an updated label was needed for the entire thiazolidinedione class of anti-diabetic drugs, including three Glaxo-SmithKline products—rosiglitazone (Avandia), rosiglitazone/glimepiride (Avandaryl), and rosiglitazone/metformin (Avandamet)—as well as pioglitazone (Actos, Takeda/Eli Lilly) and pioglitazone/glimepiride (Duetact, Takeda). These drugs are used in conjunction with diet and exercise to improve blood glucose control in adults.

The FDA's review noted cases of significant weight gain and edema, which are warning signs of heart failure. In some reports, continued therapy was associated with poor outcomes and death.

The new warning advises health care professionals to observe patients carefully for the signs and symptoms of heart failure (e.g., excessive or rapid weight gain, shortness of breath, and edema) after starting drug therapy. Patients with serious or severe heart failure whose activities are limited and who are comfortable only at rest should not take these drugs.

The FDA’s review of rosiglitazone is ongoing. On July 30, 2007, the FDA recommended that the product continue to be marketed and that the labeling include the risk of heart attacks.

(Source: FDA, August 15, 2007.)

**Warfarin (Coumadin) Labeling**

The label for warfarin (Coumadin, Bristol-Myers Squibb) now includes an explanation that one’s genetic makeup may influence how a patient responds to the drug. Warfarin is used to prevent blood clots, heart attacks, and stroke.

This change highlights the opportunity for health care providers to use genetic tests to improve their initial estimate of the reasonable warfarin dose for each patient in order to reduce the risk of bleeding complications. An analysis had indicated that patients were responding to the drug in different ways, sometimes according to whether they had variations of the genes CYP2C9 and VKO RC1.

Warfarin is a difficult drug to prescribe, because the optimal dose depends on the patient’s diet, age, and the use of other medications.

Patients who take a dose larger than they can tolerate are at risk of life-threatening bleeding; too low a dose poses a risk of blood clots. Dosing is very important at the beginning of therapy. The dosage must be individualized according to the prothrombin time and the response to the International Normalized Ratio (INR).

(Source: FDA, August 16, 2007.)

**Revised Guidelines for Unstable Angina and Non–ST-Elevation MI**

The American College of Cardiology and the American Heart Association have released revised guidelines for managing patients with unstable angina (UA)/non-ST-elevation myocardial infarction (NSTEMI). UA and NSTEMI are acute manifestations of coronary artery disease.

Major changes suggest an initial non-invasive set of preliminary tests (stress test, echocardiogram, or radionuclide angigram); antiplatelet therapy with clopidogrel (Plavix, Bristol-Myers Squibb/Sanofi) for at least one year after insertion of a drug-eluting stent; more intense lipid and blood pressure control; and cessation of nonsteroidal anti-inflammatory
drugs (NSAIDs) used for patients with UA/NSTEMI during hospitalization.

The 2002 guidelines had recommended an early invasive strategy (diagnostic angiography and revascularization) for treating UA/NSTEMI. The new guidelines distinguish high-risk from low-risk patients and recommend an early invasive strategy for unstable and high-risk patients, with an initial non-invasive strategy in stabilized and low-risk patients.

(Source: American College of Cardiology/American Heart Association, August 7, 2007.)

**Codeine Warning For Nursing Mothers**

The FDA is concerned that nursing infants might be at increased risk of a morphine overdose if the mothers are taking codeine and if they are “ultra-rapid metabolizers” of this pain-relieving agent.

In one case, a 13-day old breast-fed infant died from a morphine overdose. The morphine levels in the mother’s milk were abnormally high after she took small doses of codeine to treat episiotomy pain. A genetic test showed that she was an ultra-rapid metabolizer of codeine.

After the drug is taken, some of it is converted to morphine. Some people, as a result of their genetic makeup, metabolize codeine faster and more completely than others (the ultra-rapid metabolizers) and are more likely to have higher-than-normal levels of morphine in their blood. Mothers who are ultra-rapid metabolizers may have higher-than-usual levels of morphine in breast milk.

According to the FDA, nursing mothers have used codeine safely for many years. It is generally considered the safest choice among narcotic pain relievers for nursing women and their babies. However, to help prevent morphine overdoses in nursing infants, the FDA is requiring manufacturers of prescription codeine medications to include information about ultra-rapid metabolism in the drug package insert. The agency has also posted information on its Web site.

Signs of morphine overdose in infants include increased sleepiness, difficulty breast-feeding, breathing difficulties, or limpness.

The chance of being an ultra-rapid metabolizer varies from less than 1 per 100 to 28 per 100 people. An FDA test is available, but the results alone might not correctly predict whether the breast milk will have too much morphine.

(Source: FDA, August 20, 2007.)

**Sorafenib (Nexavar) Granted Priority Review For Liver Cancer**

Bayer HealthCare and Onyx have announced that the supplemental New Drug Application (sNDA) for sorafenib tablets (Nexavar), indicated for patients with hepatocellular carcinoma (HCC), has been accepted for review and has been granted priority review status by the FDA. HCC is the most common form of liver cancer.

Sorafenib is approved in more than 50 countries for the treatment of patients with advanced kidney cancer. It targets both the tumor cell and tumor vasculature. If approved, this agent would be the first FDA-approved therapy for HCC.

The Phase 3 SHARP trial showed that the medication extended overall survival by 44% in patients with HCC compared with those receiving placebo.

(Sources: Bayer HealthCare/Onyx, August 20, 2007; www.nexavar.com.)

**Pentostatin Injection For Hairy Cell Leukemia**

Bedford Laboratories has announced the FDA’s approval to begin shipping Pentostatin for Injection. This product is AP-rated and is equivalent to Nipent by Hospira, Inc. Pentostatin is indicated for the treatment of hairy cell leukemia.

The company will supply the latex-free injection as a sterile lyophilized powder in a single-dose vial containing 10 mg of pentostatin. Prescribing information is available upon request from the company.


**Is It Safe to Stop Digoxin?**

Because stopping treatment with digoxin (Lanoxin, GlaxoSmithKline), an antiarrhythmic agent, is associated with worsening symptoms of heart failure, the American College of Cardiology and the American Heart Association recommend keeping the treatment going. But little is known about the lasting effects of discontinuing long-term digoxin therapy in patients with ambulatory chronic heart failure.

In a multicenter study, researchers looked at data on 3,365 of 7,788 patients in the Digoxin Investigation Group trial. The patients were randomly assigned to stop or continue their long-term digoxin treatment.

Discontinuation of therapy was associated with a long-term increase in hospital admissions, but no such increase was observed in mortality rates in ambulatory patients with heart failure who were receiving angiotensin-converting enzyme (ACE)–inhibitors and diuretics. However, the data also suggested that continuing long-term therapy at low serum digoxin concentrations (i.e., 0.5–0.9 ng/mL) was associated with fewer hospital admissions and reduced mortality rates.

Mortality rates from all causes were 38% among patients who discontinued their long-term digoxin therapy, 32% among those with low serum digoxin concentrations, and 45% among those...
with high serum concentrations. Of those patients who stopped digoxin treatment, 70% were hospitalized, compared with 66% of those with low serum digoxin levels and 69% of those with high serum concentrations.

(Source: Am J Cardiol 2007;100:280–284.)

**Nebivolol (Nebilet) Effective For Older Patients**

Elderly patients with heart failure tolerated the nebivolol (Nebilet, Forest) well. In fact, 67% of 1,031 patients assigned to receive the beta blocker reached the target dose of 10 mg/day, 80% reached a maintenance dose of at least 5 mg, and approximately 70% of patients remained on the same maintenance dose until the end of the 16-week trial.

In the Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors with Heart Failure (SENIORS), a small number of patients (7%) could not tolerate a dose of nebivolol by the end of the titration phase. Those patients tended to be older; they also had lower blood pressures, lower heart rates, higher creatinine levels, and a higher prevalence of myocardial infarction as the underlying cause of heart failure. Patients with a history of hypertension tolerated the target doses better.

When patients receiving a target dose of nebivolol were compared with patients receiving placebo, the beneficial effects of nebivolol appeared early and were constant. The 5-mg dose appeared to be as beneficial as the 10-mg dose, but the lower doses showed no benefit. However, the numbers of patients in those lowest-dose groups were too small to allow a firm conclusion.

Patients who could not tolerate a maintenance dose had the worst outcomes—double the risk of death or hospitalization for cardiovascular causes.

(Source: Am Heart J 2007;154:109–115.)

**Probiotics May Curb Adverse Antibiotic Effects**

A probiotic drink twice a day can help reduce antibiotic-related diarrhea, and it may even keep health care costs down, say researchers from the United Kingdom.

One hundred thirty-five hospitalized patients (mean age, 74 years) drank Actimel (Dannon), a probiotic yogurt drink containing Lactobacillus casei, L. bulgaricus, and Streptococcus thermophilus during their course of antibiotics and for one week afterward. Control patients were given a sterile milk shake.

Diarrhea developed in only seven of 57 patients (12%) given the probiotic drink, but it affected 19 of 56 patients (34%) who were given the placebo drink (Yazoo).

The cost needed to prevent one case of antibiotic-associated diarrhea was $180, and the cost of preventing one case of Clostridium difficile-associated diarrhea (CDAD) was $120. In the U.S., it can cost an average of more than $3,600 per patient to treat CDAD, mainly because of an increased length of stay in the hospital and because vancomycin is widely used.

(Source: BMJ 2007;335:87, online version, June 11, 2007.)

**ACE-Inhibitors And Renal Shock**

Even small doses of angiotensin-converting enzyme (ACE)–inhibitors can lead to sudden renal failure in some patients, warns a physician from Northside Hospital, Atlanta.

A 70-year-old ileostomy patient received ramipril (Altace, King) 2.5 mg/day for hypertension and developed severe acute renal failure, complicated by shock, after only seven days. She was clearly in distress, with altered sensorium and labored breathing. Of note, the patient had reported increased output from her ileostomy over the previous four days. Although a cardiopulmonary examination was normal, the patient’s medical history was significant for hypertension, hyperlipidemia, and insulin-dependent (type-1) diabetes. However, she had no previous history of renal insufficiency or proteinuria.

In the intensive-care unit, ramipril was discontinued and a dopamine infusion was started. Renal ultrasonography revealed no significant abnormalities, and an echocardiogram confirmed normal left ventricular function.

The next day, the patient’s vital signs stabilized, and the dopamine dose was reduced to enhance renal perfusion. Her urine output continued to improve, and the dopamine was tapered off. Two days later, her creatinine level had dropped to 1.1 mg/dL, and her neurological status...
When Sedation Fails

After rapid-sequence intubation (RSI) has been started, there is a short period during which the induction agent ceases to be effective and continuous sedation hasn’t reached peak plasma levels. Even when a sedative infusion is started immediately, patients might begin to show signs of wakening. Waking up during sedation is not only distressing and frightening for patients; it can also lead to many adverse events—from dislodged tubes and catheters to ventilation problems, barotrauma, and hypoxemia.

In a multicenter study from England and France, patients were assigned to receive either RSI plus a bolus of etomidate (Amidate, Abbott), followed by continuous sedative infusion, or RSI plus placebo, followed by continuous sedative infusion. A composite sedation score was obtained six minutes after induction to measure the presence of the patients’ cough, pulling at the endotracheal tube, jaw relaxation, motor activity, and eye opening.

Of the 41 patients in the study, 65% who received placebo and 43% who received etomidate showed at least one sign of inadequate sedation. Half of the patients (nine in the etomidate group and 11 in the placebo arm) required additional sedation.

Etomidate starts working in seconds, and its effects last from 5 to 14 minutes. A supplementary dose of the induction agent might help. For hemodynamically stable patients, the researchers suggest that a bolus of a sedative agent with a longer duration of action than etomidate, like midazolam (Versed, Roche), right after RSI might provide better sedation.


Intrathecal Analgesia After Radical Prostatectomy

Continuous epidural analgesia had been the agent of choice for pain after radical prostatectomy at Sahlgrenska University Hospital in Gothenburg, Sweden. However, intrathecal analgesia might be the new favorite. In a study of 50 patients, the intrathecal form was as effective, more convenient, easier to manage postoperatively, and less expensive.

Before the operation, patients received lumbar intrathecal morphine 0.1–0.2 mg and hyperbaric bupivacaine 10 mg. Sedation, respiratory rate, and lower limb motor function were monitored hourly for 12 hours in the postoperative care unit. Patients also used a Visual Analogue Scale to rate pain relief.

Seven patients reported severe pain but only on the first day. Most patients reported only mild pain. In general, very small amounts of opioids were enough to achieve acceptable analgesia from day two on, the researchers say. Nausea and vomiting, reported by 16 patients on day one, corresponded to “worst pain.” High pain scores on days two and three were associated with longer stays in the postoperative care unit.

The researchers concluded that it might be worth increasing the dose on the first postoperative day, despite the conservative view that giving “systemic opioids to patients with intrathecal morphine must be avoided” unless patients are supervised in a postoperative care or an intensive-care unit. However, the researchers believe that with regular surveillance, patients receiving intrathecal analgesia can be managed safely when opioids are carefully titrated to an adequate analgesic effect.

(Source: *Acute Pain* 2007;9:65–70.)

Not Enough Morphine In Emergencies?

Raising the dose of morphine for patients in pain in the emergency department (ED) might help them, but how much should they receive?

Researchers from Albert Einstein College of Medicine in the Bronx, New York, found that boosting the dose from 0.10 to 0.15 mg/kg was safe and provided statistically superior analgesia—but not clinically superior analgesia. The question remains: are these patients being given too low a dose?

Of 280 ED patients, 138 received 0.10 mg/kg and 142 received 0.15 mg/kg (delivered in two doses). At 60 minutes, 96 of the lower-dose patients and 112 of the higher-dose patients reported “good” or “better” ratings of satisfaction.

In terms of actual pain relief, 53% of returned to normal. The patient was discharged from the hospital on the fourth day.

ACE-inhibitors are actually recommended for diabetic patients and they are considered safe in the absence of pre-existing renal insufficiency. Among antihypertensive agents, ACE-inhibitors are associated with the lowest rates of discontinuation for adverse effects. However, this patient’s ileostomy might have made her susceptible to dehydration and the resulting prerenal azotemia might have exacerbated the selective afferent arteriolar vasoconstrictive effect of ramipril, even at the low dose. Her age and weight were also factors; her body mass index was 49.1 kg/m².

In retrospect, the reporting physician concluded that despite the patient’s normal serum creatinine level, he should have calculated the creatinine clearance level, which can be affected by age and weight. A seemingly “normal” creatinine level in an elderly woman with low muscle mass might be “falsely reassuring,” he said. In this patient, the clearance rate was significantly decreased at 60.1 mL/minute.

(Source: *Heart Lung* 2007;36:298–299.)
patients receiving the higher dose reported 50% or greater pain reduction at 60 minutes. In the lower-dose group, 44% of patients reported the same amount. These findings suggest that the standard dose is inadequate.

The study team expected that a 50% increase in analgesia would increase pain relief, although with a risk of more adverse drug events (ADEs). Surprisingly, however, the additional medication did not increase pain relief or increase the frequency of ADEs.

It’s possible that higher doses have a maximum potential effect, although the researchers consider this “biologically implausible.” They also hypothesize that the relationship between analgesia and the amount of morphine administered might not be a simple linear one. That is, patients in severe pain might need to receive a threshold amount of morphine before they can feel a recognizable improvement in pain relief.

The investigators say that doses are simply not enough to reach the threshold for many patients. A better approach, they say, might be to target patients individually with higher doses or alternative analgesic agents.

(Source: Ann Emerg Med 2007;50:49–51.)

**Warfarin in Nursing Homes**

Nursing-home residents have a high risk of adverse events related to warfarin (Coumadin, Bristol-Myers Squibb), but many of those events may be preventable, say researchers from University of Massachusetts Medical School, New York University, and Duke University.

Over 12 months, the researchers performed a cohort study of all long-term-care residents, ranging from 2,946 to 3,212 per quarter, in 25 Connecticut nursing homes. During the study period, 490 residents were using warfarin. The researchers documented 720 adverse warfarin-related events and 253 potential adverse warfarin-related events. Of the definite events, 625 (87%) were characterized as minor, 82 (11%) were deemed serious, and 13 (2%) were life-threatening or fatal.

Approximately 30% of the events were preventable, and as many as 57% of the fatal, life-threatening, and serious events were avoidable, the researchers say. Prescribing and monitoring errors were the most common types. Prescribing errors were usually related to wrong dose (81%) and known drug interactions (25%). Monitoring errors generally involved inadequate laboratory monitoring of warfarin therapy or a delayed response or failure to respond to laboratory results.

Although adverse events in nursing homes might be directly linked to human error, the root cause could be defined as a defect in the system that permitted such an error. In the case of warfarin management, an important cause can be a poor flow of information.

For example, here is a frequent occurrence: A telephone call is made from the nursing home to a covering physician about a resident with a urinary tract infection, but it is not noted that the resident is taking warfarin. The result could be an order for an antibiotic that interacts with warfarin, without adequate monitoring, leading to a super-therapeutic International Normalized Ratio (INR) level and an increased risk of bleeding.

One way to solve the problem, the researchers suggest, might be to increase efforts to provide education about the safe use of warfarin. If it isn’t possible to implement changes at the systems level, efforts should at least be made to improve communication.

(Source: Am J Med 2007;120:539–544.)

**Raising Awareness of Ovarian Cancer Symptoms**

Ovarian cancer strikes more than 22,000 women in the U.S. each year. When found at an early stage, it is treatable; more than 90% of women with cancer that has not spread beyond the ovary live at least five years after diagnosis. Unfortunately, fewer than 20% of ovarian cancers are caught at this early stage.

Bloating, pelvic or abdominal pain, difficulty eating, feeling full quickly, and urinary urgency or frequency are more common in women with ovarian cancer than in women in the general population.

Patients with persistent or worsening symptoms for more than a few weeks may be candidates for a pelvic ultrasound; manual pelvic examination; and a blood test for CA-125, a tumor marker.

The tests are not recommend for low-risk women who have no symptoms.

(Sources: The New York Times and WebMD Medical News, June 13, 2007.)
Perindopril (Aceon) May Lower Risk of Myocardial Infarction

Although some studies have indicated that angiotensin-converting enzyme (ACE)–inhibitors such as quinapril (Accupril, Pfizer) andtrandolapril (Mavik, Abbott) have no real benefit for patients who have needed revascularization, there might be advantages with perindopril erbumine (Aceon, Solvay). Adding perindopril 8 mg once daily to standard preventive therapy (i.e., antiplatelets, beta blockers, and statins) reduced the rate of cardiac events by a significant 17%, suggested researchers reporting on more findings from the EUROPA study (Eu ropean trial on Reduction of cardiac events with Perindopril in stable coronary Artery disease).

In the overall EUROPA population of 12,218 patients, the incidence of cardiac events was 8% with perindopril and 9.9% with placebo. For the 6,709 patients undergoing revascularization, the incidence of cardiac events was 6.6% with perindopril and 8% with placebo. Among 3,047 patients with previous revascularization but no myocardial infarction, perindopril reduced the risk of fatal and nonfatal MI by 32%.

The researchers observed a lower risk in both men and women, whether or not they had hypertension or diabetes. The outcome was improved on top of other therapies such as lipid-lowering drugs and beta blockers. Thus, perindopril may be effective long-term therapy, even for patients who are perceived to be at low risk for ongoing medical management.

(Source: Am J Hypertens 2007;20:392–397.)

Fluoroquinolone Resistance Limits Options for Gonorrhea

The Centers for Disease Control and Prevention (CDC) no longer recommends fluoroquinolones for patients with gonococcal infections. This change thus limits the choice of medications available for treating the second most commonly reported disease requiring notification to public health departments.

Neisseria gonorrhoeae resistance to fluoroquinolones has spiked dramatically over the past decade: from a rate of less than 1% before 2002 to a rate of 38% among some populations. Homosexual men are particularly at risk.

Cephalosporins are essentially the last bastion for infected patients. For patients with penicillin or cephalosporin allergies, spectinomycin (Trobicin, Pfizer) is an alternative, but it is not available in the U.S.

Azithromycin (Zithromax, Pfizer) is effective against uncomplicated gonococcal infections, but the CDC does not recommend its widespread use because it has its own problems of resistance. However, the CDC advises that patients with gonococcal infection be given azithromycin or doxycycline (Vibramycin, Pfizer) for possible co-infection with Chlamydia trachomatis.

The CDC is urging health care workers to be on the lookout for the emergence of cephalosporin resistance.


Amiodarone-Related Blindness: A True Threat?

An antiarrhythmic agent, amiodarone (Cordarone, Sanofi-Synthelabo), has been implicated in optic neuropathy, with an estimated yearly incidence as high as 2%—12 to 200 times higher than that for idiopathic non-arteritic anterior ischemic neuropathy. Investigators from Mount Sinai, the University of Washington, and Duke University, however, suggest that the risk might be much lower. Their own study indicated that the incidence of this ocular condition was less than 0.13%.

This randomized study compared amiodarone with defibrillators in preventing sudden death. The researchers monitored 1,669 patients at three-month intervals for at least 27 months. They explained that bilateral vision loss was the main clue to amiodarone-related optical neuropathy, because logically a systemic drug would affect both eyes. They found no instances of bilateral vision loss.

In 50 out of 52 case reports of optical neuropathy, the researchers found that amiodarone treatment lasted a median of four months before vision loss occurred. One patient lost vision after 24 months of treatment. However, because the researchers’ own study went beyond 27 months, they say that the only way they might have missed a case of optical neuropathy was if the patient had died before the disease could progress to both eyes.

In the 48 case reports that mentioned continued on page 485
Because the three treatments seemed to be similar for changes in peak flow, pre-bronchodilator and post-bronchodilator FEV1 scores, and symptom scores, the main difference was in quality of life. The researchers say that the benefits of the overlapping combination were additional symptom relief via the nebulizer, with the convenience of the metered-dose inhaler when patients were away from home.

(Source: Am J Med 2007;120:435–441.)

**Paroxetine for Depressed Patients with Heart Failure**

Depression is common in patients with heart failure, but it isn’t certain how these patients might respond to antidepressant medications. Researchers from the University of Maryland and Baltimore Veterans Administration Medical Center evaluated 28 patients in a 12-week study. Controlled-release paroxetine (Paxil, GlaxoSmithKline) significantly relieved depression in 69% of patients, compared with 23% of patients receiving placebo. Simultaneously, treatment also dramatically improved quality of life.

Paroxetine was well tolerated. Only one patient could not tolerate an increase to 25 mg/day and continued therapy with 12.5 mg.

It was interesting—but not surprising—that even the placebo patients experienced a lifting of depression. Social isolation needs to be carefully considered in the treatment of patients with heart failure, the researchers said.

(Source: Am J Heart J 2007;153:868–873.)

**NEW MEDICAL DEVICES**

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

**Name:** C-flex Intraocular Lens, Model 570C

**Manufacturer:** Rayner Surgical, Inc., Los Angeles, CA

**Approval Date:** May 3, 2007

**Use Classification:** Rayner C-flex intraocular lenses are indicated for correcting aphakia (absence of the lens) when a lens has been removed during cataract surgery.

**Description:** The single-piece, ultra-violet-absorbing posterior chamber lens is implanted into the capsular bag of the human eye to replace the crystalline lens following phacoemulsification. The lens is made from Rayacryl, a copolymer. The lenses range from +8.0 to +30.0 dipters with 0.5-diopeter steps.

**Purpose:** The plastic lens is used to restore vision and to replace the natural lens of the eye after cataract surgery.

**Contraindications:** The lens should not be implanted in patients who are younger than 21 years of age, who have extremely small eyes, who have chronic or active eye disease (excluding cataracts), and who are pregnant or nursing.

**Benefit:** The lens works as a healthy eye to focus light on the retina correctly and to restore vision. The hydrophilic nature of the Rayacryl material and the design features of the lens reduce the problems of silicone oil adhesion.

**Source:** FDA, www.fda.gov

**Name:** Mynx Vascular Closure System

**Manufacturer:** AccessClosure, Inc., Mountain View, CA

**Approval Date:** May 16, 2007

**Use Classification:** The system is designed to seal a puncture site in the femoral artery and to stop bleeding after cardiac catheterization. The procedure is also performed to determine pressure and blood flow in the heart’s chambers, to collect blood samples from the heart, and to visualize the arteries with fluoroscopy.

**Description:** A catheter is passed into the right or left side of the heart, usually to obtain diagnostic information about the heart or its blood vessels or to provide treatment in some heart conditions. After the cardiac catheterization, the Mynx balloon catheter is inserted through the introducer sheath into a blood vessel in the femoral artery to temporarily stop bleeding at the puncture.
site. The Hydrogel sealant is injected through the introducer sheath at the puncture site and within the tissue tract, thus stopping the bleeding and sealing the access site.

After the site is sealed, the balloon catheter is deflated and removed along with the introducer sheath. Manual compression is applied for one to two minutes to ensure that bleeding stops. The gel is absorbed into the body within 30 days.

**Purpose:** The system delivers an extravascular gel to seal the puncture site after cardiac catheterization. It is used for patients who have undergone diagnostic or interventional endovascular procedures.

**Benefit:** The time needed to achieve hemostasis and ambulation is reduced.

**Contraindications:** There are no known contraindications for its use.

**Source:** FDA, www.fda.gov

**Name:** Immulite 1000 and 2000 Free PSA Tests

**Manufacturer:** Siemens Medical Solutions Diagnostic, Los Angeles, CA

**Approval Date:** May 11, 2007

**Use Classification:** Two laboratory tests are used along with digital rectal examination to help detect prostate cancer in men 50 years of age and older. The tests measure the level of free prostate-specific antigen (PSA) in the blood.

**Description:** A sample of blood is drawn and is added to chemicals in the Free PSA test. When a specific chemical is added, a light reaction is produced and is measured inside an instrument. The amount of light emitted shows the level of free PSA in the blood.

The free PSA level is used with total PSA, measured in the same sample, to calculate the fraction of total PSA that is free PSA. The test is used only with a total PSA test from the same company and on the same instrument system.

**Purpose:** The risk of cancerous and noncancerous conditions (e.g., benign prostatic hyperplasia) increases as men grow older. Both benign and malignant conditions can result in elevated total PSA levels; in cancer, however, the fraction of free PSA to total PSA is decreased.

This laboratory test assists the doctor in determining the chances of cancer in a patient with a total PSA value between 4 and 10 ng/mL and whether a biopsy of the prostate gland is needed.

**Contraindications:** The test should not be used when the total PSA value is outside the range of 4 to 10 ng/mL or with PSA tests developed by other companies.

**Benefit:** The tests may help to reduce the number of unnecessary biopsies in men with total PSA values between 4 and 10 ng/mL and who are unlikely to have cancer.

**Source:** FDA, www.fda.gov

**Name:** Electronic Medication Management Assistant (EMMA)

**Manufacturer:** InRange Systems, Altoona, PA

**Approval Date:** June 21, 2007

**Use Classification:** “EMMA” is a programmable device that stores and dispenses prescription medications for patients to use at home. The computerized medication box is designed to be used under the supervision of a licensed health care provider.

**Description:** A drug-delivery unit and two-way communication software enable health care professionals to manage prescriptions. The delivery unit is about the size of a bread box and plugs into a standard power outlet.

EMMA stores medications, emits an audible alert when patients are scheduled to take them, and releases the drugs onto a delivery tray when patients activate the device at the appropriate time. A Web-based application allows doctors and pharmacists to schedule or to adjust the medications from a remote location. Health care professionals thus have a record of each time patients access their medications.

**Benefits:** The remote system puts an important safety tool directly in the hands of patients and their health care providers and helps to reduce errors by minimizing some of the confusion that patients can experience when taking prescription medications. Physicians can monitor patients’ medications between office visits.

EMMA may be especially useful for elderly patients and for those with complex drug regimens.

**Source:** FDA, www.fda.gov

**Infusion Pump Recall**

Baxter Healthcare Corp. and the FDA have notified health care professionals and consumers of a Class I Recall of Baxter Upgraded Colleague Triple Channel Volumetric Infusion Pumps, Models 2M8153, 2M8163, and 2M9163. The pumps deliver controlled amounts of medications or other fluids to patients through an IV, intra-arterial, epidural, or other direct line into the bloodstream.

A software irregularity had caused the newly upgraded pumps to emit an alarm, to display an error code (16:310:867:0002), and to stop the infusion. This occurred during user programming, and all three channels were infusing fluids at the same time.

Serious injuries have been reported, and in some cases, the pump stopped infusing, causing an audible and a visual alarm to be activated.

Interruption of life-sustaining therapy can lead to serious injury or death. All affected triple-channel pumps should be removed from service immediately.

**Source:** FDA, June 20, 2007, www.fda.gov