**NEW DRUGS**

**Tentative Approval of Generic AIDS Trio**

The Food and Drug Administration (FDA) has tentatively approved a package of three antiretroviral drugs to be used together in the initial treatment of HIV/AIDS in adults.

The regimen, manufactured by Aurobindo Pharma of India, consists of a lamivudine/zidovudine fixed-dose combination (Combivir, GlaxoSmithKline) and efavirenz (Sustiva, Bristol-Myers Squibb). These drugs help keep the AIDS virus from reproducing during its life cycle.

The product will be available for purchase under the President’s Emergency Plan for AIDS Relief (PEPFAR).

(Source: FDA, www.fda.gov/oashi/aids/hiv.html.)

**Generic Pravachol Available For Hyperlipidemia**

The first generic version of Bristol-Myers Squibb’s Pravachol (Pravastatin Sodium Tablets) has been approved.

Pravastatin is indicated for the treatment of patients with high cholesterol levels or who are at increased risk for atherosclerosis-related cardiac and cardiovascular events (e.g., heart attack and stroke). Bristol-Myers Squibb’s patent for the drug expired on April 20, 2006.

Pravastatin sodium tablets, available in strengths of 10, 20, and 40 mg, are manufactured by Teva Pharmaceuticals.

(Source: FDA, April 24, 2006.)

**Orphan Drug for Pompe Disease Approved in Europe**

Genzyme Corporation has received authorization to market alglucosidase alfa (Myozyme) as an orphan drug in the European Union. Myozyme has been approved for long-term enzyme replacement therapy in patients with Pompe disease. This debilitating and often fatal disorder affects fewer than 10,000 people worldwide.

The product is the first therapy for Pompe disease and one of the first for an inherited muscle disorder.

Pompe disease, a lysosomal storage disorder, is also known as acid maltase deficiency or glycogen storage disease type II. People born with Pompe disease have an inherited deficiency of the enzyme acid alpha-glucosidase.

Patients typically experience progressive muscle weakness and breathing difficulty. When symptoms appear shortly after birth, babies often have an enlarged heart and die within the first year of life. When symptoms first appear later in life, patients may experience steadily progressive debilitation and premature mortality because of respiratory failure.

(Source: Genzyme, April 3, 2006.)

**NEW INDICATIONS**

**Preventing Influenza with Zanamivir**

Zanamivir for inhalation (Relenza, GlaxoSmithKline) has been approved to prevent influenza in adults and children five years of age and older. This antiviral medication was previously approved to treat influenza A and B virus infections in this population.

The new approval for prevention provides another option in addition to oseltamivir phosphate (Tamiflu, Roche), which is indicated for both preventing and treating the flu.

The effectiveness of zanamivir was demonstrated in four large-scale studies.

This drug is not recommended to treat or prevent seasonal influenza in people with asthma or chronic obstructive pulmonary disease, and it is not a substitute for the flu vaccine.

In preparation for a potential pandemic, the FDA has assembled a task force to develop a comprehensive plan to accelerate the development of antiviral agents and other countermeasures. Both Relenza and Tamiflu have been identified for stockpiling.

(Source: FDA, March 29, 2006.)

**Tacrolimus Now Approved For Heart Transplantation**

Astellas Pharma US, Inc., has received approval to market tacrolimus (Prograf) as an immunosuppressant to prevent organ rejection in patients who have received a heart transplant. Prograf is also used to treat patients undergoing kidney and liver transplantation.

The FDA’s review was based on one U.S. study and one European study. Tacrolimus is available in approximately 70 countries.

(Sources: Astellas, March 31, 2006; www.prograf.com.)

**Docetaxel for Stomach Cancer**

Following a priority review of a supplemental New Drug Application, the FDA has approved docetaxel concentrate (Taxotere Injection, sanofi aventis) in combination with cisplatin and 5-fluorouracil to treat advanced stomach cancer, including gastroesophageal junction cancer, in patients who have not received prior chemotherapy for advanced disease.

This is the first FDA approval of a therapy for advanced stomach cancer that has shown a survival advantage in more than a decade. Stomach cancer is the fourth most common type of cancer worldwide.

The docetaxel-based regimen demonstrated a 23% reduction in the risk of death. About 80% of the treated patients experienced at least one severe adverse event (usually neutropenia), compared with 75.4% in the control arm. Dexamethasone is administered before treat-
Pregabalin Approved in Europe For Generalized Anxiety Disorder

The European Commission has approved pregabalin capsules (Lyrica, Pfizer) to treat Generalized Anxiety Disorder (GAD) in adults. About 5% of people experience GAD at some point in their lives.

This approval was based on five randomized, double-blind clinical trials involving more than 2,000 patients. As early as the first week of treatment, it provided relief for emotional symptoms (e.g., depression and panic) and physical symptoms (e.g., headaches and muscle aches).

In the U.S., pregabalin is indicated for the management of diabetic peripheral neuropathy and postherpetic neuralgia and as an adjunctive therapy for partial-onset seizures. It is an alpha2-delta ligand that appears to calm hyperexcited neurons.

(Source: Pfizer Inc., March 27, 2006.)

NEW FORMULATIONS

First Generic HIV/AIDS Capsule

Aurobindo Pharma’s zidovudine, the first generic capsule dosage form to treat HIV/AIDS, is now approved for patients in the U.S. The tablet and oral solution dosage forms of zidovudine were previously approved for sale in the U.S. when the patent on those dosage forms expired in September 2005.

The approval of the capsule formulation follows the expiration of GlaxoSmithKline’s patent on its capsule form of the product marketed under the trade name Retrovir.


Injectable Naltrexone For Alcohol Dependence

Naltrexone for extended-release injectable suspension (Vivitrol, Alkermes/Cephalon) has been approved for the treatment of alcohol dependence.

This once-monthly injectable medication is indicated for alcohol-dependent patients who are able to abstain from drinking in an outpatient setting and who are not actively drinking when they begin treatment. This agent should be used in combination with psychosocial support.

Vivitrol will be available as a single-dose 380-mg IM injection by the end of June.

(Sources: Alkermes/Cephalon, April 13, 2006; National Institutes of Health, www.niaaa.nih.gov; www.vivitrol.com.)

Skin Patch for ADHD

A methylphenidate transdermal system (Daytrana, Shire) offers another option for children six to 12 years of age with Attention Deficit Hyperactivity Disorder (ADHD). This is the first non-oral medication for ADHD.

The patch, in strengths of 10, 15, 20 and 30 mg, is designed to be worn during a child’s normal daily activities. It should be applied daily to clean, dry, non-irritated skin. Because the body absorbs four times the amount of drug when the patch is heated, children should not sit in a hot bathtub or use a heating pad or electric blanket while they are wearing the patch.

In clinical trials, wearing the patch for nine hours provided a 12-hour duration of effect. The patch is to be left on for nine hours, followed by 15 hours of non-wear, and alternate sites should be used. Parents must be advised to follow instructions carefully to prevent excess absorption of the medication. In 2003, the FDA rejected the ADHD patch in a 12-hour form because of an excess of adverse reactions.

The label will include warnings about insomnia, decreased appetite, and nausea.

(Sources: Shire, April 6, 2006; www.daytrana.com; The Philadelphia Inquirer, April 12, 2006.)

DRUG SAFETY ALERTS

Advisory: Diazepam Gel For Seizures

The FDA is advising patients with epilepsy of a potential hazard caused by cracks in the applicator tips of diazepam rectal gel (Diastat AcuDial, Valeant). These cracks can result in the leakage of gel while it is being applied; this may cause patients to not get enough of the medication to control seizures.

The pre-filled syringes are designed to deliver the gel rectally in patients with acute repetitive seizures. The drug is usually administered by family members or caregivers at home.

At least once a month, patients and their caregivers should examine the syringes for cracks in the applicator tip. The cap should not be removed during inspection. Syringes with cracks should be returned to the pharmacist and exchanged for new ones at no cost. Valeant Pharmaceuticals can be reached at 1-877-361-2719.

A new version of this product is expected to be available in June or July. Until then, the current syringes are still being sold.

(Sources: FDA, April 4, 2006; Valeant, www.diastat.com.)

Label Changes for an Ocular Injectable Drug, Pegaptanib

Pfizer has notified health care professionals of important changes in the approved product labeling for pegaptanib sodium injection (Macugen).
Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration. It is administered once every six weeks by injection within the vitreous.

The changes affect the Contraindications, Precautions, Adverse Events Post-Marketing, and the Dosage and Administration sections.

Rare reports of anaphylaxis or anaphylactoid reactions, including angioedema, were described. These reactions occurred following the administration of Macugen along with various medications given as part of the injection preparation.

Clinicians should evaluate the patient’s medical history for hypersensitivity reactions to Macugen before prescribing it.

(Source: FDA, MedWatch, April 10, 2006.)

**Promethazine in Children**

The FDA has notified health care professionals and patients that serious and sometimes fatal breathing problems have occurred in children younger than two years of age who were given the antihistamine agent promethazine HCl (e.g., Phenergan, Wyeth). Parents and caregivers should obtain a doctor’s advice about giving promethazine in any form to children age two and older.

The labeling on all promethazine brand-name and generic products has been changed to reflect these strengthened warnings.

(Source: FDA MedWatch, April 25, 2006.)

**Drug News**

**Committee Votes Against Accepting Modafinil for ADHD**

The FDA’s Psychopharmacologic Drugs Advisory Committee has voted not to recommend approval of modafinil tablets (Sparlon, Cephalon), an investigational medication for children and adolescents with ADHD. Cephalon had received an approvable letter from the FDA in October 2005. Modafinil was deemed effective for its intended use, but more safety data were needed.

Sparlon is a new formulation and dosage strength of modafinil, the active ingredient in Provigil, which is indicated for adults with excessive sleepiness associated with narcolepsy, sleep apnea, and shiftwork sleep disorder. Sparlon is chemically distinct from currently approved therapies.

Provigil is not approved to treat ADHD; it is available only in 100- and 200-mg strengths. Sparlon should not be used in combination with Provigil or any other medications that contain modafinil.

(Source: Cephalon, Inc., March 23, 2006.)

**Hyperactivity Drugs and Risk of Adverse Events**

An FDA review of drugs used to treat attention-deficit/hyperactivity disorder (ADHD) reveals that 81 deaths and 54 nonfatal cardiovascular events from 1999 to 2003 might have been related. During those five years, about 78 million ADHD prescriptions were written for children and more than 14 million were written for adults.

The reports of deaths and serious ADEs involved an amphetamine/salt mixture (e.g., Adderall, Shire), methylphenidate (Concerta, McNeil Consumer/Johnston & Johnson; Ritalin, Novartis), and generic drugs.

The FDA said it would provide updates on deaths and nonfatal serious events for all of the drugs, including a newer ADHD drug, atomoxetine (Strattera, Eli Lilly).

The case reports themselves did not establish a causal link and suggested that these ADEs could have occurred for another reason.

The agency began reviewing ADHD drugs in 2005 after Adderall was ordered off the market in Canada because of reports of 20 sudden deaths and 12 strokes. The drug was later returned to the market.

(Source: The Wall Street Journal, February 9, 2006.)

**Preventing Clots in Hospitals**

Can hospitals do a better job of preventing dangerous blood clots in hospitalized patients? According to a review of more than 250,000 patient records by Premier, Inc., an alliance of hospitals, and researchers from the University of California–Irvine, the answer is yes.

The research, funded by sanofi aventis, supports the findings of the National Quality Forum and the Joint Commission for the Accreditation of Healthcare Organizations. These and other groups are promoting the adoption of regimens for preventing deep vein thrombosis (DVT).

DVT occurs when a blood clot forms in a vein, usually in the legs. If the clot travels to the lungs, the result is a pulmonary embolism.

Researchers found that nonsurgical patients received recommended treatment as little as 27% of the time and only half the time at best; surgical patients, only 13% of the time; and patients undergoing major orthopedic surgery, as often as 83% of the time.

Some patients either did not receive any recommended preventive regimen at all or did not receive treatment for enough days during their hospital stay. When patients did receive the recommended medication, they usually received the appropriate dose.


**More Time for tPA Therapy**

Can the window of time for giving tissue plasminogen activator (tPA) to patients with ischemic stroke safely be opened wider, from the standard three
hours to six hours? Researchers from university hospitals in Hamburg, Heidelberg, and Cologne, Germany, suggest that instead of a one-size-fits-all approach based on clock time, it might be possible to tailor treatment to individual needs—with the help of magnetic resonance imaging (MRI).

They administered IV tPA within three hours to 108 patients and within three to six hours to 66 others. They then compared outcomes with those of pooled placebo patients and pooled tPA patients from three major stroke trials.

The extra effect of using MRI to select patients was “quite remarkable,” the researchers say. They found an 8% absolute increase of favorable outcome, compared with unselected tPA patients, and 14%, compared with placebo. Outcomes were not related to the onset-to-treatment time.

Mortality rates were lower in the patients undergoing MRI (7.5%) than in both the pooled tPA group (13%) and the pooled placebo group (12%). Death after 90 days was also less likely in the MRI-selected tPA patients.

Why does MRI help? In one sample, the number of patients likely to benefit from thrombolysis wanes over time, as does the overall treatment effect. However, a high percentage of patients who have had an acute ischemic stroke have penumbral patterns beyond the first three hours; MRI might be able to help identify those patients whose tissue is at risk for infarction.

(Source: Stroke 2006;37:852–858.)

Antibiotic Resistance: Patients Are Bringing ‘Bugs’ into Hospitals . . .

Antibiotic-resistant bacteria, a major problem in hospitals, seem to be arriving with the patients. One particularly high-risk group: everyone who has been in the hospital in the last year.

Researchers from the University of Maryland, the Veterans Affairs and Maryland Health Care System, and the National Institutes of Health say that screening programs must look beyond intensive care units. They found that 11% of 699 patients entering the hospital had methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant enterococci (VRE) infection.

Simply requiring patients to self-report that they have received antibiotics and a hospital admission in the previous year identified 76% of patients with MRSA infection, 100% of those with VRE, and 90% of those infected with either organism.

(Source: Arch Intern Med 2006;166:580–585.)

...And They Are Not Using Antibiotics Correctly

A survey of 4,500 people in 11 countries who reported taking an antibiotic within the previous 12 months found that many respondents were concerned about antibiotic resistance but did not usually understand how their improper use of antibiotic medications was contributing to the problem.

Preliminary results from the COMpli ance, Modalities by Population, Lifestyle and Geography (COMPLY) survey showed that 80% of patients considered antibiotic-resistant germs to be a serious problem, but only 60% believed that taking an antibiotic improperly reduced its effectiveness the next time it was used.

Of the respondents, 22% were considered “noncompliant” with their last antibiotic treatment because they skipped treatment days or doses or did not take all doses even after being instructed to do so. Half of the respondents thought that leftover antibiotics could be saved and used again, and 73% of those who had leftover antibiotics said that they saved them.

Noncompliance can lead to antibiotic resistance and is associated with treatment failure, deterioration of health, hospital admissions, and additional costs. Repeated and improper use of antibiotics are the two main causes of the increase in resistant bacteria.

Younger patients were less likely than older patients to be compliant.

(Source: Pfizer-supported study, April 4, 2006; European Congress of Clinical Microbiology and Infectious Diseases.)

Tenofovir Gel: A New Microbicide for Women?

Tenofovir disoproxil fumarate (Viread, Gilead), an oral medication that inhibits retroviral replication, could have a new life as a convenient vaginal gel, say researchers from Harlem Hospital Center, Bronx-Lebanon Hospital/Center, University of Pennsylvania, and Miriam Hospital in Providence, Rhode Island.

In the first phase 1 clinical trial to evaluate an antiretroviral agent as a vaginal microbicide, tenofovir vaginal gel was well tolerated. The study included 60 HIV-negative women and 24 HIV-positive women.

The women used either 0.1% or 0.3% tenofovir gel for 14 consecutive days between menstrual periods. Adverse events were generally mild; most of the women and their male partners said that they would probably use the gel if it were available. Pharmacokinetic testing demons trated that 14 of 25 women had detectable plasma levels of tenofovir at least once.

Longer-term studies are needed to determine whether the drug accumulates to toxic levels or whether tissue penetration enhances the gel’s protective effects. However, thousands of HIV-positive patients have tolerated daily tenofovir for up to five years.

None of the HIV-positive women with detectable plasma or cervicovaginal HIV
RNA developed mutations associated with tenofovir resistance—a “reassuring” finding, the researchers note. Longer-term studies are recommended to evaluate chronic use.

(Source: AIDS 2006;20:543–551.)

Dexmedetomidine for Sedation?

Dexmedetomidine HCl injection (DEX, Precedex, Abbott) may be a better alternative to conventional sedatives and analgesics during carotid endarterectomy, suggest researchers from St. Vincent’s Hospital in Melbourne, Australia. DEX is used as a sedative in intensive care settings.

DEX offers sedation without respiratory depression. It has a short half-life, allowing titration via an intravenous (IV) infusion, and it offers mild analgesia with easy arousability of patients.

The researchers compared DEX with a conventional technique using midazolam (Versed, Roche) with fentanyl as standard treatment in 56 patients who underwent carotid endarterectomy with regional anesthesia. Successful sedation was achieved with both techniques.

About 80% of patients in both groups needed at least one hemodynamic intervention. However, fewer DEX patients required intervention for hypertension or tachycardia; conversely, they were more likely to have postoperative hypertension and bradycardia.

DEX’s analgesic effects meant that fewer patients needed supplementary pain medication in the postanesthetic care unit (PACU), even though fentanyl was part of the standard treatment. Pain experienced by the DEX patients was also more likely to be controllable with simple acetaminophen, codeine, or tramadol (Ultram, Ortho-McNeil). Those patients receiving the standard therapy needed parenteral medications more often.

In small concentrations, DEX is associated with a lack of amnesic effects, but this may be a drawback. In a postoperative questionnaire, the DEX patients tended to recall intraoperative discomfort more than the standard group and requested techniques for a repeated procedure in the awake state less frequently. Despite similar levels of sedation, the use of midazolam may have blunted the recall of intraoperative events.

The researchers suggest that the ideal sedation-plus-amnesia technique might combine DEX with small doses of a benzodiazepine.

(Source: Anesth Analg 2006;102:668–675.)

A Timely Transformation for Pralidoxime Antidote

Pralidoxime (Protopam, Wyeth, Baxter), an antidote for organophosphate poisoning from insecticides, is also a potential antidote in the event of mass casualties resulting from nerve agents. The IV form, which is easy to administer and titrate, is preferable in emergency departments and intensive care units. Researchers from Ohio State University tested a method to convert the intramuscular (IM) formulation to an IV form.

The researchers were concerned to find only 36 g of IV pralidoxime available for the 1.1 million people of Franklin County, Ohio—less than 4 g per hospital. They say that a national purchasing restriction of Protopam, the only formulation marketed for IV use, is partly responsible for the low stockpile. However, the study also revealed the availability of a large supply of supply of IM pralidoxime (4,398 g), mostly outside of hospital settings.

The authors injected five autoinjectors, each containing 2 ml of a 300-mg/L solution of pralidoxime, into sterile empty, vented 30-ml vials. The resulting 3-g (10-ml) pralidoxime contents of each vented vial were used to prepare two concentrations diluted for IV administration. The solution was found to be stable under various conditions at temperatures ranging from –20° to 50°C for up to 28 days.

For many years, Wyeth had been the sole manufacturer of Protopam. In November 2003, Wyeth stated that the product was out of stock. This product line had been sold to Baxter, Inc., in August 2003.

(Sources: Ann Emerg Med 2006;47:272–277; Wyeth.)

Venlafaxine: A Cause of Hepatitis?

Venlafaxine (Effexor, Wyeth), an antidepressant sometimes indicated for women with vasomotor symptoms of menopause, may lead to drug-induced hepatitis, warn pharmacists from the University of Iowa.

A healthy 60-year-old woman developed hepatitis after taking venlafaxine 75 mg/day for one month. At her first visit, she had fever, cough, headache, and myalgia. An upper respiratory tract infection was the diagnosis. Three days later, she had persistent fever, chills, congestion, sharp abdominal pain, and marked upper-quadrant tenderness. She had nausea and no appetite, but she was not vomiting.

A sonogram revealed an enlarged liver (18.2 cm), a dilated mid-common bile duct, lymph nodes near the pancreatic head (up to 1 cm), and fluid collection between the gallbladder and liver. She had no gallstones, and the gallbladder wall was not thickened. Her blood cell counts, as well as lipase, amylase, and total bilirubin levels, were normal, but liver enzymes were greatly elevated.

The next diagnosis was sinusitis. The patient’s abdominal tenderness was presumed to be a result of exacerbation of her gastroesophageal reflux disease,
Cataracts. Women taking either drug had less likely than tamoxifen to cause retinopathy, which can become invasive. In those cases, tamoxifen is known to decrease this risk by half.

In other cases, venlafaxine caused dramatic liver problems, but values normalized after the drug was stopped. (Source: Ann Pharmacother 2006;40:323–327.)

Raloxifene as Effective as Tamoxifen in Lowering Breast Cancer Risk

Raloxifene (Evista, Eli Lilly), which is indicated for preventing and treating osteoporosis in postmenopausal women, seems to work as well as tamoxifen citrate (Nolvadex, AstraZeneca) in reducing the risk of invasive breast cancer.

In the National Cancer Institute’s Study of Tamoxifen and Raloxifene (STAR) trial, raloxifene and tamoxifen reduced the risk of invasive breast cancer by about 50% in women at high risk for the disease; however, raloxifene did not lower the risk of earlier forms (lobular and ductal carcinomas in situ), which can become invasive. In those cases, tamoxifen is known to decrease that risk by half.

Women who took raloxifene 60 mg daily and who were monitored for about four years had 36% fewer uterine cancers and 29% fewer blood clots than the women who were assigned to take tamoxifen 20 mg. Raloxifene was also less likely than tamoxifen to cause cataracts. Women taking either drug had equivalent numbers of strokes, heart attacks, and bone fractures.

Eli Lilly is expected to apply to the FDA for permission to market raloxifene for breast cancer prevention in high-risk postmenopausal women. (Sources: The New York Times, April 18, 2006; National Cancer Institute, April 17, 2006.)

Health Plan Changes Affect 22 Drugs In Medicare Part D

Independence Blue Cross (IBC) of Philadelphia plans to make 22 changes to its formulary for Medicare recipients starting June 1. These changes affect only a small fraction of the 3,000 drugs on its list, but some experts are concerned that insurers can add and remove drugs from their formulary every month, whereas Medicare recipients can change plans only once a year.

Drug plans can change the drugs as many times as they want in a year as long as they give advance notice to enrollees. Patients can appeal to keep getting their old drugs.

Pre-approval will be needed for three sleeping aids (Lunesta, Ambien CR, and Rozerem) and for three new drugs (Revlimid, Nexavar, and Sutent). Six drugs for erectile dysfunction (Caverject, Edex, Levitra, Muse, Viagra, and Cialis) will be limited to eight pills per month.

Generic forms will be substituted for 10 brand-name drugs: Zithromax, Tri-Pak, Z-Pak; Brovex-D; Metrogel Vaginal Gel; Miacalcin Spray; Retrovir; Amaryl; Didronel; Augmentin, Flexeril; and Lofibra.

(Sources: PR Web, March 10, 2006; www.appellatebrief.com/ambien.html.)

Panel Rejects Gemcitabine For Ovarian Cancer

An FDA advisory panel has voted 9–2 against approving Eli Lilly’s cancer drug gemcitabine (Gemzar) to treat advanced ovarian cancer.

The panel said that the data did not support this use for the drug, which has already been approved in the U.S. to treat lung, pancreatic, and breast cancers.

Lilly is seeking to market Gemzar for relapsed cases of advanced ovarian cancer when used with the chemotherapy drug carboplatin. The FDA will make a final decision, but it usually follows the recommendation of its advisory panels.

Although company officials said the goal was to prevent the cancer from worsening, not to help patients live longer overall, most panel members said they were not convinced that the goal was worth their support. (Sources: Yahoo! and Reuters Limited, March 16, 2006.)

Class Action Suit on Sleep Aid Reflects Need for Warnings

At least 26.5 million prescriptions of the sleeping aid zolpidem tartrate (Ambien, sanofi aventis) were filled this past year, but some users nationwide have experienced bizarre side effects of sleepwalking, sleep eating, and memory loss from this powerful hypnotic agent.

New York City Attorney Susan Chana Lask filed a class action complaint in the Southern District of New York on March 6, 2006, to ensure that the manufacturer warns consumers and doctors about the drug’s adverse effects.

Four representatives of the class complained that they took the drug to sleep and woke up only to find themselves in jail, driving cars while in a hypnotic state, and binge-eating at night. Another complainant discovered she had been arrested for driving her car in a zombie-like state and crashing into parked vehicles. Another woman was arrested for shoplifting but had no memory of the incident. Finally, a woman opened her door for a stranger and was assaulted. (Sources: PR Web, March 10, 2006; www.appellatebrief.com/ambien.html.)

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Histamine Blockers for Reflux May Cause Bowel Infection in Infants

Researchers at the National Institute of Child Health and Human Development Neonatal Research Network have found that premature infants receiving a common class of nonprescription drugs (histamine H₂ blockers), which are used to treat acid reflux, may have a higher risk for developing a potentially fatal bowel disorder than infants who do not receive the drugs.

H₂ blockers such as famotidine (Pepcid, Merck), nizatidine (Axid, Reliant), and GlaxoSmithKline’s cimetidine (Tagamet) and ranitidine (Zantac) inhibit the production of stomach acid, but they may also cause necrotizing enterocolitis, a serious intestinal inflammation.

Necrotizing enterocolitis affects 5% to 10% of infants born very prematurely. The tissue lining the intestinal wall dies, the surviving tissue becomes swollen and inflamed, and the GI tract cannot digest or transport food. Sometimes parts of the intestines must be removed, or the damage may be so severe that the infant dies.

Physicians sometimes prescribe H₂ blockers for premature infants to prevent esophageal damage if the infant is experiencing acid reflux, to reduce excessive stomach acid (which can lead to stomach ulcers) in infants being fed through an esophageal tube, and to possibly prevent sleep apnea (although data are inconclusive).

The researchers hypothesized that by decreasing acidity in the digestive tract, H₂ blockers might cause an excess level of gram-negative bacteria, which in turn might lead to necrotizing enterocolitis. Gram-negative bacteria are usually harmless, but their numbers can increase to unhealthy levels when sufficient stomach acid is lacking. They also advise that the drugs be prescribed with caution for premature infants.

(Sources: Pediatrics, February 2006; National Institutes of Health, February 8, 2006.)

Can Nalmefene Curb Compulsive Gambling?

Researchers at the University of Minnesota have found that daily doses of an experimental drug called nalmefene (Revex, BioTie Therapies, Finland), which has been used to treat alcoholism, may be able to reduce the urge to gamble.

Nalmefene, an opioid antagonist, helps to take the compulsive thrill out of winning and losing by interfering with sensations of pleasure and reward. Treated patients report that gambling no longer seemed as thrilling or compelling.

Of 207 people undergoing treatment for compulsive gambling at 15 centers in the U.S., almost two thirds of the patients who were given nalmefene showed “significant” improvement during the four months of treatment; about one-third in the placebo group responded favorably. One-third of the original participants dropped out because of nausea and other ADEs.

In the past, serotonin inhibitors and lithium showed mixed results. Naltrexone (ReVia, Duramed Pharmaceuticals, DuPont), now indicated for alcoholism, might be a promising treatment for pathological gambling, but it has been linked to severe liver damage.

Nalmefene seems to be most effective when used with traditional counseling and therapy. It is structurally similar to naloxone (Narcan, Endo) and naltrexone.

(Sources: Am J Psychiatry, February 2006; The Los Angeles Times, February 1, 2006.)

Taking Aspirin before Stroke May Worsen Prognosis

A study from Oulu University Hospital indicates that aspirin use may double the risk of death in patients with intracerebral hemorrhage (ICH). Regular aspirin use was a significant independent predictor of death within the first three months after the index stroke; it was also significantly associated with early hematoma growth.

The researchers evaluated 208 patients with ICH; 44 had used aspirin, 26 used warfarin (Coumadin, Bristol-Myers Squibb), and 138 used neither. On hospital admission, the warfarin users had significantly larger hematomas than the aspirin users and non-users. In the 47 patients with an ICH score of 2 or higher, 55% had a Glasgow Coma Scale score of 3–4, 40% had a score of 5–12, and 74% had a hematoma volume of 30 cm³ or more.

Most patients (89%) had intraventricular hemorrhages, and 13% had infratentorial hemorrhages. Twenty-five percent were 80 years of age or older; these patients were also more likely to be taking aspirin.

The high mortality rate among warfarin users reflects the fact that most of these patients had large hematomas on admission, and no effective measures to reverse the anticoagulant effect were used. The researchers attributed the “untoward effect” of aspirin use on short-term outcome to early enlargement of hematomas, perhaps caused by impaired hemostasis. However, they could not prove this hypothesis because a second CT scan was available for only 104 patients.

By contrast, the mortality rate during the first four days after the onset of ICH was higher (18%) in aspirin users than in non-users (11%), even though the aspirin users did not have larger hematomas on admission than the non-users.

If early hematoma growth is the problem, using transfusions to reverse aspirin’s antiplatelet effects might be beneficial, just as emergency reversal of

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anticoagulation is indicated for patients taking warfarin.

(Source: Stroke 2006;37:129–133.)

**Ropinirole for Restless Legs**

Ropinirole (Requip, GlaxoSmithKline), a non–ergot-based, second-generation dopamine agonist, was recently approved as a therapy for moderate-to-severe primary restless legs syndrome (RLS). Results from clinical trials suggest that it significantly improves symptoms and quality of life, compared with placebo, and it is well tolerated over the long term (up to 52 weeks).

The largest study of RLS to date, the Therapy with Ropinirole Efficacy and Tolerability in RLS US Study (TREAT RLS US), supports those findings. Compared with placebo, once-daily ropinirole (0.25–4 mg/day) reduced overall symptoms of RLS. Improvements were observed as early as the third day and the first week, even with low starting doses. Ropinirole was also more effective than placebo in reducing sleep disturbances.

Earlier studies showed that patients with RLS frequently become anxious and depressed. In the current study, a subset of ropinirole patients with mild anxiety symptoms, as well as a small subset of patients, also improved. Ropinirole directly stimulates dopamine receptors in the brain.


**NEW MEDICAL DEVICES**

**The FDA and E-Health Records**

The FDA is advancing the government’s effort to create electronic health records for Americans within the next decade by making it easier to access and share drug information more efficiently.

The FDA is adopting the Systematized Nomenclature of Medicine (SNOMED) as the standard computerized medical vocabulary system for coding important terms in the Highlights section of prescribing information. For instance, one code would be for the terms “heart attack,” “myocardial infarction,” “infarct,” and “MI.” SNOMED, developed by the College of American Pathologists, is one of the terminologies chosen by the U.S. government as part of the health information technology infrastructure for clinical language. This format will be required beginning June 30, 2006, for recently and newly approved drugs.


**Heart Group Wants Safety Panels for Medical Devices**

The Heart Rhythm Society is recommending changes in how medical device manufacturers and the government oversee implanted heart devices, such as defibrillators and pacemakers. The group is requesting that (1) companies use outside experts to help them decide when to issue alerts about potential safety problems; (2) doctors test a heart unit at the time of a patient’s death to see whether it played any role; (3) the FDA create forms to track reports of problems; and (4) a consistent way be found to alert doctors and patients to defects.

(Source: The New York Times, April 27, 2006.)

**NEW DRUGS**

**The Excimer Laser**

The Excimer Laser is indicated for use in the U.S. as part of its Zyoptix Personalized Laser Vision Correction System for refractive surgery. Surgeons in the U.S. will be the first in the world to operate the company’s Planoscan standard treatment at 100 Hz when the 217z100 Laser becomes available in July.

**Description:** The laser operates at twice the speed of the company’s current system.

**Purpose:** The laser is used to reshape or “sculpt” the anterior corneal surface, thus changing the eye’s focal length.

**Benefit:** The combination of beam diameters and laser speed enables treatment time to be reduced by half.

**Sources:** www.pharmacyonesource.com; www.dcmsonline.org

**Name:** BoneGen-TR

**Manufacturer:** BioLok International, Deerfield Beach, FL

**Approval Date:** March 23, 2006

**Use Classification:** BoneGen-TR is a clinically safe, nano-composite, time-release calcium sulfate product used for bone regeneration and augmentation. It is also used as a soft-tissue barrier in implantation, periodontology, endodontics and oral surgery.

**Description:** BoneGen-TR is an unusual complement to the Laser-Lok dental implant, which promotes tissue and bone attachment.

**Purpose:** This stand-alone device is used to fill small voids in bone augmentation. It can be an additive to more expensive bone augmentation products to “stretch” the volume and enhance bone formation.

**Benefits:** BoneGen-TR takes longer to be absorbed and costs less than other calcium sulfate materials on the market. It is resorbed over 18 weeks, compared with four weeks for other calcium sulfate products, which may be absorbed too quickly. This longer time period allows larger voids to be filled and full bone regeneration to be achieved. The application method is not technique-sensitive. This product is simple to use, and excellent results are obtained.

**Sources:** www.pharmacyonesource.com/News/article.cfm?Article_ID=24457

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Name: Luma Cervical Imaging System
Manufacturer: MediSpectra, Inc., Lexington, MA
Approval Date: March 16, 2006
Use Classification: This imaging system can help detect and identify sites on the female cervix that may contain precancerous cells.

Description: The optical detection system shines a light on the cervix and analyzes how various areas of the cervix respond to the light. The system assigns a score to tiny areas of the cervix and produces a color map that helps the physician decide where to obtain a biopsy specimen. The map’s colors and patterns enable the physician to distinguish between healthy and potentially cancerous tissue.

The physician performs a colposcopy, identifies areas on the cervix to sample, and then evaluates the Luma image to determine whether additional areas of the cervix need to be sampled. The biopsy is performed only after the colposcopy and the Luma procedures are completed.

Purpose: The system, as an adjunct to colposcopy, identifies high-grade disease in women with carcinoma in situ. The device provides a high-magnification evaluation of the cervix for women who have recently had an abnormal Pap smear.

Benefit: The Luma system has been able to detect cancer precursors that remained undetected by colposcopy. Of 50 cases of precancerous cervical lesions detected, 41 cases were caught by colposcopy and nine more lesions were detected by the Luma system.

Source: www.fda.gov/bbs/topics/NEWS/2006/NEW01338.html

Medical Device Safety Alerts

Guidant Corporation stated that it would remove Xience heart stents that had been manufactured for sale in Europe and for clinical testing in Japan after finding defects in some of the stents. Guidant did not identify the defects. No patients were reported to have been harmed by the faulty units.


Ossur hf., based in Iceland, has voluntarily recalled the 1100, 1900, 2000, and 2100 models of its Total Knee prosthetic device because some units may have contained faulty pins based in the axis of the knee. No incidents or injuries have been reported to the company.

(Source: FDA, www.fda.gov/oc/po/firmrecalls/ossur03_06.html.)