NEW INDICATIONS

Zoledronic Acid (Reclast) To Prevent New Fractures

The Food and Drug Administration (FDA) has broadened the U.S. indication for once-yearly zoledronic acid Injection (Reclast, Novartis) to include the prevention of new clinical fractures in patients who have recently had a low-trauma hip fracture. This fracture results from a fall from standing height or less.

The new indication was based on data from the Recurrent Fracture Trial, which included more than 2,100 men and women aged 50 and older with osteoporosis who had experienced a recent low-trauma hip fracture. Reclast increased bone mineral density and reduced the risk of new clinical fractures by 35%, compared with placebo. The risk of new spine fractures was reduced by 46%.

Known as Aclasta in Europe, Reclast is given once yearly as a 15-minute intravenous infusion. It is already approved to treat postmenopausal osteoporosis and Paget's disease of bone. Zoledronic acid is also available as Zometa Injection for cancer treatment.

(Sources: *N Engl J Med* 2008;59:762–784; Novartis, June 5, 2008, www. reclast.com.)

Duloxetine for Fibromyalgia

Eli Lilly's duloxetine HCl (Cymbalta) has been approved for the management of fibromyalgia, a chronic pain disorder. This agent is a serotonin–norepinephrine reuptake inhibitor (SNRI).

The cause of fibromyalgia remains unknown, but it might be related to a combination of changes in brain and spinal cord chemistry, genetics, and stress. Fibromyalgia affects about 2% of the U.S. population (five million people), and most patients are women.

Duloxetine is also approved for adults with diabetic peripheral neuropathic pain, major depressive disorder, and generalized anxiety disorder.

(Source: Eli Lilly, June 16, 2008.)

Bortezomib (Velcade) for Untreated Multiple Myeloma

Millennium Pharmaceuticals, Takeda Oncology, and Takeda Pharmaceutical Company Ltd. have announced the FDA's approval of bortezomib (Velcade) for patients with previously untreated multiple myeloma (MM). In the U.S., this agent is indicated for patients with MM and for patients with mantle-cell lymphoma who have received at least one previous therapy. This medication is contraindicated for patients with a hypersensitivity to bortezomib, boron, or mannitol.

(Source: Millennium, June 20, 2008.)

DRUG NEWS

Recalls

Xiadafil VIP Tabs

The FDA has requested that SEI Pharmaceuticals recall all Xiadafil VIP Tabs sold in eight-tablet bottles (Lot No. 6K029) or blister cards of two tablets (Lot No. 6K029-SEI) with an expiration date of September 2009. These products contain a potentially harmful, undeclared ingredient that can lower blood pressure to dangerous levels. The tablets are marketed as a dietary supplement for sexual enhancement and for treating erectile dysfunction.

The illegal ingredient, hydroxyhomosildenafil, is an analogue of sildenafil, the active ingredient in Pfizer's Viagra. It may interact with nitrates such as nitroglycerin.

The FDA has not approved Xiadafil VIP Tabs for erectile dysfunction or any other use. The product is sold over the Internet, as free samples at trade shows, and in health food stores. The FDA is advising consumers not to buy or use this product.

(Source: FDA, May 29, 2008.)

Morphine Sulfate Tablets

Ethex Corporation has notified health care professionals of a voluntary recall of a single lot of morphine sulfate 60-mg extended-release tablets (Lot No. 91762), because a tablet with twice the appropriate thickness was reported. Oversized tablets may contain as much as two times the labeled level of active drug. The lot was distributed under an Ethex label between April 16 and 27, 2008. Debilitated patients might not be able to tell that a tablet is overweight or oversized. Overdoses of opioids such as morphine can be life-threatening.

(Sources: FDA, June 10, 2008; Ethex.)

Boxed Warnings Added

Older Antipsychotic Drugs

The FDA is requiring manufacturers of conventional (first-generation, or "typical") antipsychotic drugs to make safety-related changes to the labeling to warn about an increased risk of death associated with the off-label use of these drugs to treat behavioral problems in older people with dementia. In 2005, the FDA announced similar labeling changes for "atypical" (second-generation) antipsychotic drugs, and boxed warnings were added at that time. The warnings will now apply to both drug classes, and all of the drug labels will carry uniform language.

Both classes of drugs block naturally occurring dopamine in the brain. Atypical drugs are associated with fewer neurological side effects such as involuntary movements. However, neither drug class is approved for treating dementia-related symptoms. The agents are approved primarily to treat symptoms associated with schizophrenia. The decision to use these drugs off-label to treat dementia symptoms is left to the discretion of the physician.

The conventional agents include prochlorperazine (Compazine); haloperidol

(Haldol); loxapine (Loxitane); thioridazine (Mellaril); molindone (Moban); thiothixene (Navane); pimozide (Orap); fluphenazine (Prolixin); trifluoperazine (Stelazine); chlorpromazine (Thorazine); and perphenazine (Trilafon).

The atypical drugs include aripiprazole (Abilify); clozapine (Clozaril); clozapine (FazaClo); ziprasidone (Geodon); paliperidone (Invega); risperidone (Risperdal); quetiapine (Seroquel); olanzapine (Zyprexa); and olanzapine with fluoxetine (Symbyax).

(Source: FDA, June 17, 2008.)

Becaplermin (Regranex Gel) For Leg and Foot Ulcers

A boxed warning about a risk of cancer is being added to the labeling for becaplermin (Regranex Gel 0.01%, Ortho-McNeil) when patients use three or more tubes of the product. This topical agent is used by diabetic patients to treat leg and foot ulcers that are not healing.

As a recombinant form of human platelet-derived growth factor, the gel is applied directly to the ulcer. Growth factors cause cells to divide more rapidly. For this reason, the manufacturer continued to monitor studies that began before the product's approval in December 1997 for any evidence of adverse effects, such as an increase in cancer.

(Source: FDA, June 9, 2008, www.fda.gov; www.medicalnewstoday.com)

New Inhalers Required For Asthma and COPD

The FDA has alerted patients, caregivers, and health care professionals to switch to hydrofluoroalkane (HFA)-propelled albuterol inhalers. Chlorofluorocarbon (CFC)-propelled inhalers are being phased out and will not be available in the U.S. after December 31, 2008. The CFC type is considered harmful to the environment by contributing to depletion of the earth's ozone layer.

Three HFA-propelled albuterol inhalers have been approved: ProAir, Proventil, and Ventolin Aerosol. Another HFA-propelled inhaler containing levalbuterol is also available as Xopenex Aerosol. Manufacturers have been increasing production of HFA albuterol inhalers, and adequate supplies are available.

Albuterol inhalers are used to treat bronchospasm in patients with asthma and chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema.

The spray of an HFA-propelled albuterol inhaler may feel softer than that of the CFC type. Patients must clean HFA-propelled albuterol inhalers to prevent the buildup of the drug in the device.

(Source: FDA, June 4, 2008.)

Pain Relief: Ice Water or Ethyl Chloride?

The lowly ice cube may be better than the vapocoolant ethyl chloride spray in controlling pain induced by an antibiotic skin test. Researchers from Korea compared the two treatments in a randomized study. Fifty healthy volunteers received an intradermal skin test on both arms. Only one volunteer considered the spray a more effective analgesic than the ice, and seven participants noted no difference in pain. The 42 others said ice pretreatment was better as analgesia, although 32 volunteers said that the ice cube was more uncomfortable than the spray. Nonetheless, nearly all—45 volunteers—preferred the ice.

(Source: *Am J Emerg Med* 2008;26:59–61.)

Clopidogrel (Plavix) Safe With Glycoprotein Inhibitors

Pretreatment with clopidogrel (Plavix, Bristol-Myers Squibb/Sanofi-Aventis) for patients undergoing percutaneous coronary intervention (PCI) may be able to reduce the risk of death and ischemic complications. However, its use has been debated for patients who are receiving a glycoprotein IIb/IIIa inhibitor (GPI), because both drugs are associated with a higher risk of bleeding.

A meta-analysis of three trials (PCI-CURE, CREDO, and PCI-CLARITY) involving 6,325 patients found a "consistent benefit," according to researchers from Brigham and Women's Hospital and Harvard Medical School, University of Kentucky, McMaster University, and University of Edinburgh. Overall, pretreatment reduced the odds of cardiovascular death, MI, or stroke after PCI by roughly 29% in both groups, whether or not the patients were receiving a GPI. Moreover, clopidogrel pretreatment was not associated with significantly more major or minor bleeding in either group.

(Source: *Am Heart J* 2008;155:910–917.)

Disulfiram (Antabuse) Yields Success In Alcohol Dependence

Alcohol-dependent patients went 54 days longer without a relapse when they were treated with disulfiram (Antabuse, Odyssey), compared with patients receiving topiramate (Topamax, Ortho-McNeil). In a study from Mumbai, India, 90% of 50 patients receiving disulfiram were still abstinent from alcohol at nine months, compared with 56% of 50 patients receiving topiramate.

Nausea was more common with disulfiram than with topiramate (4% vs. 1%), but the side effects abated in the first two weeks. The topiramate patients also had lower alcohol-craving scores.

The researchers say supportive families might have kept the dropout rate low, and they emphasized that treatment works best when patients are supervised

by family members or professionals.

(Source: *J Substance Abuse Treat* 2008; 34:460–463.)

Antihypertensive Agents Benefit All Age Groups

Strong support for the use of medications to lower blood pressure in *all* adults, regardless of age, comes from a meta-analysis of 31 trials involving nearly 200,000 patients. The studies showed no clear difference between age groups in terms of antihypertensive effects, say researchers from the Blood Pressure Lowering Treatment Trialists' Collaboration. Their findings, they suggest, should greatly simplify decision making for millions of health care providers.

Although some guidelines advocate particular types of drugs according to a patient's age on the basis of possible differences in effects, the researchers saw no evidence of differences between beta blockers and other classes of drugs in older and younger patients.

Among patients older than age 65, there were usually perceived benefits from reducing blood pressure, and in no case was there evidence of harm. Moreover, the absolute benefits of treatment are likely to be great in older patients because of their higher average risk. As long as blood pressure is managed effectively, factors such as tolerability and cost are probably "reasonable" bases for choice.

(Source: *BMJ* 2008;336:1121–1123, online.)

DRUG DEVELOPMENT

Creating New Drugs With Polyketides

Many drugs used to treat cancer and lower cholesterol are made from organic compounds called polyketides. These compounds are found in nature but are difficult for chemists to alter and reproduce in large quantities. Scientists at the University of California at Irvine have now discovered how polyketides form a unique ring-like shape. This can make it easier for chemists to manipulate polyketides into new drugs.

The key is an enzyme called aromatase/cyclase, which forms a C-shaped mold in which polyketides can form one molecule at a time. By changing this mold, chemists can control the size and shape of the polyketide to form new drugs. Polyketide-based drugs include antibiotics (tetracycline, erythromycin); chemotherapy agents (doxorubicin); antioxidants (resveratrol); and statins. Green tea and red wine also contain polyketides.

Bacteria, fungi, plants, and marine animals produce polyketides to kill predators. Before this study, it was not known how nature controlled the ring shape, which is essential for the antibiotic and anticancer properties. Researchers hope that the discovery of the ring pattern will lead to advances in cancer, obesity, and stem cell treatments.

(Sources: *Proc Natl Acad Sci* online; Science Daily, April 9, 2008.)

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: SynerGraft Valve

Manufacturer: CryoLife, Inc., Kennesaw, Ga.

Approval Date: February 7, 2008

Use Classification: The SynerGraft Valve is the first replacement heart valve obtained from donated human tissue in which the cells have been removed.

Description: The tissue's cells and cellular debris are removed, but a scaffold of connective tissue remains and functions like a human heart valve, potentially lowering the risk of an immune response and tissue rejection. The pulmonary valve directs blood flow from the right ventricle to the lungs.

Purpose: The device is indicated for patients whose pulmonary valve must be replaced because of disease, malformation or malfunction of their own pulmonary valve, or as part of another surgical procedure.

Benefit: Allograft (human) heart valves are popular choices for children because they obviate the need for blood-thinning medications on a long-term basis. Allograft heart valves, compared with heart valves from a pig or cow, are less likely to calcify. In a study, the SynerGraft valve performed at least as well as traditional allograft valves.

Source: FDA, February 7, 2008; www.fda.gov

Name: iFix Interference Screws

Manufacturer: Cayenne Medical, Inc., Scottsdale, Ariz.

Approval Date: February 27, 2008

Use Classification: This iFix Screw System is used in reconstruction procedures for bones, tendons, and the anterior cruciate ligament (ACL). The ACL is the major stabilizing ligament of the knee and helps to prevent buckling or instability.

Description: These screws use polyetheretherketone (PEEK), a form of plastic that is highly biocompatible, biomechanically strong, and radiolucent.

Purpose: The screw system offers ACL reconstruction technology to surgeons who practice the bone–tendon–bone technique.

Benefit: iFix surgical screws have better biomechanical strength than bioabsorbable and biocomposite interference screws. They are also superior to metallic screws, which can interfere with imaging. The iFix tip design is unique, and no tapping is necessary before insertion. Some patients react to foreign bodies or may have inflammatory responses to traditional screw materials. iFix screws overcome this problem because PEEK is biologically inert.

Sources: www.pharmacyonesource.com; Medical News Today, February 28, 2008; www.medicalnewstoday.com

Name: CellSearch Circulating Tumor Cell Kit

Manufacturer: Immunicon Corporation, Huntingdon Valley, Pa.

Approval Date: February 27, 2008

Use Classification: The kit is used as an aid in monitoring patients with metastatic prostate cancer.

Description: A sample of the patient's blood is processed to capture and count circulating tumor cells.

Purpose: Evaluating the circulating tumor cell count during the treatment of metastatic disease allows assessment of the patient's prognosis and predicts survival.

Benefit: Oncologists must often wait several months before they can determine whether a treatment is beneficial. With this kit, physicians can assess changes in the circulating tumor cell count in three to five weeks rather than in eight to 12 weeks, the usual period required to complete imaging studies. The serial test results can help physicians assess disease progression and make more informed decisions earlier.

Sources: www.pharmacyonesource.com; Medical News Today, March 3, 2008, www.medicalnewstoday.com.

Name: InPlex Cystic Fibrosis Molecular Test

Manufacturer: Third Wave Technologies, Inc., Madison, Wisc.

Approval Date: March 14, 2008

Use Classification: This genotyping test identifies cystic fibrosis mutations in DNA samples from isolated human whole peripheral blood specimens.

Description: Cystic fibrosis is a fatal genetic disease that affects more than 30,000 Americans. The test provides information to determine the carrier status of adults of reproductive age, serves as an aid in screening newborns, and confirms diagnostic results in newborns and children. The test delivers the accuracy of the company's Invader chemistry in a microfluidic card, developed in collaboration with the 3M Company.

Purpose: The test is used to identify cystic fibrosis mutations in DNA samples of patients.

Benefit: Compared with DNA sequencing (the standard for genotype determination), the Inplex test achieved 100% agreement on samples positive for cystic fibrosis and 99.96% overall agreement. The InPlex CF card was sensitive and specific. Minimal hands-on time and training were required, and the data generated were easily decipherable.

Source: www.pharmacyonesource.com; www.inplexcf.com.

Name: Silk'n

Manufacturer: Home Skinovations, Ltd., Yokneam, Israel

Approval Date: March 24, 2008

Use Classification: Silk'n is indicated for the home-based removal of unwanted hair under the direction of a physician.

Description: Silk'n has been clinically tested and physician-approved for removing hair safely and effectively in the privacy of the home. The unit is available only by prescription.

Purpose: Unwanted hair is removed via a photothermal treatment. This device is designed to be used with guidance from a physician.

Benefit: An average reduction of 50% in the hair count was monitored three months after three biweekly treatment sessions in a study in North America and Israel. No adverse effects were noted. Subjects were extremely satisfied with the device.

Sources: www.pharmacyonesource.com; www.medgadget.com; www.silkn.com

Name: FreeStyle Navigator Continuous Glucose Monitoring System

Manufacturer: Abbott Diabetes Care, Alameda, Calif.

Approval Date: March 12, 2008

Use Classification: This system is used to record interstitial fluid glucose levels in diabetic patients.

Description: A sensor reports glucose values continuously for up to 120 hours. The sensor is inserted in either the abdomen or the back of the upper arm. After a 10-hour start-up period, the system is calibrated with a fingerstick measurement taken by a built-in glucose meter. After calibration, the system provides glucose readings and updated information on trends for viewing. A built-in alarm can be programmed to alert patients when results fall below preset low and preset high levels; another alarm alerts users before their results reach preset levels.

Purpose: With this monitoring system, patients (18 years of age and older) can continually record their interstitial fluid glucose levels to improve diabetes management. Traditional blood glucose tests must be performed before therapy is adjusted for diabetes management based on the results and alarms in the system.

Benefit: This system provides real-time readings, graphs, trends, and alarms directly to patients. It can be used at home to aid patients in detecting episodes of hypoglycemia and hyperglycemia and in clinical settings to aid health care professionals in evaluating glucose control. The system is available only by prescription, and it can provide more information than that obtained by fingerstick measurements alone.

Sources: FDA, www.fda.com; Abbott, www.abbottdiabetescare.com ■