NEW DRUGS

Ziconotide for Pain Relief

The Food and Drug Administration (FDA) has approved ziconotide (Prialt®, Elan) for severe pain. The new drug offers an option for patients who no longer benefit from morphine or other traditional pain medications and who need a pump that delivers medicine directly to the area around the spine.

Ziconotide selectively blocks the nerve channels that transmit pain signals. It is part of a new class of drugs known as N-type calcium-channel blockers.


Trypan Blue In Cataract Surgery

The FDA has approved trypan blue ophthalmic solution (Vision Blue, DORC International), the first product in the U.S. for staining the anterior lens capsule during cataract surgery.

It is expected that the use of trypan blue will enhance the ability of ophthalmologists to remove advanced “white” cataracts, which typically occur in countries where medical care is not widely available. The surgeon will be able to view the capsule as it is cut and removed. Selective staining of the anterior lens capsule with trypan blue makes it easier to visualize, manipulate, and remove the cloudy lens through a surgical incision.

The solution appears safe in both older and younger patients. It is currently marketed in 30 countries.

(Source: FDA, December 16, 2004.)

Iloprost Helps the Lungs

An inhaled drug solution (Ventavis™, CoTherix) has been approved for the treatment of pulmonary arterial hypertension, a debilitating and potentially fatal disease characterized by high blood pressure in the pulmonary arteries of the lungs.

Iloprost is a synthetic compound that is structurally similar to prostacyclins, which are naturally occurring molecules that cause blood vessels to dilate.

The solution is marketed by Schering AG in Europe and Australia and will be made available in the U.S.


Orphan Drug Clofarabine For Leukemia Patients

The FDA has granted marketing approval for clofarabine (Clolar™, Genzyme) to treat refractory or relapsed acute lymphoblastic leukemia (ALL) in children aged one to 21 years. This is the first new leukemia treatment approved specifically for children in more than a decade. The drug is approved for children who do not respond to initial therapy, who relapse, or whose prognosis for survival is poor.

(Source: The Wall Street Journal, December 30, 2004; www.clolar.com; Genzyme.)

Darifenacin Relieves Overactive Bladder

Darifenacin (Enablex®, Novartis) extended-release tablets (7.5 and 15 mg) have been approved for patients with overactive bladder. The product blocks the M3 receptor, which is primarily responsible for bladder muscle contraction; helps lower the number of incontinence episodes; increases the amount of urine the bladder can hold; reduces the frequency of urination episodes; and decreases the pressure associated with the urge to urinate.

Darifenacin is not indicated in patients with urinary or gastric retention or with uncontrolled narrow-angle glaucoma.

(Source: Novartis, December 22, 2004.)

Omeprazole Powder Reduces GI Bleeding

The FDA has approved a New Drug Application (NDA) for omeprazole (Zegerid™ Powder for Oral Suspension, Santarus) 40 mg to reduce the risk of upper gastrointestinal bleeding in critically ill patients and for the short-term treatment of active benign gastric ulcers.

An immediate-release oral proton-pump inhibitor (PPI), the powder is the only PPI approved for the indicated use in these ill patients. This formulation reaches peak plasma levels within 30 minutes and provides strong acid control throughout the day. Repeated once-daily dosing of the 40-mg form before bedtime also controls nighttime gastric acidity.

An antacid protects the omeprazole from acid degradation in the stomach, allowing the drug to be quickly absorbed into the bloodstream. (Other available oral PPIs are delayed-release formulations that use an enteric coating to protect the PPI from acid degradation, delaying absorption and initial acid suppression.)

Clinicians should carefully evaluate
the agent's use for patients who follow sodium-restricted diets. Sodium bicarbonate is contraindicated in patients with metabolic alkalosis and hypocalcemia.

Otsuka America Pharmaceutical, Inc., is co-promoting this PPI.

(Source: Santarus, December 22, 2004.)

**Diphtheria Toxoid Vaccine Approved**

Sanofi-Pasteur, the vaccines division of the Sanofi-Aventis Group, has announced the approval of polysaccharide diphtheria toxoid conjugate vaccine (Menactra™) for protection against meningococcal disease in adolescents and adults aged 11 to 55 years.

This is the first quadrivalent conjugate vaccine licensed in the U.S. for preventing meningococcal disease. It is designed to protect against four serogroups of Neisseria meningitidis, the bacterium that causes meningococcal infection.

(Source: www.medicalnewstoday.com, January 17, 2005.)

**NEW FORMULATIONS**

**Aripiprazole Oral Solution For Psychiatric Disorders**

Bristol-Myers Squibb and Otsuka have received approval to market an oral solution form of aripiprazole (Abilify®) for adults who cannot swallow tablets.

Aripiprazole is indicated for the treatment of schizophrenia and acute manic and mixed episodes associated with bipolar disorder. The product is the first dopamine partial agonist.

(Sources: Bristol-Myers Squibb, January 4, 2005; www.abilify.com.)

**Albumin Form of Paclitaxel For Metastatic Breast Cancer**

Patients with breast cancer that has spread may now have a new option: paclitaxel protein-bound particles for injectable suspension (albumin-bound) (Abraxane™, American Pharmaceutical Partners/American BioScience).

This new form of paclitaxel is indicated for the treatment of breast cancer after unsuccessful combination chemotherapy for metastatic disease or after relapse within six months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless it was clinically contraindicated.

Albumin-bound paclitaxel showed a superior response rate, when compared with solvent-based paclitaxel (Taxol®, Bristol-Myers Squibb Oncology) in a prospectively randomized trial.

Because the albumin form contains no toxic solvents, this next-generation taxane product enables 50% more chemotherapy to be administered. The product can be given over 30 minutes via standard intravenous tubing.

(Source: BioScience/Abraxis Oncology, January 8, 2005.)

**DRUG NEWS**

**Osteonecrosis and HIV**

If an HIV-infected patient has unexplained bone pain, it might be a result of long-term highly active antiretroviral therapy (HAART). Between 1999 and 2002, researchers from France diagnosed avascular necrosis (AVN) in six patients, all of whom had received HAART.

In both HIV-infected and noninfected patients, risk factors for AVN include femoral neck fractures, corticosteroid therapy, and dyslipidemia; however, HIV-infected patients seem to be at higher risk for AVN. Case reports have appeared since 1990. In addition to known risk factors, AVN might also be a consequence of longer survival of patients with HIV, a complication of longstanding infection, or simply increased awareness.

The authors suggest several reasons for the higher risk among HIV patients. HAART may affect lipids or humoral immunity, increasing the production of antiphospholipid antibodies, for instance, which can predispose these patients to intraosseous platelet aggregation and subsequent bone necrosis.

(Source: Ann Pharmacother 2004;38: 2050–2054.)

**Alzheimer’s Disease, Anticholinergics Don’t Mix**

The treatment of Alzheimer’s disease (AD) relies heavily on cholinesterase inhibitors, which help salvage acetylcholine and maintain function in the cholinergic system. However, these agents are expensive and affect cognition only slightly. Patients with AD are sensitive to cognitive impairments induced by anticholinergic drugs.

Avoidance of anticholinergic agents should be the rule for patients with AD, the researchers say, because of the “exquisite sensitivity” of these patients to the cognitive and other psychiatric adverse effects associated with these agents, whether or not they are receiving a cholinesterase inhibitor.

If a patient is already receiving the drugs in combination, the researchers advise stopping the anticholinergic medication or choosing a “less” anticholinergic drug. They also advise substituting cautiously, because an anticholinergic withdrawal syndrome can cause seizures if the drug is stopped too abruptly.


**New Warning for Atomoxetine**

The long-term use of atomoxetine (Strattera®, Eli Lilly), a drug for attention deficit hyperactivity disorder (ADHD), may cause severe liver damage, the FDA warns. The drug’s labeling is being updated to include the warning after two reports about severe liver injury in a teenager and an adult (both patients recovered).
The labeling now states that the injury may progress to liver failure, resulting in death or the need for a transplant in a small percentage of patients.

(Sources: FDA, December 17, 2004; Eli Lilly; J Atten Disord 1996;1:147–161.)

Epilepsy Drugs May Raise Fracture Risk
The risk of fracture has been found to be almost twice as high in patients with epilepsy as in other people. A study from Utrecht Institute for Pharmaceutical Sciences in The Netherlands revealed that although menopause might be a contributing factor to low bone mineral density, antiepileptic drugs clearly exacerbated the hormonal effect on bone loss.


Mixing Valdecoxib, Aspirin May Raise Blood Clot Risk
Combining aspirin with the pain medication valdecoxib (Bextra®, Pfizer) may increase the risk of high blood clots that can trigger a heart attack or stroke. In December, the FDA warned that valdecoxib should not be used in candidates for heart bypass surgery.

Low-dose aspirin can slow the development of atherosclerosis in mice, but it seems ineffective once the disease is established. Adding a COX-2 inhibitor does not enhance the beneficial effects of aspirin; instead, the combination of valdecoxib and aspirin produces potentially dangerous changes in the makeup of the plaque within the arteries. The added COX-2 inhibitor causes changes that—if they occurred in humans—would result in a loss of stability of the plaque, making it more likely to rupture and activate clotting, causing heart attack or stroke.

Researchers say aspirin prevents atherosclerosis by blocking COX-1. Adding a COX-2 inhibitor may cause the beneficial effects of aspirin to be lost. This could increase the chance of developing dangerous blood clots.

Researchers caution that these results should not be taken out of context; the patients were at high risk for heart problems because they were undergoing heart bypass surgery. However, they say the findings represent a class effect of the COX-2 inhibitors.

(Sources: Circulation, 2005;111; American Heart Association; University of Pennsylvania Medical Center; WebMD Medical News; www.foxnews.com, January 18, 2005.)

Setback for Pregabalin, A Nerve Pain Agent
Federal regulators have decided to classify pregabalin (Lyrica™, Pfizer), a drug to treat persistent nerve pain, as a controlled substance, even as the FDA finally approved it in December 2004.

The mixed decision is a major setback for Pfizer, which has been counting on strong sales of pregabalin to offset declines in gabapentin (Neurontin®), a similar Pfizer medication that was released as a generic drug last year.

The FDA still is reviewing pregabalin as an aid in managing epileptic seizures. The drug had been approved to treat pain from nerves damaged by diabetes and by shingles, a herpes viral infection. In September 2004, the FDA rejected pregabalin as a treatment for generalized anxiety disorder, although Pfizer has not given up on that use. If approved to treat anxiety, pregabalin would be an alternative to antidepressants and older anxiety drugs such as the benzodiazepines (e.g., Valium®).

European regulators approved pregabalin in July 2004 to treat nerve pain and as an adjunct to other drugs in managing epilepsy.

(Source: The Wall Street Journal, January 3, 2005.)

Thymosin Beta4 Protein May Prevent Heart Damage
Researchers are hopeful that a protein that is critical in prenatal heart development will prove effective in preventing damage caused by heart attacks.

Thymosin beta4 (RegeneRx Biopharmaceuticals), when given to mice that were induced to have heart attacks, protected heart muscle cells from dying and was associated with improved heart function. After several weeks, the protein-treated mice had less muscle damage and stronger hearts than mice that were given saline solution.


Long-Term NSAID Use And Severe GI Damage
Chronic users of non-steroidal anti-inflammatory drugs (NSAIDs) face an increased risk of bleeding and visible damage to the small intestine, according to a study from the Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine in Houston, Texas.

Forty-three generally healthy patients, including those who used NSAIDs daily for relief of osteoarthritis, rheumatoid
arthritis, or nonspecific arthritis, were compared with a control group who did not use NSAIDs or aspirin. Of those patients who used NSAIDs for more than 90 days, 71% had visible small-intestinal injuries ranging from erosions to ulcers.

Symptoms of indigestion associated with NSAID use are common with long-term use. It has always been known that NSAIDs could cause stomach complications, but the extent of the impact had been unclear. The introduction of video capsule endoscopy has given physicians an opportunity to examine the small intestine and to see the adverse effects of NSAIDs on this organ.

More than 30 million people take over-the-counter and prescription NSAIDs for pain relief, headaches, and arthritis. Approximately 20 NSAIDs are available by prescription only.

Each year, the side effects of long-term NSAID use cause nearly 103,000 hospitalizations and 16,500 deaths. (Sources: Clin Gastroenterol Hepatol 2005;3:55–59; American Gastroenterological Association.)

**Delayed: Eszopiclone For Insomnia**

Sepracor, Inc., has announced a revision to the anticipated commercial availability of eszopiclone (Lunesta™) for the treatment of insomnia.

On December 15, 2004, the FDA had approved the New Drug Application (NDA) for this product. As expected, the FDA recommended that eszopiclone, like all other non-benzodiazepine hypnotics, be classified as a Schedule IV controlled substance by the Drug Enforcement Administration (DEA).

Sepracor is working with the FDA and the DEA on scheduling and anticipates that the product will be available nationwide within the first quarter of 2005. (Source: Sepracor, January 11, 2005.)

**Fast-Track Status: AMG 531 for ITP, AMG 706 for Stromal Tumors**

Amgen, Inc., has announced a “fast-track” designation for two experimental therapies, AMG 531 and AMG 706.

AMG 531, which received orphan drug designation in 2003, represents a new approach to treating immune thrombocytopenic purpura (ITP), an autoimmune bleeding disorder. AMG 706 is in phase 2 trials for the treatment of imatinib-resistant gastrointestinal stromal tumors (GISTs), which are fatal.

(Sources: Amgen, December 6, 2004; www.amgentrials.com.)

**BAY 43-9006 on Fast Track For Liver and Renal Cancer**

In April 2004, the FDA granted fast-track status to BAY 43-9006 (sorafenib, Bayer). This anticancer agent is being co-developed with Onyx Pharmaceuticals, Inc.

BAY 43-9006 is intended to prevent tumor growth by inhibiting tumor cell proliferation and angiogenesis (new blood vessel formation).

(Sources: www.onyx-pharm.com; www.pharma.bayer.com; November 22, 2004; www.HealthNewsDigest.com.)

**Eisai Distributor to Change**

Eisai, Inc., has announced that Cardinal Health will no longer serve as a distributor of record for the company’s U.S. pharmaceutical products.

Eisai is working to move pharmacy customers to its other distributors in an effort to avoid disruptions for patients who are taking donepezil HCl (tablets) (Aricept®, Eisai/Pfizer) for Alzheimer’s disease, rabeprazole sodium (Aciphex®, Eisai/Janssen) for ulcers and gastrointestinal reflux, and zonisamide (Zonegran®, Dainippon/Eisai), an anticonvulsant agent.

(Sources: FDA; BioWorld Online, December 29, 2004, www.bioworld.com.)

**Hormones and Ovarian Cancer**

Oral hormone replacement therapy (HT) is associated with a risk of ovarian cancer in women who have not undergone hysterectomy, according to findings from a study of 1,487 women in Denmark. However, reducing the daily dose of estrogen from oral HT might lower the cancer risk.

The risk increased with the cumulative intake of the estrogen component of HT but not with the duration or the cumulative intake of the progestogen component. Each additional gram of estrogen produced the same relative increase in risk.

If a woman is taking HT for irregular bleeding only, treatment with progestogen alone might be preferable. If an estrogen component is required to alleviate menopausal symptoms, the lowest possible daily dose should be used.

(Source: Arch Intern Med 2004;164: 2253–2259.)

**Twice-Weekly Simvastatin As Effective as Daily Doses**

Twice-weekly simvastatin (Zocor®, Merck) is just as effective, and perhaps safer, than daily doses of the drug, say researchers from Southern Arizona Veterans Affairs HealthCare System. They switched 31 patients from simvastatin 10 or 20 mg once a day to 40 or 80 mg once a week for 12 weeks and then compared lipid profiles at enrollment and at the sixth and 12th weeks.

After 12 weeks, two thirds of the patients remained at their goal for low-density lipoprotein-cholesterol (LDL-C). Most of the patients who did remain at their level had LDL-C goals of below 160 mg/dl or below 130 mg/dl.

Three patients reported not adhering to the regimen. A slight majority of patients found the twice-weekly regimen

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the same or easier to follow compared with taking daily doses. A larger clinical trial is needed to confirm the efficacy and safety of this approach.

(Source: *Ann Pharmacother* 2004;38:1789–1793.)

**Rosiglitazone Reduces Restenosis in Diabetic Patients**

Rosiglitazone maleate (Avandia®, GlaxoSmithKline) significantly reduced restenosis after coronary stent implantation in patients with type-2 diabetes, according to a study in Korea.

Of 83 patients, nine (17.6%) who took rosiglitazone experienced restenosis, compared with 21 controls (38.2%). The researchers attribute the outcomes in part to rosiglitazone’s anti-inflammatory properties. The anti-restenosis effect is probably independent of the known hypoglycemic action of the drug.

(Source: *Diabetes Care* 2004;27:2654–2660.)

**Diabetes Plan: 99 Cents a Day**

Sigma Medical, a division of Sigma Global Corporation, plans to offer a comprehensive health maintenance program for diabetic patients at only 99 cents a day ($0.99). The program is designed to aid elderly patients and uninsured Americans with diabetes who might be managing their condition improperly because of the cost or a lack of information.

(Sources: Sigma, October 27, 2004; American Diabetes Association.)

**Transdermal Pain System After Gynecological Surgery**

A novel patient-controlled, analgesic system that delivers fentanyl through the skin appears to be comparable to intravenous patient-controlled analgesia (IV PCA) after gynecological surgery. This needle-free system, called Ionsys™, is indicated for managing acute pain in hospitals. The system was granted approval status in June 2004 and is now being reviewed by the FDA. Findings were presented at the fall 2004 meeting of the American Society of Regional Anesthesia and Pain Medicine.

Fentanyl, an opioid agonist and a Schedule II controlled substance, is associated with a high potential for abuse. Patients should not let fentanyl gels touch their fingers or mouth. Oral contact or ingestion of the gel may cause life-threatening hypoventilation or death.

(Sources: www.alza.com, November 14, 2004; www.ortho-mcneil.com; www.janssencilag.com.)

**NEW MEDICAL DEVICES**

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

**Name:** Advanced D-Dimer Assay

**Manufacturer:** Dade-Behring, Deerfield, IL

**Approval Date:** January 4, 2005

**Use Classification:** This assay is used as an aid in the diagnosis of venous thromboembolism (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE).

**Description:** Polystyrene particles, covalently linked to a monoclonal antibody (DD5) to the cross-linkage region of cross-linked fibrin degradation products (D-dimer), are agglutinated when mixed with samples containing D-dimer. The cross-linkage region has a stereosymmetrical structure; that is, the epitope for the monoclonal antibody occurs twice. Consequently, one antibody is enough to trigger an agglutination reaction, which is then detected via the increase in turbidity.

**Purpose:** This immunoturbidimetric assay provides excellent sensitivity and negative predictive value for the diagnosis of disseminated intravascular coagulation associated with VTE.

**Benefit:** Early diagnosis and treatment of thromboembolic disorders are essential. The use of pretest probability

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assessment, together with this assay, aids in the diagnosis of VTE.

Sources: www.pharmacyonesource.com; www.fda.gov.

Name: ThyroTest™
Manufacturer: ThyroTec, Inc., Honey Brook, PA
Approval Date: December 28, 2004
Use Classification: This rapid diagnostic screening device can detect hypothyroidism (underactivity of the thyroid gland).

Description: This rapid immunoassay is similar to a quick pregnancy test. With two drops of blood from a fingerstick and five drops of diluent, a qualitative level of thyroid-stimulating hormone (TSH, thyrotropin) is indicated in 10 minutes.

Purpose: This is the first product to receive FDA approval and the Clinical Laboratory Improvement Amendment (CLIA) waiver for identifying above-normal levels of TSH in a rapid format. This simple diagnostic tool enables physicians to quickly screen patients for hypothyroidism with a whole blood sample.

Benefit: In the U.S., thyroid disease is more common than diabetes and cancer combined. Currently, patients with symptoms of hypothyroidism must wait days to discover laboratory results. Because of the CLIA waiver status, patients can now obtain test results in minutes, right in the doctor’s office.


Name: Reflection Ceramic-on-Ceramic Hip
Manufacturer: Smith & Nephew, Inc., Orthopaedics Division, Memphis, TN
Approval Date: December 22, 2004
Use Classification: The ceramic-on-ceramic hip is a product with “advanced bearing” performance for patients who need total hip replacement surgery.

Description: Lower-friction alumina (Al₂O₃, aluminum oxide) surfaces provide easier mobility and reduced wear. Surgeons believe that the ceramic-based implants, unlike traditional implants with an average life of 10 years, will offer a long-term solution.

Purpose: Hip implants, or total hip replacements, are used to replace hip joints in patients with diseased or damaged hips. Hip replacement devices are designed to replicate the function of a ball-and-socket hip joint.

Benefit: Until now, implants have typically consisted of metal-on-plastic surfaces, such as titanium, stainless steel, and cobalt chrome alloy femoral heads that articulate on ultra-high-molecular-weight polyethylene acetabular cups. These implants were known to produce wear debris that would lodge in the surrounding tissues over time. Osteolysis (loss of bone) was also associated with traditional implants and was often blamed for implant failure. The new implants use advanced bearing materials and are longer-wearing than the standard devices. They are especially suited for younger, active patients.


Name: Smoothbeam® Diode Laser
Supplier: Candela Corp., Wayland, MA
Approval Date: December 2, 2004
Use Classification: This laser is indicated for the treatment of sebaceous hyperplasia, a common skin condition that usually affects middle-aged to older adults. This benign proliferation of the sebaceous glands appears on the skin as small, soft, yellowish papules. These lesions are often located near the nose, cheeks, and forehead; they also occur on the chest.

Benefit: Rare side effects include hyperpigmentation and hypopigmentation of the treated areas. These effects usually disappear with time. Any redness that results generally disappears within an hour. Until now, existing therapies were invasive and created a socially unacceptable appearance for the patient.


Recalls

Automated Defibrillators
Access Cardiosystems, Inc., has recalled some of its automated external defibrillators (AEDs). In some units, the shock delivery circuit failed so that the AED could not deliver a shock. In other units, the AED unexpectedly turned itself on and could not be turned off.

Source: www.accessdata.fda.gov.

Airway Adapters
Unomedical’s adapter is typically used as an accessory connector to extend the airway circuits and to attach various breathing circuit components, such as reservoir bags. Although the adapter is distributed primarily to medical facilities, some units may have been distributed for home use. The adapters were found to be blocked or occluded, potentially preventing patients from exhaling or inhaling.

Source: www.fda.gov.