**NEW DRUGS**

*Actemra*

**For Rheumatoid Arthritis**

Tocilizumab (Actemra) has been approved for adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor antagonist therapies. This interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody may be used alone, with methotrexate, or with other disease-modifying anti-rheumatic drugs. Several cytokines (proteins) are involved in inflammation, including IL-6, levels of which are elevated in patients with RA.

The FDA's approval was based on data from five phase 3 studies. Tocilizumab was approved with a Risk Evaluation and Mitigation Strategy (REMS).

Source: Genentech, www.actemra.com, January 8, 2010

*Wilate for Bleeding In von Willebrand Disease*

Octapharma has received orphan drug exclusivity approval for Wilate. This agent is indicated for the treatment of spontaneous and trauma-induced bleeding episodes in patients with von Willebrand disease (vWD). Wilate is a high-purity, double-virus-inactivated von Willebrand factor/coagulation factor III concentrate (human). It has shown efficacy for all types of vWD in four prospective clinical trials. vWD results from the body’s inability to make von Willebrand factor (vWF), the human protein that helps clot blood. Wilate is exclusively derived from large pools of human plasma collected at plasma-donation centers approved by the FDA.

For more information, please see this month’s Pharmaceutical Approval Update column on page 109.

Sources: Medical News Today, December 8, 2009; Octapharma, January 13, 2010

*Ampyra for Multiple Sclerosis*

The FDA has approved dalfampridine extended-release tablets (Ampyra, Elan/Acordia) to improve walking in patients with multiple sclerosis (MS). In clinical trials, treated patients could walk more quickly than those receiving placebo.

A matrix tablet form of the investigational drug Fampridine SR, it is designed to block specialized potassium channel leaks from axons and to restore nerve impulses to damaged myelin sheaths. The progression and severity of symptoms in MS vary among patients. Mild symptoms can include numbness in the limbs; severe symptoms may include paralysis and loss of vision.

In clinical trials, dalfampridine caused seizures when given at doses greater than the recommended dose of 10 mg twice daily. Dalfampridine should not be used in patients with moderate-to-severe kidney disease.

Source: FDA, January 22, 2010

**NEW FORMULATION**

*Morphine Sulfate Oral Solution For Opioid-Tolerant Patients*

Roxane’s Morphine Sulfate Oral Solution has been approved for the relief of moderate-to-severe, acute, and chronic pain in opioid-tolerant patients. This medication will be available in doses of 100 mg/5 mL or 20 mg/1 mL. This is the only FDA-approved morphine sulfate oral solution available at this concentration.

The approval is part of the FDA’s unapproved drugs initiative. As part of this program, the FDA worked with Roxane to ensure that a sufficient amount of the drug will be available for patients.

For this formulation of morphine, Roxane had to develop a safety program before approval to address the known risks of morphine misuse, abuse, and overdose.

Source: January 26, 2010

**DRUG NEWS**

*Eszopiclone (Lunesta) May Ease Apnea*

The first few months—even the first few days—of continuous positive airway pressure (CPAP) therapy for patients with sleep apnea can predict how patients will be doing at six and 12 months. Approximately 50% of patients stop using CPAP within the first year, and most discontinue within the first month, usually because of discomfort, intolerance, or a lack of perceived benefit. However, in a Walter Reed Army Medical Center study of 160 patients with severe obstructive sleep apnea, two weeks of receiving eszopiclone (Lunesta, Sepracor), a non-benzodiazepine sedative-hypnotic drug, at the beginning of therapy led to increased CPAP adherence for the first six months.

Patients in the eszopiclone group used CPAP for nearly 21% more nights. Among the entire group of patients, CPAP was used on 62% of nights during follow-up. Mean nightly use was three hours for all patients. Patients receiving eszopiclone used CPAP for 64% of nights, compared with a rate of 45% among patients receiving placebo. The eszopiclone patients used CPAP for 3.57 hours per night, compared with 2.42 hours in the placebo group.

Eszopiclone was well tolerated. Any adverse events occurred within the first week of treatment. After two days, two patients withdrew from therapy, both from the eszopiclone group.


*Ribavirin (Copegus) Does Not Benefit Respiratory Syndrome*

During worldwide outbreaks of severe acute respiratory syndrome (SARS), the combination of ribavirin (Copegus, Roche) and corticosteroids was used widely; however, studies about efficacy
have been uncontrolled and inconclusive. After analyzing data for 1,934 patients, researchers from the University of Hong Kong and St. Michael’s Hospital in Toronto concluded that early combination treatment had no significant benefit.

Initially in the epidemic, when the causative agent was still unknown, ribavirin was used because of its in vitro activity against a broad spectrum of viral agents. It was thought that ribavirin had the potential to suppress acute viral replication in the early phase of SARS. Early treatment with ribavirin was considered important because the viral load peaked at day 10 after symptoms appeared. However, the in vivo inhibitory effect of ribavirin at clinically achievable doses remains controversial, and significant adverse events have been reported. Moreover, corticosteroids given during the early stage of viral replication might have suppressed the immune response and allowed a higher peak viral level.

In the absence of further evidence, the researchers advised that clinicians not use ribavirin and corticosteroids to treat SARS because of the lack of benefit for survival.


2009 Survey: Recession Is Affecting Drug Safety

In a survey conducted by the Institute for Safe Medication Practices (ISMP) in the fall of 2009, nurses and pharmacists working in hospitals responded that the current recession in the U.S. was having the effects of compromising drug safety and placing patients at risk. Of 848 respondents, 20% reported a negative impact on medication safety and 21% reported a moderately negative impact.

Adverse changes included staff reductions, fewer purchases of equipment, less participation in education and certification programs, a lack of time to report errors and to conduct double-checks of high-alert medications, an absence or a reduced availability of a medication safety officer, more potentially unsafe drug-purchasing decisions (choosing multiple-dose vials instead of single-use vials and prefilled syringes), a shortage of available medications, fewer pharmacists on patient-care units, and shortcuts in administering drugs.


Cochrane Reviews

Chemotherapy plus Radiation Improves Survival in Cervical Cancer

Combining drugs and radiotherapy may improve survival rates in women with cervical cancer, according to Cochrane researchers.

Treatments have changed markedly over the last decade. In 1999, the National Cancer Institute (NCI) recommended that chemoradiotherapy, which combines drugs and x-ray treatment, should be considered an alternative to radiotherapy.

Researchers analyzed data from 15 trials involving 3,452 women. Compared with women who had radiotherapy alone, women receiving chemoradiotherapy were more likely to live longer after treatment and had a reduced chance of recurrence and metastasis. The benefits of chemoradiotherapy were not restricted solely to the platinum-based drugs that the NCI had recommended.

Source: Cochrane Database Syst Rev 2010(1), Article No. CD000825

NSAIDs Are More Effective Than Paracetamol for Menstrual Pain

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, aspirin, and naproxen may be more effective in alleviating pain during a woman’s menstrual period than paracetamol (acetaminophen), yet it is not clear whether any one NSAID is safer or more effective than another.

In an Australian survey of 16- to 49-year-old females, up to 72% of respondents reported menstrual pain. The pain is thought to be caused by an excess or imbalance of certain hormones (e.g., prostaglandins) released during the menstrual period.

The updated review includes data from 73 trials conducted in 18 countries and involving a total of 5,156 women. The trials compared NSAIDs with placebo, with each other, and with paracetamol. All NSAIDs, except aspirin, were more effective in relieving pain, compared with placebo, and appeared to work better than paracetamol, although there were only three relevant studies.

Overall, NSAIDs carried a higher risk of adverse effects, such as indigestion, headaches, and drowsiness, compared with placebo.

Source: Cochrane Database Syst Rev 2010(1), Article No. CD001751

Adding Beta-Blockers Reduces Hypertension

Using beta blockers as a second-line therapy with antihypertensive drugs seems to lower blood pressure (BP) in patients with hypertension. Beta blockers are commonly used in hypertension to help reduce the risk of stroke and cardiovascular disease. They can be used alone or as a second-line therapy with other antihypertensive drugs.

The idea behind combining two different drugs is that each agent has a different mechanism of action and the combination may result in greater decreases in BP than can be achieved with monotherapy.

In 20 trials involving 3,744 patients, adding beta blockers as a second-line drug, along with thiazide diuretics or calcium-channel blockers, caused an addi-
tional reduction in BP as well as a 30% greater decrease when the dose was doubled. In an earlier review of second-line thiazide diuretics, second-line beta blockers were more effective in reducing diastolic BP but had little or no effect on pulse pressure, whereas second-line thiazides decreased pulse pressure in a dose-related manner. More study is needed to explain why beta blockers might seem less effective than thiazide diuretics in reducing adverse cardiovascular outcomes, particularly in older individuals.

Source: Cochrane Database Syst Rev 2010(1), Article No. CD007185

**RESEARCH NEWS**

**Protein Mutations Linked To Huntington’s Disease**

In patients with Huntington’s disease (HD), a mutated protein in the body becomes toxic to brain cells. A small region next to the altered segment might play a role in the toxicity. Two new studies suggest that slight changes to this region can eliminate signs of the disease in mice. It is not clear why the protein (mutant huntingtin) is toxic, but it accumulates in clumps of fibrils and might be clogging the internal functions of the cells.

HD is inherited, usually striking in middle age. Patients experience uncontrollable muscle movements and changes in personality and intellect. Individuals with HD carry mutations that affect the huntingtin protein. The mutations involve a triple-repeat DNA sequence, a type of genetic miscue similar to those found in Friedreich’s ataxia, Kennedy’s disease, fragile X syndrome, and other neurodegenerative disorders.

The normal huntingtin protein consists of about 3,150 amino acids, but in patients with HD, the mutated protein contains an abnormally long string of a single amino acid repeat; longer chains are associated with worse symptoms and earlier disease onset.

Researchers have been examining the effects of other nearby amino acids. In one study, they investigated how phosphorylation (the attachment of phosphates onto amino acids) in a protein affects huntingtin. This natural process is a way of marking proteins for destruction. In the study, phosphorylation of just two amino acids, located at one end of huntingtin, targeted the protein for destruction and protected against the toxic effects of the mutant protein. It is thought that boosting phosphorylation of those two amino acids might reduce the build-up of huntingtin and thus alleviate symptoms.

In an animal model, mice that carry the mutant huntingtin gene were created. Symptoms reminiscent of HD in humans developed (poor coordination, anxiety, loss of brain tissue, and clumps of huntingtin in brain cells). The researchers altered the same two critical amino acids at the end of the mutant huntingtin protein to either mimic phosphorylation (phosphomimetic) or resist it (phosphoresistant). Mice with the phosphoresistant version experienced HD symptoms, but mice with the phosphomimetic version remained free of symptoms and clumps for up to one year.

In other experiments, phosphomimetic modification of a huntingtin fragment reduced its tendency to form clumps. The nearly complete lack of any signs of disease in the phosphomimetic Huntington mice may point toward new strategies to treat the disorder. Drugs that enhance or mimic the effects of phosphorylation may help to detoxify the mutant huntingtin protein. Such drugs, if developed, would probably be most effective in early disease.

Sources: Neuron online, NIH, December 24, 2009; J Cell Biol online, December 21, 2009

**NEW DRUGS**

**DEVICES IN THE NEWS**

**Left Ventricular Assist System For Severe Heart Failure**

The FDA has approved a new indication for Thoratec’s HeartMate II, a continuous flow, left ventricular support system for patients with severe heart failure who are not appropriate candidates for heart transplantation. HeartMate II is already approved for patients who are awaiting further treatment, such as transplants or other cardiac procedures.

Heart-assist devices are surgically implanted mechanical pumps that help the heart’s ventricle pump blood to the rest of the body.

Source: January 20, 2010

**Synthes Spine Device Recalled**

The FDA has notified health care professionals of a Class I recall of all lots of the Synthes USA, Ti Synex II Vertebral Body Replacement. This device is used in the T1–L5 portion of the spine to replace a collapsed, damaged, or unstable vertebral body. Moderate-to-severe loss of vertebral body replacement height (caused by failure of the central body component) in situ was reported six to 15 months after implantation. Potential health problems that can result from this defect include neural injury, increased pain, spinal kyphosis, failure of supplementary fixation, and the need for reoperation. Surgeons and hospitals that have these devices should stop implanting them immediately.

This product was manufactured from June 8, 2007, through September 9, 2009, and was distributed from July 2, 2007, through September 8, 2009.

Source: FDA, November 12, 2009

**Sybaritic Is Ordered To Stop Making Devices**

Sybaritic, Inc., has agreed to stop producing and distributing medical products until it is in compliance with FDA
quality standards. The devices, which are used in laser surgery, dermatology, and spa treatments, are considered to be unapproved because they lack appropriate FDA clearance review and approval for safety and effectiveness. The consent decree was signed on January 4, 2010, in Minnesota.

The company designs, manufactures, and distributes moist steam cabinets (Dermalife), laser systems, ultrasound and noninvasive subdermal therapy systems to reduce the appearance of cellulite (Dermosonic), and microdermabrasion systems (SkinBella).

FDA inspections have revealed violations related to design controls, the handling of complaints, corrective and preventive actions, and quality audits. The FDA is not aware of any adverse events associated with the devices but is advising consumers to stop using these products.

After the company makes corrections, it must hire an independent auditor to conduct annual inspections of all its facilities for at least four years and to report the results to the FDA. The company may be required to pay damages of $15,000 per day if it does not comply with any provisions of the decree and an additional $15,000 for each violation.

Source: FDA, January 8, 2010

Stricter Criteria Needed For Device Approvals

The FDA’s criteria for evaluating medical devices appear to be less stringent than those for approving drugs. Two studies that examined premarket device approvals from 2000 to 2007 found that about 40% of pivotal trials lacked precise targets for how safety would be measured. It was also revealed that many devices were approved on the basis of small trials (300 patients on average) or just one study. Only 27% of the studies were randomized, only 14% used blinding, and only 50% included control groups; 31% were retrospective. Many studies had not been conducted in the U.S.

The U.S. Supreme Court has ruled that after a device is approved, consumers can no longer sue for problems in safety or effectiveness. Implantable defibrillators, valves, and stents are considered high-risk devices, and they must undergo the strictest review before they can be marketed.

The FDA counters that devices and drugs are not the same; it says that different processes are required for approval and that randomized, controlled trials are not always appropriate for testing devices. For example, patients cannot ethically be blinded to whether they are receiving a stent, bypass, or a drug; the agency adds that large-scale trials might be impractical for expensive or experimental devices.

The studies did not address whether the current approval process led to actual harm in patients. The FDA plans to study its device program and wants manufacturers to adhere to tougher research guidelines, to be published in 2010.


Fees for Medical Devices

With the passage of the Senate’s version of health care reform legislation in December 2009, there is a good chance that manufacturers of medical devices will be facing a new government fee for the long term. The fee would collect about $20 billion by 2019 and in subsequent decades. It is not certain when payments would start and which companies might be exempt.

Under the Senate bill, starting in 2011, companies would start paying their share of a $2 billion non–tax-deductible industry fee each year. Each company’s contribution is to be calculated from its share of total industry sales from the previous year. Revenues of $5 million or less would be excluded, and revenues between $5 million and $25 million would contribute only half of their value to calculations. Sales of FDA Class I products, as well as Class II products sold at retail for less than $100, would be exempt. The total fee would be increased to $3 billion in 2018.

Source: Medical Devices Today, December 24, 2009

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: Conserve Plus Total Resurfacing Hip System

Manufacturer: Wright Medical Technology, Arlington, Tenn.

Approval Date: November 3, 2009

Purpose: The Conserve system is surgically implanted to replace a hip joint. This single-use device is intended for hybrid fixation utilizing a cemented femoral head component and a cementless acetabular component. The device is designed to reduce or relieve pain and to improve hip function in skeletally mature patients with inflammatory (rheumatoid) arthritis, non-inflammatory degenerative joint disease (e.g., osteoarthritis), traumatic arthritis, avascular necrosis, or dysplasia, or developmental dislocation of the hip.

Description: Only the surface of the femoral head is removed to implant the femoral resurfacing component. The device has two parts: a socket in the shape of a shallow cup (the acetabular component) and a cap in the form of a ball head (the femoral resurfacing component). The cup replaces the damaged surface of the hip socket (the acetabulum). The cap covers the ball-shaped bone at the top of the thigh. The cap also has a small stem that is inserted into the top of the thigh.

continued on page 105
bone. The cap moves within the cup. The surfaces that rub against each other are made from highly polished metal, known as a metal-on-metal type of bearing couple.

**Benefit:** This artificial hip-replacement system is designed for patients who, because of their relatively younger age or increased activity level, might not be suitable candidates for traditional total hip arthroplasty, in that they may need ipsilateral hip joint revision in the future.

**Sources:** www.fda.gov; www.wmt.com

---

**Name:** OIS EyeScan

**Manufacturer:** Ophthalmic Imaging Systems, Sacramento, Calif.

**Approval Date:** December 2, 2009

**Purpose:** The EyeScan is a portable device that captures images of the anterior and posterior segments of the eye.

**Description:** The scanner can take pictures from a customized chin rest or a slit-lamp adapter, or it can be used as a hand-held device.

**Benefit:** The device is small, light, and portable, and its versatility should add value to an ophthalmologist’s practice.

**Precautions:** The light emitted from this instrument is potentially hazardous. The longer the duration of exposure, the greater the risk of ocular damage. Safety guidelines are provided in the user manual.

**Sources:** www.news-medical.net; www.oisi.com

---

**Name:** Pherocious CT Apheresis Catheter

**Manufacturer:** r4 Vascular, Inc., Maple Grove, Minn.

**Approval Date:** December 8, 2009

**Purpose:** The apheresis catheter is indicated for power injection of contrast media for contrast-enhanced computed tomography (CT). More than a quarter of a million patients undergo apheresis each year for the treatment of neurological, immunological, hematological, or oncologic disorders and for stem-cell transplantation. The device is designed for patient comfort and reliable long-term use.

**Description:** A staggered medial or proximal lumen location and power-injection capability at the distal tip make the catheter the new standard for addressing the challenges of long-term apheresis. The catheter is available in both 12.5 and 10.5 French sizes. All sizes are rated a maximum power injection rate of 5 mL/second at 300 pounds per square inch (psi).

**Benefit:** This product has the potential to reduce the number of needlesticks that patients currently require for CT studies. There have been few innovations in vascular access for these patients. The triple-lumen catheter offers a major advantage.

**Source:** http://r4vascular.com/pherocious.html

---

*continued from page 81*