

**NEW DRUGS**

**Stelara for Psoriasis**

Ustekinumab (Stelara, Centocor Ortho Biotech Inc.), a biologic agent, has been approved for adults with moderate-to-severe psoriasis, an immune system disorder that results in the rapid overproduction of skin cells. Plaque psoriasis is characterized by thickened patches of inflamed, red skin, often covered with silvery scales.

A monoclonal antibody that mimics the body’s own antibodies, ustekinumab blocks the action of two proteins that contribute to the overproduction of skin cells and inflammation. Because ustekinumab reduces the immune system’s ability to fight infections, it may pose a risk of infection and cancer. The FDA is requiring a Risk Evaluation and Mitigation Strategy (REMS) that includes information for health care professionals and a medication guide for patients.

Source: FDA, September 25, 2009

**Votrient and Kidney Cancer**

Pazopanib (Votrient) is now approved for patients with advanced renal cell carcinoma, a form of kidney cancer that is highly resistant to chemotherapy.

A once-daily oral medication, pazopanib is an angiogenesis inhibitor that may help prevent the growth of new blood vessels, which tumors need to survive. In a phase 3 trial, the drug reduced the risk of disease progression or death by 54% compared with placebo, regardless of any previous treatment. Treated patients gained an average of 9.2 months of progression-free survival, compared with 4.2 months for those not receiving the drug. Patients did not experience a significant decline in health-related quality of life. Adverse reactions were generally mild to moderate. However, 4% of treated patients died, compared with 3% of placebo patients.

This product has not yet been approved outside the U.S.

Sources: FDA, GlaxoSmithKline, October 19, 2009

**Berinert for Symptoms Of Hereditary Angioedema**

The FDA has approved Berinert, a C1-esterase inhibitor, for adolescents and adults with acute abdominal attacks and facial swelling associated with a potentially life-threatening genetic disease, hereditary angioedema (HAE). This protein product is derived from human plasma. Attacks can occur spontaneously or during stress, surgery, or infection in patients with HAE. Berinert regulates clotting and inflammatory reactions that, when impaired, can lead to local tissue swelling.

Berinert is contraindicated in patients with a history of life-threatening hypersensitivity reactions to C1-esterase inhibitors. Adverse reactions may include subsequent HAE attacks, headache, abdominal pain, nausea, muscle spasms, pain, diarrhea, and vomiting.

Source: FDA, October 12, 2009

**Generic Topamax Sprinkle Capsules for Seizures**

Mylan Pharmaceuticals has received approval for its Abbreviated New Drug Application (ANDA) for Topiramate Sprinkle Capsules (Sprinkle) in strengths of 15 mg and 25 mg. The capsules are the generic version of Janssen/Ortho-McNeil’s anticonvulsant Topamax Sprinkle Capsules in dosages of 15 and 25 mg.

Sources: Mylan; PharmaLive, October 15, 2009, www.pharmalive.com

**Folotyn and Peripheral T-Cell Lymphoma**

Pralatrexate (Folotyn, Allos) has been approved as the first agent to treat peripheral T-cell lymphoma (PTCL), often an aggressive type of non-Hodgkin’s lymphoma. Pralatrexate was designated as an orphan drug under the agency’s accelerated approval process.

The approval was based on evidence that it reduced tumor size, as shown on imaging scans in one study.

Adverse reactions included irritation or sores of the oral and digestive mucous membranes; low platelet cell and white blood cell counts; fever; nausea; and fatigue. Patients who take pralatrexate should take folate and vitamin B₁₂ supplements to reduce mucous membrane irritation.

For more information, please see this month’s Pharmaceutical Approval Update on page 636.

Source: FDA, September 25, 2009

**Cervarix Vaccine For Preventing Cervical Cancer**

Cervarix (GlaxoSmithKline) has been approved to prevent cervical cancer and precancerous lesions caused by human papillomavirus (HPV) types 16 and 18 in girls and women 10 through 25 years of age. HPV types 16 and 18 cause about 70% of cervical cancers worldwide.

In a clinical study involving more than 18,000 women 15 years through 25 years of age, the vaccine was about 93% effective in preventing precancerous cervical lesions caused by these HPV types among participants who had not already been infected by types 16 and/or 18 before the start of the study. Cervarix was approximately 53% effective in preventing precancerous cervical lesions among all Cervarix vaccinees, which included those who tested negative for HPV types 16 and/or 18 and those who tested positive at the start of the study. In other studies, girls 10 through 14 years of age had an immune response that was similar to that of the older group.

The vaccine provides protection for approximately 6.4 years; it does not protect against current HPV infections at the time of vaccination or against HPV
types not in the vaccine. Therefore, regular Pap tests are still recommended for all patients receiving Cervarix.

Pregnant women or women who think that they might be pregnant or who plan to become pregnant during the vaccination course should not use Cervarix.

The vaccine is administered in three separate injections. The initial dose is followed by two additional injections at one and six months.

Source: FDA, October 19, 2009

**NEW INDICATIONS**

**Welchol Tablets**

**For LDL-Cholesterol In Children**

Daiichi Sankyo, Inc., has announced the approval of its supplemental New Drug Application (sNDA) for colesevelam HCl (Welchol) to be used as an adjunct to diet and exercise, as monotherapy or with a statin, to reduce elevated low-density lipoprotein-cholesterol (LDL-C) levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia who have not responded to a trial of diet therapy.

The approval was based on data from a study of doses of 1.875 or 3.75 g/day as monotherapy or with a statin, to reduce elevated low-density lipoprotein-cholesterol (LDL-C) levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia who have not responded to a trial of diet therapy.

Source: Daiichi Sankyo, October 7, 2009

**Elitek Reduces Uric Acid In Adults with Blood Cancers**

Rasburicase (Elitek, Sanofi-Aventis U.S.) has been approved for the initial management of plasma uric acid levels in adult patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anti-cancer therapy that is expected to cause tumor lysis syndrome (TLS) and elevations of plasma uric acid.

Rasburicase was first approved in 2002 to manage plasma uric acid levels in pediatric patients receiving anti-cancer treatment and at risk for TLS. The new approval was based on pivotal phase 3 trial results showing that the drug significantly reduced PUA levels when compared to the current standard of care (oral allopurinol) in adults with hematological cancers at risk for TLS.

Based on the results of the study, rasburicase is now indicated at a daily dose of 0.20 mg/kg intravenously for up to five days. This is the first recombinant uricolytic FDA-approved agent in the U.S. for maintaining uric acid levels in patients undergoing cancer treatment. The drug rapidly catabolizes circulating uric acid into allantoin, which can be easily excreted by the kidneys in as little as four hours after the first dose.


**Preventing Genital Warts With Gardasil in Males**

Merck’s Gardasil vaccine is now indicated for the prevention of genital warts (condyloma acuminata) caused by human papillomavirus (HPV) types 6 and 11 in boys and men 9 through 26 years of age. Gardasil is currently approved for use in girls and women 9 through 26 years of age for preventing cervical, vulvar, and vaginal cancer caused by HPV types 16 and 18; precancerous lesions caused by types 6, 11, 16, and 18; and genital warts caused by types 6 and 11 at the start of the study, Gardasil was nearly 90% effective in preventing genital warts caused by infection with these HPV types.

In a randomized trial, for males who were not infected by types 6 and 11 at the start of the study, Gardasil was almost 90% effective in preventing genital warts caused by infection with these HPV types.

Gardasil is given as three injections over a six-month period.

Source: FDA, Oct 19, 2009

**Fluarix Vaccine For Pediatric Use**

The FDA has approved use of the seasonal influenza vaccine Fluarix (Glaxo-SmithKline) for children 3 to 17 years of age. Previously, this vaccine, which contains inactivated (killed) influenza A and B viruses, had been approved for use in adults 18 years of age and older.

The safety and effectiveness of Fluarix for use in children 3 years of age and older were documented in a study comparing children who received this agent with children who received Fluzone, an influenza vaccine already licensed for those 6 months of age and older. Children who received both vaccines produced similar amounts of antibodies in the blood at levels considered likely to be protective against seasonal influenza.

With this approval, four companies are now authorized to manufacture the seasonal influenza vaccine for children.

Fluarix does not protect against the 2009 H1N1 influenza virus, and it should not be administered to anyone who is allergic to eggs or egg products.

Source: FDA, October 21, 2009

**NEW FORMULATION**

**Welchol Oral Suspension for Glycemic Control, Cholesterol**

The FDA has approved an oral suspension of colesevelam (Welchol) (alone
or with a statin) for patients with difficulty swallowing tablets. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes and to reduce elevated LDL-C levels in adults with primary hyperlipidemia (Fredrickson type IIa). Colesevelam has also been used as an adjunct to diet and exercise for reducing elevated LDL-C levels in boys and menarchal girls 10 to 17 years of age and who have heterozygous familial hypercholesterolemia after they have tried dietary modifications. The recommended dose is one 3.75-gram packet once daily.

To avoid esophageal distress, patients should not take the suspension in its dry form. The suspension contains 48 mg of phenylalanine per 3.75-gram dose.

Source: Daiichi Sankyo, October 7, 2009

**DRUG NEWS**

**Heparin Potency Reduced**

Heparin, an anticoagulant, has been reformulated to improve its safety and to guard against potential contamination. The new formulation is 10% less potent than before. The change should make it easier for manufacturers to spot impurities in the drug; however, the FDA is advising physicians that extra heparin might be needed to treat some patients.

The formulation was revised because of heparin contamination in 2007 and 2008 involving a manufacturing step in China. The product was associated with deaths and other adverse events in the U.S. The change now includes a test for the contaminant.

Four companies in the U.S. produce heparin: B. Braun, APP, Hospira, and Baxter.

For more information, see the FDA Alert on heparin on page 634.

Sources: FDA, United Press International, and Associated Press, October 1, 2009

**Increased Adverse Drug Events in 2008**

The Institute for Safe Medication Practices (ISMP) has found that fatal, disabling, and serious adverse drug events (ADEs), as reported to the FDA, increased by 25% from 2007 to 2008 (from 80,600 to 100,800). The number of patient deaths also increased by 56% (from 9,800 to 15,200) in that time span.

One factor in the increase was a large number of recalls of generic drugs, including heparin, digoxin, morphine, isosorbide, and propafenone, because of poor product quality. Other reasons included an increase in voluntary reporting by health care professionals to the FDA and the growing number of Internet links to the FDA’s MedWatch site. Manufacturers also learned of ADEs through contact with patients.

Fentanyl (Duragesic, Ortho-McNeil Janssen) ranked first among drugs causing ADEs that were described as medication errors. The ISMP recommends that new prescriptions for fentanyl not be dispensed unless special instructions are communicated to patients considered appropriate to receive the drug.

A series of drug recalls led to the near collapse of KV Pharmaceuticals. In 2008, the company recalled a large quantity of morphine tablets exported to Canada because of superpotent, oversized tablets. It also began recalling morphine, isosorbide, dextroamphetamine, and propafenone. In 2009, the company announced that it was recalling most of its products.

In 2009, the FDA and Pfizer strengthened the warnings regarding the risks of violence to oneself and others associated with varenicline (Chantix). The ISMP suggests that the warning about accidents emphasize the possibility of severe ADEs when the drug is started, throughout therapy, and even after therapy stops. The ISMP also recommends that the Department of Defense and the Federal Aviation Administration extend its present ban (for pilots, air controllers, and missile crews) to all uniformed military personnel, police, and firefighters.

The number of reports of psychiatric side effects associated with Merck’s montelukast (Singulair) also grew. In 2009, the company noted the potential for psychiatric ADEs in its Web-based information for patients.


**Shortage of Tamiflu Oral Suspension May Lead to Errors**

Shortages of Roche’s oral suspension of oseltamivir phosphate (Tamiflu) in some areas in the U.S. is posing a risk of dosing errors related to the product’s concentration.

Tamiflu is provided in a 12-mg/mL suspension and is available for children and adults who have difficulty swallowing capsules. Because of the influenza epidemic, some pharmacies have been unable to buy the commercial oral suspension from Roche or drug wholesalers. As a result, they’ve been compounding the product on an emergency basis by following FDA-approved directions in the labeling.

The suspension is made from the powder in Tamiflu capsules, which are still available. However, the compounding directions in the labeling result in a 15-mg/mL oseltamivir base concentration, not the normally available 12-mg/mL base concentration. Unless prescribers specify the patient’s dose in milligrams, a dosing error is possible. In some cases, prescribers expected the 12-mg/mL product to be used because they were unaware of the shortage. The 15-mg/mL concentration is resulting in a dose that is too large for children.

The ISMP is advising prescribers to communicate suspension doses in mil-
ligrams rather than by volume. In hospitals with computerized prescribing, only the available concentration should be listed; otherwise, there must be direct communication between prescriber and pharmacist to ensure that the intended dose reaches the patient.

If pharmacists experience a shortage, they can communicate with medical practices in their area to reduce the possibility of dosing errors when dispensing the pharmacy-compounded solution. Roche is also providing instructions for an extemporaneous preparation of capsule contents (30, 45, and 75 mg) mixed with sweetened liquids for single doses.


**Does Metformin (Glucophage) Lower Cancer Risk?**

Metformin (Glucophage, Bristol-Myers Squibb) may help protect against cancer. Researchers from the University of Dundee in the United Kingdom found a 37% reduced risk with metformin and say that their findings warrant a randomized trial. During 10 years of follow-up, cancer occurred in 297 of 4,085 patients (7.3%) new to using metformin, compared with 474 (11.6%) of 4,085 non-users. Because this was an observational study, the researchers could not control for all differences between study groups. The metformin population seemed to be a different group clinically from the non-users, with a much lower rate of mortality. Some of these rates might have been explained by lower risk of cardiovascular mortality.

The metformin patients also might have had a lower baseline risk of cancer, because they were younger than the non-users; however, their mean body mass index and glycosylated hemoglobin (HbA1c) values were higher. However, having adjusted for known potential confounders, such as other diabetic drugs, smoking, and age, the researchers say that it is unlikely that unknown or residual confounders could account for the entire 37% reduced risk.

The metformin users also had a longer median time before cancer developed (3.6 years vs. 2.5 years), but a dose-response analysis showed that their cancer risk was higher during the first two years of follow-up. The reason might be that patients who are just starting to take metformin have more contact with healthcare professionals and thus cancer would be more likely to be diagnosed. In later years, high maximum doses of metformin were associated with the greatest reduction in risk of cancer.

Source: *Diabetes Care* 2009;32:1620–1625

**Shorter Hospital Stays And Eplerenone (Inspra)**

Adding eplerenone (Inspra, Pharmacia/Pfizer) to standard therapy for patients who have had heart attacks can shorten the length of hospitalization, say researchers for the EPHESUS study (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival).

The multicenter trial included 6,632 patients who were given eplerenone 25 mg, titrated to 50 mg daily, or placebo. The mean follow-up was 16 months. Eplerenone was associated with a 15% reduction in the number of patients hospitalized for heart failure. Patients given eplerenone also spent 1.6 fewer days in the hospital than patients given placebo (13.3 vs. 14.9 days). A separate cost-effectiveness analysis showed that using eplerenone with standard therapy cut total rehospitalization costs significantly, by $275 per hospitalization, compared with placebo.

Source: *Am Heart J* 2009;158:437–443

**Chorea Linked To Gabapentin (Neurontin)**

A 75-year-old patient who was given gabapentin (Neurontin, Pfizer) for severe anxiety developed choreiform movements, according to doctors at Richmond University, New York, and the University of Connecticut.

The patient’s memory complaints, attributed to dementia and comorbid anxiety disorder, were present before the first evaluation. Neuropsychological evaluation confirmed global cognitive dysfunction, including memory loss. The cause was believed to be vascular.

The patient took citalopram (Celexa, Forest), which was discontinued after four months because it wasn’t effective. Gabapentin was initiated, and the dose was titrated up to 300 mg three times daily.

Chorea began a month after gabapentin was started, lasted for about four months, and resolved two days after the drug was discontinued. The patient’s medical history was negative for psychiatric and neurological disease, and his medication history did not reveal treatment with antipsychotic drugs or dopamine antagonists. He did have hyperlipidemia, coronary artery disease, and temporal arteritis, and he had undergone multiple coronary artery bypass grafts and an aortic valve replacement. In addition to gabapentin, he was also taking 25 mg of trazodone (Desyrel, Apothecan) at night and lidocaine (e.g., Xylocaine, AstraZeneca) for mouth ulcers.

The patient began taking haloperidol (Haldol, Ortho-McNeil) for chorea, but it had little effect. However, when gabapentin was stopped, his speech was clearer, the chorea was improved, and anxiety symptoms were also alleviated within two days. He was discharged after eight days and has had no recurrence of abnormal movements. His previous diagnosis of dementia was reversed.

continued on page 601
This was the first case to describe chorea development with low-dose gabapentin, the authors say. In other cases, chorea usually developed with doses ranging from 1,200 to 2,100 mg/day.


**Acetylcysteine: Timing Is Everything**

Which is more effective in preventing hepatotoxicity for patients with acute acetaminophen poisoning: 20-hour intravenous (IV) or 72-hour oral N-acetylcysteine? According to a Canadian study, it’s important to know when the overdose occurred.

Of 2,086 patients in the 20-hour IV group, 13.9% experienced hepatotoxicity, compared with 15.8% among the 1,962 patients in the 72-hour oral group. The relative risk of hepatotoxicity was lower in the 20-hour IV group when the acetylcysteine was started within 12 hours of ingestion. The risk was lower in the 72-hour group when acetylcysteine was started later than 18 hours after ingestion. The researchers observed no significant difference in risk between the two groups when acetylcysteine treatment was started 12 to 18 hours after ingestion.


**Many Patients Have Stopped Osteoporosis Therapy**

In a study from Israel, about one-fifth of women taking anti-osteoporosis drugs stopped taking them after two years, often without reporting any defined reason.

The study included 178 patients who had been receiving alendronate (Fosamax, Merck) or raloxifene (Evista, Lilly). The researchers assessed adherence at a clinic visit after six months and by telephone two years after the patients began treatment.

After six months, 137 women (77%) were still taking the drugs. After two years, the number had dropped to 78 (44%). At two years, 22% had stopped taking these agents, 10% had changed to another therapy, and 12% were lost to treatment. Of 41 women who stopped treatment at six months, 17 restarted with one of the anti–bone resorptive medications.

Age, a family history of osteoporosis, and previous fracture history did not influence patients’ adherence. Eight women discontinued taking alendronate because of upper gastrointestinal (GI) adverse effects. In three cases, women stopped taking the drug because of perceived benefit: bone mineral density had increased.

Source: *Arch Gerontol Geriatr* 2009;49:360–363
NEW DRUGS

‘Traditional’ Chinese Therapy And Rheumatoid Arthritis

In Chinese medicine, an extract of *Tripterygium wilfordii* Hook F (TwHF) has been used to treat autoimmune and inflammatory conditions for generations. Now a study supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases has shown that TwHF extract worked better than sulfasalazine in attaining 20% improvement in American College of Rheumatology (ACR) criteria at 24 weeks.

During the six-month study, TwHF extract resulted in rapid improvement in joint pain, swelling, and markers of inflammation. The study involved 121 patients, although only 62 completed the 24 weeks (62% of those taking TwHF and 41% of those taking sulfasalazine). Of those patients, 68% of the patients receiving TwHF showed at least a 20% improvement in disease activity, compared with only 36% of those on sulfasalazine. Similar improvements in ACR 50 and ACR 70 responses were observed.

Improvements in C-reactive protein, erythrocyte sedimentation rate, and interleukin-6 (a pro-inflammatory cytokine) translated into better patient function. The rapid improvement might have been a result of both TwHF’s potent anti-inflammatory and immunomodulatory effects and its ability to inhibit transcription of cyclooxygenase-2 (COX-2), which may reduce prostaglandin E₂ production and thus might have a direct analgesic effect.

Adverse effects included GI symptoms, which subsided in more patients receiving TwHF than those who continued receiving sulfasalazine. The investigators say that a lower dose at the beginning of treatment or a gradual dose increase might improve tolerability.


Companies Warned about Illegal Opioid Pain Relievers

The FDA has ordered four companies to stop marketing unapproved codeine sulfate tablets. These opioid analgesics are narcotic pain relievers that have not been approved, and there is no evidence that they are safe and effective. The products are as follows:

- Codeine Sulfate Tablets, 30 mg, 60 mg, Lehigh Valley Technologies
- Codeine Sulfate Tablets, 30 mg, 60 mg, Cerovene, Inc.
- Codeine Sulfate Tablets, 30 mg, Dava International, Inc.
- Codeine Sulfate Tablets, 30 mg, 60 mg, Glenmark Generics

The FDA does not anticipate a shortage; Roxane markets FDA-approved codeine sulfate tablets and is able to meet the demand for the drug.

Source: FDA, October 13, 2009

A Gender Gap In Pain Management

A patient’s sex seems to matter when it comes to the type of analgesia given, according to a study from Monash University, Victoria, British Columbia, and the University of Melbourne, Australia.

Of 3,357 patients transported to the hospital by ambulance, 1,766 reported pain; 50% of the patients were women. Their median initial pain score was 6 on a verbal scale of 0 to 10. The patients received analgesia in roughly the same proportions, with no significant difference between the sexes.

Of the patients reporting pain, 15% received morphine, 34% received methadone, and 6% received both. However, 17% of the men, but only 13% of the women, received morphine; this difference remained significant when the researchers controlled for type of pain, age, and pain severity.

One explanation for gender bias might have been the reluctance of female patients to accept morphine. However, equal percentages of men and women (11%) declined analgesia. In other studies, both men and women expect women to be more likely to report pain, to be more sensitive to pain, and to be less tolerant of pain than men. Such beliefs might influence a paramedic’s decision to administer or withhold morphine, which is seen as an analgesic agent reserved for severe pain. The researchers cite studies in which the treating physician’s sex influenced pain-management decisions and studies involving an experimental pain setting in which the sex of the experimenter influenced pain reporting.


DEVICE BRIEFS

Optase Wound Gel

Eloquest Healthcare, Inc., has joined with Onset Therapeutics to market Optase (Balsam of Peru, castor oil, trypsin), a topical gel that promotes healing of debrided ulcers, varicose ulcers, and diabetic wounds. The gel helps to protect the wound and increases capillary blood flow.


Donor Screening HIV Test

Abbott Laboratories has received approval for the first fully automated blood screening test for HIV-1 and HIV-2, the Abbott Prism HIV O Plus. The test was approved for screening donated blood and specimens from living organ donors.

HIV type 1 incudes group M, the most common subgroup of the virus in the U.S., and group O, found primarily in Cameroon and other areas of West Africa. HIV type 2 is found mostly in West Africa. Both types have been detected in the U.S. and Europe.
**New Use for Bone Graft Substitute (EquivaBone)**

EquivaBone (Etex Corp.) is indicated for filling bone voids or defects of the skeletal system that are not intrinsic to the stability of the bone structure. With this new indication, the device can now be used in postero-lateral spine fusion; it can also be mixed with autologous blood, adding greater procedural flexibility. The resultant viscous putty can then be molded and packed or injected into a defect.

This bone graft substitute was the first moldable and injectable combination product. Both trauma and spine fusion data were included in the 510k submission, which was approved in April 2008.


**OVA1, a Test for Ovarian Cancer**

A new test, called OVA1 (Vermillion, Inc.), can help detect ovarian cancer in a pelvic mass. OVA1 identifies some women who will benefit from referral to a gynecological oncologist for surgery despite negative results from other tests for ovarian cancer. If other test results suggest cancer, referral to an oncologist is appropriate even with a negative OVA1 result.

OVA1 should be used as an adjunctive test to complement, not replace, other diagnostic and clinical procedures. A blood sample is obtained to test for levels of five proteins that change in the presence of ovarian cancer.

The test is intended only for women 18 years of age and older who are already candidates for surgery because of a pelvic mass. OVA1 is not indicated for ovarian cancer screening or for arriving at a definitive diagnosis of ovarian cancer.

Source: FDA, September 11, 2009

**Resuscitator Recalled**


This recall is being conducted because of a potential malfunction of certain units of the MPR, which may impair the ability of the device to generate the positive pressure necessary to function properly. Such a malfunction may create a situation in which the use of the product could potentially cause serious adverse health consequences or death.

Unomedical is contacting customers to arrange for the return and credit of all MPR units subject to this recall by sending notification letters to distributors and customers. The company has also set up a Web page with a list of affected lot numbers, diagram, photos, and instructions.

To distinguish between the recalled product and an unaffected product, customers may examine the patient valve housing immediately below the right-angle exhalation port, where the retention ring should be visible. MPR units with a clear or transparent ring, as well as those where no ring can be seen, should be returned to the company. MPR units with a clearly visible blue retention ring are not affected and do not need to be returned. Unomedical notified the FDA of its decision to voluntarily recall the product on October 1, 2009. Customers can call Unomedical at 1-800-634-6003.

Source: FDA, October 6, 2009; www.unomedical.com/?pageid=H3160.

**Zolinza Reduces Brain Metastases in Mice**

In a new study, Merck’s drug vorinostat (Zolinza), a histone deacetylase inhibitor also known as suberoylanilide hydroxamic acid (SAHA), was able to cross the blood–brain barrier and reduce the development of large metastatic tumors in mice brains by 62% when compared with mice not receiving the drug. Vorinostat is approved to treat patients...
with cutaneous T-cell lymphoma.

The incidence of breast cancer spread to the brain is increasing. These metastases have been largely untreatable because the blood–brain barrier limits drug access to the brain and many drugs are carried out of the brain at this barrier.

Vorinostat appears to slow the growth of primary tumors of several different types of cancer in mice. Previous studies suggested that the drug could be taken up by the brain, but little was known about its effects on metastatic tumors. To study the drug’s effect on the formation of brain metastases, scientists used a mouse model of human breast cancer. Human breast cells were cultured in the laboratory and were injected into mice with compromised immune systems. The breast cancer cells then migrated to the brain, forming metastases.

Urgently needed are medications that can cross the blood–brain barrier and reduce the size and incidence of metastatic tumors. Vorinostat was easily absorbed into normal mouse brains and reduced the development of tiny tumors by 28% compared with the rate in control mice.

Vorinostat’s action may be linked to the fact that it can cause breaks in both strands of a DNA helix and can lower the activity of a DNA repair gene called Rad52. The researchers hypothesize that the drug could enhance the effect of radiation therapy in mice with brain cancer metastasis. Mice that received implants of human breast tumors in their brains lived the longest after receiving both vorinostat and radiation, suggesting that the drug enhances the sensitivity of cancer cells to radiation therapy.

Sources: Clin Cancer Res 2009;15(19); NIH, September 29, 2009

Cocaine Vaccine Shows Promise

An experimental anti-cocaine vaccine appears to result in a substantial reduction in cocaine use, according to a clinical trial supported by the National Institute on Drug Abuse (NIDA).

The anti-cocaine vaccine stimulates the immune system to produce antibodies. Unlike antibodies against infectious diseases, which deactivate disease-causing agents, anti-cocaine antibodies attach themselves to cocaine molecules in the blood, preventing them from passing through the blood-brain barrier. By preventing the drug’s entry into the brain, the vaccine inhibits or blocks the cocaine-induced euphoria.

This study included 115 patients from a methadone maintenance program who received the anti-cocaine vaccine or a placebo vaccine. Participants in both groups received five vaccinations over a 12-week period and were followed for an additional 12 weeks. Participants also took part in weekly relapse-prevention sessions with a substance abuse counselor; their blood was tested for antibodies to cocaine, and their urine was tested three times a week for the presence of opioids and cocaine.

The subjects differed in the levels of antibodies generated in response to vaccination; 38% attained blood levels of anti-cocaine antibodies thought to be sufficient to block cocaine’s euphoric effects. During weeks 9 to 16 (when antibody levels peaked), these patients had significantly more cocaine-free urine samples than the placebo subjects or those with active vaccine but low levels of anti-cocaine antibodies. Patients with the highest antibody levels had the greatest reductions in cocaine use. No serious adverse effects were noted.

Of participants in the high-antibody group, 53% were abstinent from cocaine more than half the time during weeks 8 to 20, compared with only 23% of those with lower antibody levels. Immunization did not achieve complete abstinence from cocaine use, but previous research had shown that a reduction in use was associated with improved social functioning, and the results were thus therapeutically meaningful.

Sources: Arch Gen Psychiatry, October 2009; NIH, www.nih.gov, October 5, 2009

Gaucher’s Disease Gene Linked to Parkinson’s Disease

Carriers of a rare, genetic condition called Gaucher’s disease, compared with the general public, have a five-times-greater risk of developing Parkinson’s disease (PD). A study from the National Institutes of Health suggests that mutations in the gene responsible for Gaucher’s disease are among the most significant risk factors found to date for PD.

A neurological condition, PD affects about 1% to 2% of people over the age of 60. Gaucher’s disease occurs when an individual inherits two defective copies of the GBA gene, which codes for an enzyme called glucocerebrosidase. This enzyme breaks down a fatty substance called glucocerebroside, which, if not properly disposed of, can harm the spleen, liver, lungs, bone marrow, and brain.

The research team examined the frequency of GBA mutations in 5,691 patients with PD, including 780 Ashkenazi Jews, in whom a particular type of Gaucher’s disease is more prevalent. Those data were matched against 4,898 unaffected volunteers, including 387 Ashkenazi Jews. At least one of the two common GBA alterations was found in 3.2% of PD patients and 0.6% of controls. Among the Ashkenazi patients, 15.3% of those with PD carried a GBA alteration compared with 3.4% of Ashkenazi controls.

GBA mutations also appear to increase the likelihood of early PD onset. In this
study, PD patients with GBA alterations developed earlier symptoms an average of four years earlier than other PD patients.

In the general population, GBA alterations occur in fewer than 1 in 100 people; in those of Ashkenazi descent, GBA alterations occur in at least one in 16 people. However, many carriers of the GBA mutation as well as patients with Gaucher’s disease never develop PD.


**NEW MEDICAL DEVICES**

Marvin M. Goldenberg, PhD, RPh, MS

**Name:** IsoFlow Infusion Catheter

**Manufacturer:** Vascular Designs, Inc., San Jose, Calif.

**Approval Date:** September 2, 2009

**Use Classification:** The dual-balloon catheter is used to deliver medications directly into a highly targeted area in patients with critical illnesses.

**Description:** This infusion catheter is designed to isolate a specific treatment region within the body from blood flow. It allows the infusion of fluids into the region and the perfusion of blood past the region to keep the blood flow intact during treatment. This catheter can deliver medications sideways while pressure is used to push the medication into the targeted area.

**Purpose:** Sideways perfusion enables physicians to precisely target areas within the body where the infused drugs are delivered. Local delivery may cause tumors that were previously unresponsive to systemic chemotherapy to respond.

**Benefit:** Drug concentrations can be increased at specific sites, and systemic exposure to medication is reduced, which improves outcomes in patients receiving chemotherapy. Drugs can be delivered into areas that could not previously be treated directly, such as a cancerous tumor. Delivering a local endovascular drug dose without systemic exposure can reduce complications.

**Source:** www.vasculardesigns.com

**Name:** DuraSeal Sealant

**Manufacturer:** Covidien, Waltham, Mass.

**Approval Date:** September 8, 2009

**Use Classification:** This sealant is used to repair tissue tears that occur during spinal surgery.

**Description:** The synthetic polymer is sprayed onto surgical sites to close gaps and create a watertight seal.

**Purpose:** The product is indicated for sutured dural tears, which occur in almost 10% of all spinal surgeries.

**Benefit:** DuraSeal is fast-acting and can be prepared in only two minutes; it sets in three seconds, and surgeons can quickly continue with their procedures.

**Source:** The Wall Street Journal, September 8, 2009; http://investor.covidien.com

**Name:** PsoriasisDX Genetic Test

**Manufacturer:** PharmaGenoma, Inc., Irvine, Calif.

**Approval Date:** September 19, 2009

**Use Classification:** The genetic test is used to identify persons at high risk for the development of psoriatic arthritis (PsA) before they experience arthritic symptoms.

**Description:** At a cost of $399, the device is available through qualified physicians. A cheek swab is performed to collect a genetic sample. The sample is mailed for analysis to the PsoriasisDX laboratory, and the test results are reported to the doctor.

**Purpose:** This is the first commercial genetic test for PsA.

**Benefit:** This genetic test provides an opportunity to lessen joint damage through early medical intervention. PsA eventually develops in 20% to 40% of psoriasis patients.

**Sources:** www.psoriasisdx.com; www.genomeweb.com

**Safety Alerts**

**Fetal Monitors.** The FDA has notified health care professionals and facilities of complaints of inaccurate readings during the use of Philips Avalon Fetal Monitors (Models FM20, FM30, FM40, and FM50) with the ultrasound transducer. On September 4, 2009, Philips issued a device safety alert. Inaccurate output readings, if not properly addressed, can lead to unnecessary interventions, failure to identify the need for interventions, and an inability to identify fetal distress. The complaints most often occurred during the second stage of labor.

Recognizing these conditions and responding appropriately is important to avoiding serious adverse health consequences. The FDA’s alert describes steps for clients to take to minimize risks.

**Source:** FDA, September 4, 2009

**Recall.** The Pedi-Cap End-Tidal Carbon Dioxide Detector (Pedi-Cap and Pedi-Cap 6) has been recalled. It was noticed that the device might increase the resistance of the flow of air into the lungs, resulting in ineffective ventilation and the inability to verify the correct placement of a breathing tube when it is inserted into the windpipe. The Pedi-Cap is used in pediatric patients weighing 2.2 to 33 pounds during ventilation. There is a reasonable probability that using the recalled PediCap would cause serious adverse health consequences or death.

Covidien has informed its distributors and customers to stop selling and using the affected devices and to return them to the company.

**Source:** FDA, September 10, 2009