**NEW DRUGS**

**Rotarix Oral Vaccine For Rotavirus Gastroenteritis**

Avant Immunotherapeutics has announced that its partner, GlaxoSmithKline, has received approval from the Food and Drug Administration (FDA) to market Rotarix vaccine to prevent rotavirus gastroenteritis in infants.

The Centers for Disease Control and Prevention (CDC) currently recommends that children complete the rotavirus immunization series by six months of age. Rotavirus infects virtually every child in the U.S. by five years of age and is the leading cause of severe gastroenteritis in infants and young children worldwide. In the U.S., the rotavirus season typically begins in the southwest during November and December and spreads to the northeast by April and May.

Avant licensed the technology to GlaxoSmithKline in 1997.


**Generic Ocuflox (Ofloxacin) For Eye Infections**

Akorn’s Abbreviated New Drug Application (ANDA) for Ofloxacin Ophthalmic Solution USP, 0.3%, has been approved. This sterile anti-infective agent is used to treat ocular infections caused by bacteria in conjunctivitis and corneal ulcers. This product is the generic version of Allergan’s Ocuflox. The launch is scheduled for the third quarter of 2008.

(Source: Akorn, April 17, 2008.)

**Sumatriptan/Naproxen (Treximet) for Migraine**

Treximet (GlaxoSmithKline/Pozen), a combination tablet, has been approved for the acute treatment of migraine with or without aura in adults.

Treximet contains 85 mg of sumatriptan (Imitrex) and 500 mg of naproxen sodium. Available in 25-mg, 50-mg and 100-mg strengths, it is the first migraine product that combines a triptan and an anti-inflammatory pain reliever in a single tablet.

In clinical trials, the tablet provided more pain relief at two hours compared with sumatriptan 85 mg or naproxen sodium 500 mg alone. Fewer patients receiving Treximet needed a rescue medication to treat their migraine attack than those taking sumatriptan 85 mg.

(Source: GlaxoSmithKline/Pozen, April 15, 2008.)

**Aplenzin for Depression In Adults**

Biovail Corporation has received the FDA’s approval for its New Drug Application (NDA) for Aplenzin (BVF-033), a once-daily formulation of bupropion hydrobromide for the treatment of depression in adults. This alcohol-resistant formulation of a new bupropion salt has been approved as 174-mg, 348-mg, and 522-mg extended-release tablets.

(Source: Biovail, April 23, 2008.)

**Certolizumab (Cimzia) For Crohn’s Disease**

Certolizumab pegol (Cimzia, UCB) has been approved for adults with moderate-to-severe Crohn’s disease who have not responded to conventional therapies. This product was approved with a Medication Guide.

This debilitating inflammatory bowel disease affects more than one million men and women worldwide. Certolizumab reduces signs and symptoms of the disease, but patients must be closely monitored. Patients receive an injection every two weeks for the first three injections. After the benefit has been established, the medication is given once every four weeks.

Patients receiving this drug are at increased risk for serious adverse effects, including serious infections that can lead to hospitalization or death. Because certolizumab affects the immune system, it can lower the body’s ability to fight infections and may cause malignancies. In cases of serious infections, the drug should be discontinued immediately.

(Source: FDA, April 23, 2008.)

**Regadenoson (Lexiscan) For Cardiac Stress Tests**

CV Therapeutics, Inc., and Astellas have announced the approval of regadenoson injection (Lexiscan) for use in a test that detects coronary artery disease in patients who cannot undergo an exercise stress test. This pharmacological stress agent is used in radionuclide myocardial perfusion imaging (MPI). It is delivered as a rapid bolus in about 10 seconds without regard to body weight.

Cardiac stress tests identify areas of poor blood flow in the heart.

Lexiscan is not indicated for patients with second-degree or third-degree atrioventricular block or sinus node dysfunction who do not have a functioning artificial pacemaker.

(Sources: CV Therapeutics/Astellas, April 10, 2008; www.Lexiscan.com.)

**NEW INDICATIONS**

**Abatacept (Orenica) For Juvenile Rheumatoid Arthritis**

Bristol-Myers Squibb has received approval to market abatacept (Orenica) to reduce signs and symptoms in pediatric patients six years of age and older with moderately to severely active juvenile rheumatoid arthritis (JRA), also called juvenile idiopathic arthritis. It may be used as monotherapy or concomitantly with methotrexate (MTX).

The approval of this indication was based on the AWAKEN trial (Abatacept Withdrawal study to Assess efficacy and
safety in Key Endpoints in juvenile idiopathic arthritis Not responding to current treatment).
(Source: FDA, April 8, 2008.)

Vyvanse for ADHD in Adults
The FDA has approved Shire’s lisdexamfetamine dimesylate (Vyvanse) for treating Attention-Deficit/Hyperactivity Disorder (ADHD) in adults. Introduced in July 2007 for the treatment of ADHD in children 6 to 12 years of age, it is now the first once-daily prodrug stimulant approved to treat adults with ADHD.

Vyvanse is now available in strengths of 30 mg, 50 mg, and 70 mg for once-daily dosing. Dosage strengths of 20 mg, 40 mg, and 60 mg are expected to be available in pharmacies this summer.
(Source: FDA, April 23, 2008; www.vyvanse.com.)

DRUG NEWS
Recalled: Rotigotine (Neupro), Parkinson Patch

Schwarz Pharma has announced the recall of Neupro, a transdermal delivery system worn on the skin to treat early-stage Parkinson’s disease, because of the formation of rotigotine crystals in the patches. When the drug crystallizes, less of the drug is available to be absorbed through the skin and the efficacy of the product may vary.

Health care professionals should not prescribe the patch for new patients, and they should start lowering the dose for patients who are currently using the product. Patients should not abruptly discontinue therapy because of the possibility of neuroleptic malignant-like syndrome or an akinetic crisis.
(Source: FDA, April 9, 2008.)

Alert for Tussionex, A Cough Medication

The FDA has issued an alert concerning the safe and correct use of a potent cough medication, Tussionex Penn-kinetic Extended-Release Suspension (UCB) in response to reports of adverse events, including death. The product contains hydrocodone, a narcotic ingredient, and the antihistamine chlorpheniramine. The alert does not apply to short-acting hydrocodone cough products that can be given every four to six hours.
(Source: FDA, March 13, 2008.)

Revised Dosing For PegIntron/Ribavirin In Hepatitis C

The FDA has approved label revisions for Schering-Plough’s combination agent peginterferon alfa-2b (PegIntron) plus ribavirin (Rebetol) for chronic hepatitis C virus (HCV) infection. The revised label includes recommendations for weight-based dosing of Rebetol (800–1,400 mg daily) and recommends a shorter, 24-week course of the combination for patients with chronic HCV genotype 2 or 3.

In the U.S., PegIntron is indicated for use alone or with Rebetol for treating chronic HCV in patients with compensated liver disease who have not used interferon-alpha and who are at least 18 years of age.

The label changes were based on the results of the WIN-R trial (Weight-Based Dosing of PegIntron and Rebetol), which showed higher sustained virological responses, when compared with PegIntron plus a flat 800-mg daily dose of Rebetol (the previously accepted dose).
(Source: FDA, March 27, 2008.)

New Medicare Guidelines For Erythropoietin in Dialysis

The Centers for Medicare and Medicaid Services (CMS) has completed guidelines for kidney dialysis patients that do not include changes in anemia treatment.

Last year, the agency had set restrictions on the use of anemia drugs such as Amgen’s Epogen and Aranesp and Johnson & Johnson’s Procrit for cancer patients. The revised regulations address patients’ rights, patients’ safety, and their participation in health care procedures.

Epogen is used to treat anemia in patients undergoing kidney dialysis, and Aranesp is used in patients with kidney disease and cancer patients undergoing chemotherapy. Under a license from Amgen, J&J sells Procrit for treating cancer patients. The drugs are genetically engineered versions of erythropoietin.

(Sources: Reuters, April 3, 2008; CMS, www.cms.hhs.gov.)

AIDS Drugs
And Heart Attack Risk

In a European study, an antiretroviral drug used to fight AIDS, GlaxoSmithKline’s abacavir (Ziagen), appeared to double the risk of a heart attack. Didanosine (Videx, Bristol-Meyers Squibb), a less commonly used agent, also increased heart attack risk by about 50%.

Researchers from the University of Copenhagen analyzed data from more than 33,000 patients with HIV infection in Europe, the U.S., and Australia who were enrolled from 1999 to 2005. The authors looked for heart problems that occurred before February 2007. Of 517 patients who had heart attacks, 124 had recently taken didanosine and 192 had recently taken abacavir.

Patients taking abacavir had twice the chances of a heart attack compared with those using other antiretroviral agents. Those using didanosine had a 50% higher risk, but the risk disappeared six months after patients stopped taking the drugs.

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GlaxoSmithKline did not agree with the study and noted that abacavir does not increase lipids or glucose levels.

Patients who smoke or who are obese are already susceptible to heart problems and may face the highest risk. In
people with HIV infection, heart attacks do not appear to be more deadly than in healthy people; however, after patients with HIV infection have a heart attack, they are more likely than others to have another attack. As HIV patients who use antiretroviral therapy continue to live longer, more rare effects may emerge.

(Sources: Lancet online, March 2008; Associated Press/Sci-Tech Today.)

**Reversing Atherosclerosis In Diabetes**

Aggressively lowering cholesterol and blood pressure (BP) levels below current targets in adults with type-2 diabetes may help to prevent and reverse hardening of the arteries. Diabetic patients are two to four times more likely than nondiabetic people to die of heart disease.

A three-year study, supported by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH), is the first to compare two treatment targets for LDL-cholesterol and systolic BP in diabetic patients. In the Stop Atherosclerosis in Native Diabetics Study (SANDS), 50% of the participants were enrolled to try to decrease LDL-cholesterol levels to 100 mg/dL and systolic BP to 130 mm Hg or below. The other 50% aimed for more aggressive reductions (LDL-cholesterol to 70 mg/dL or below and systolic BP to 115 mm Hg or below).

All of the enrollees were American Indians 40 years of age or older who had diabetes, high blood cholesterol, and high BP but no history of heart attack or other evidence of heart disease. Patients were encouraged to follow a heart-healthy eating plan, be physically active, maintain a healthy weight, and not to smoke.

Participants in both groups reached and maintained their target goals for cholesterol and BP. The rate of heart attacks and other cardiovascular events was similar for the two groups and lower than expected. Carotid artery thickness increased slightly with standard treatment but regressed with aggressive treatment, indicating a partial reversal of atherosclerosis. Heart size decreased in both groups, but this benefit was greater with intensive therapy.

Patients receiving intensive treatment needed more drugs and higher doses, and were more likely to experience side effects from BP-lowering medications, compared with those in the standard group. Adverse effects usually resolved after the drug was changed or after the dose was reduced.

(Sources: JAMA, April 9, 2008; NIH.)

**Warning for Inhaled Insulin (Exubera) and Lung Cancer**

Pfizer has updated its product labeling for inhaled insulin of rDNA origin (Exubera Inhalation Powder) to include a warning about lung cancer. Over the course of the clinical trial program, six of 4,740 treated patients and one of 4,292 untreated patients developed lung cancer. The update states that all patients who developed lung cancer had a history of cigarette smoking and that there were too few cases to determine whether the cancer was related to the use of the product.

Pfizer announced in October 2007 that it would stop marketing Exubera because it did not meet customers’ needs or the company’s financial expectations. It is recommended that physicians prescribe other therapies for glycemic control.

(Sources: Pfizer, April 9, 2008; www.exubera.com.)

**Can Statins Prevent Kidney Disease?**

Small studies have found that statins may help keep kidneys from deteriorating. Pravastatin (Pravachol, Bristol-Myers Squibb), for instance, slows the loss of renal function in patients with coronary artery disease, proteinuria, and moderate chronic and advanced kidney disease. Could statins do the same for other patients?

Researchers studied the effects of statins on renal dysfunction in 197,551 veterans from 10 hospitals in the southern states. Of those patients, 58,332 (30%) were using statins. Renal dysfunction was defined as a doubling of baseline creatinine or an increase in serum creatinine of 0.5 mg/dL from the first to the last measurement with at least 90 days in between.

Over three years of follow-up, renal dysfunction developed in 6,654 (3.4%) patients. After the authors made adjustments for diabetes, smoking, and medications, statins reduced the odds of renal dysfunction by 13%. The benefits appeared to be independent of the reduction in cholesterol.

In a meta-analysis on the same topic, another research group concluded that statins could safely reduce lipid concentrations and cardiovascular endpoints in patients with chronic kidney disease, irrespective of stage of disease. However, they did not find a benefit in all-cause mortality, perhaps because patients with stages 3 to 5 chronic kidney disease are understudied. They add that renoprotective effects of statins are uncertain because of relatively sparse data.

Although research has confirmed the role of statins in the secondary prevention of chronic kidney disease, more studies are needed to establish their role in primary prevention.

(Sources: Am J Cardiol 2008:101:975–979; BMJ 2008;336:645–651.)

**Estrogen and Breast Cancer Recurrence**

Women whose breast cancer returned after treatment had almost twice as much estrogen in their blood compared with women who remained free of cancer—
Breast Cancer and Overweight

Overweight women with breast cancer seem to have more aggressive disease and lower survival. Scientists think that fat tissue may increase inflammation.

In a study of 606 women with locally advanced breast cancer, at five years, overall survival rates were 56.8% in obese women, 56.3% in overweight women, and 67.4% in normal-weight women. Ten-year survival rates were 42.7% in obese women, 41.8% in overweight women, and 56.5% in normal-weight women. Rates of inflammatory breast cancer were 45% in obese women, 30% in overweight women, and 15% in normal-weight women. By five years, 50.8% of obese women had a recurrence, compared with 38.5% of normal-weight women. By 10 years, recurrence rates were 58% in obese women and 45.4% in normal-weight women.

Drugs used after chemotherapy, such as tamoxifen (Nolvadex, AstraZeneca), may increase weight gain during treatment. Following resolution of nausea, patients may overeat, or they might have decreased their exercise during treatment; this can also lead to weight gain.

(Source: Clin Cancer Res 2008;14:1718–1725.)

Heparin Imports Halted; Contaminant Identified

Health authorities in the U.S. have ordered a halt to all imported heparin anticoagulants to test them for contaminants possibly linked to dozens of deaths and hundreds of severe allergic reactions. On March 5, the FDA said it had detected a contaminant in heparin injections sold by Baxter Pharmaceuticals. Most of the active ingredients came from China, which has been supplying heparin raw materials to the U.S. for more than a decade. As of April 29, 81 deaths had been reported.

The contaminant—identified as over-sulfated chondroitin sulfate—seems to have been deliberately altered chemically to mimic heparin. Chondroitin sulfate is widely sold as a dietary supplement to treat pain. The over-sulfated version does not occur in nature and was probably chemically modified. The FDA now considers that the product was deliberately altered for economic reasons.

Baxter, which made about half of all the heparin used in the U.S., recalled all of its heparin products in February. There is no shortage, though; another company, APP, has increased production, and no contaminants have been noted in its heparin products.

Although the Chinese plant agreed not to export heparin products to the U.S., the FDA issued the alert to detain all heparin products that the plant might ship in the future. China’s drug safety agency has agreed to require stricter controls for heparin production. Earlier it said that ensuring quality was up to the company, APP, has increased production, and no contaminants have been noted in its heparin products.

Antithrombotic Therapy And Acute Coronary Syndrome

Triple anticoagulation with aspirin, clopidogrel (Plavix), and anticoagulant therapy can be an unattractive option for many clinicians, according to a multicenter study, and it’s apparently one of the reasons why hospital discharge strategies vary widely for patients with acute coronary syndrome (ACS).

Researchers analyzed data from 5,673 patients enrolled in the CRUSADE trial (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines?). They found that 25% of patients hospitalized for ACS were discharged without a prescription for continuing warfarin (Coumadin, Bristol-Myers Squibb). The perceived risk of bleeding appeared to be the overriding factor in the clinicians’ decisions to not use a triple-anticoagulant therapy, even though thrombosis-related events are possible.

Women, patients with a history of coronary artery bypass grafting or heart failure, and those with higher hematocrit levels at hospital admission were more likely to be prescribed continuing warfarin therapy at discharge. Clinicians also tended not to add warfarin later, after they had made their decision, based on risks and benefits, particularly if they anticipated a long course of dual antiplatelet therapy.

(Source: Am Heart J 2008;155:361–368.)

Do Cardiovascular Drugs Hurt or Help Cocaine Users?

Emergency physicians who see young patients with symptoms of a heart attack should ask them whether they have recently used cocaine. Symptoms of a heart attack
attack in younger patients with no risk factors for cardiovascular disease may signify cocaine use, and some treatments intended for heart attacks can be fatal for these individuals.

Cocaine, like heart attacks, can cause chest pain, shortness of breath, anxiety, palpitations, dizziness, nausea, and sweating. Only about 1% to 6% of patients with cocaine-associated chest pain are actually having a heart attack. Cocaine raises the heart rate and blood pressure.

Two typical heart attack treatments can be dangerous to those using cocaine: clot-busting drugs carry a risk of bleeding into the brain in patients with hypertension that is caused by cocaine use, and beta blockers that lower blood pressure without constricting arteries in typical heart attack patients may actually raise blood pressure and squeeze arteries narrowed by cocaine use.


**Zotarolimus Coronary Stent**

The FDA has approved Medtronic’s Endeavor Zotarolimus-Eluting Coronary Stent to treat narrowed coronary arteries. This is the first drug-eluting stent approved since 2004.

(Source: FDA, February 4, 2008.)

**NEW MEDICAL DEVICES**

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

**Name:** NexGen LPS-Flex and LPS-Mobile Bearing Knees

**Manufacturer:** Zimmer, Inc., Warsaw, Ind.

**Approval Date:** December 10, 2007

**Use Classification:** These artificial mobile bearing knee systems are designed to replace the knee joint.

**Description:** The knee systems have three parts: a metal curve-shaped part (a femoral component), which a doctor cements onto the end of the thigh bone; a flat metal tray cemented onto the top of the shin bone (tibia); and a plastic support (bearing) that sits on the tibial tray and mates with the curved femoral component. The plastic bearing slides in between the tibial tray and femoral component, which allows the artificial knee joint to move.

**Purpose:** Patients may need knee replacement because of osteoarthritis, traumatic arthritis or physical injury; avascular necrosis of the femoral condyle; or a moderate varus, valgus, or flexion deformity of the knee.

**Benefit:** The painful portion of the knee joint is replaced, and the joint’s alignment and movement are restored.

**Source:** www.fda.gov/cdrh/mda/docs/p060037.html

**Name:** ProDisc-C Total Disc Replacement

**Manufacturer:** Synthes Spine, Inc., West Chester, Pa.

**Approval Date:** December 17, 2007

**Use Classification:** The device is used to replace a diseased cervical disc.

**Description:** The replacement consists of two metal (cobalt–chrome alloy) end-plates and an ultra-high-molecular-weight polyethylene (plastic) inlay that fits between the two end-plates.

**Purpose:** The plastic inlay and end-plates restore the natural distance between the two vertebrae. The top end-plate slides over the domed part of the plastic inlay, which allows movement at the level where it is implanted. The device is intended for skeletally mature patients for reconstruction of the disc from C3 to C7 cervical vertebrae after removal of the disc at one level for intractable symptomatic cervical disc disease.

**Contraindications:** The replacement should not be implanted in patients with an active infection, an allergy to any of the device materials, osteoporosis, cervical instability, severe spondylitis, clinically compromised vertebral bodies at the level to be treated, or symptomatic cervical disc disease at more than one level.

**Benefit:** The device stabilizes the spinal level after surgery. Unlike a fusion procedure, the replacement allows motion at the spinal level that has undergone surgery. After the diseased disc is removed, patients should experience pain relief and improved function.

**Source:** www.fda.gov/cdrh/mda/docs/p070001.html

**Name:** Evicel Fibrin Sealant (Human)

**Manufacturer:** Ethicon, Inc., and Omrix Biopharmaceuticals, Somerville, N.J.

**Approval Date:** January 10, 2008

**Use Classification:** Evicel is the first fibrin sealant to be indicated as an adjunct to hemostasis for use in patients undergoing surgery when control of bleeding by standard surgical techniques is ineffective or impractical. The FDA originally licensed the predecessor of Evicel (Crosseal) in 2003 for use during liver surgery.

**Description:** This sealant is sold as a frozen liquid. Less than one minute of preparation time is needed after thawing.

**Purpose:** This is the only human plasma-derived fibrin sealant commercially available in the U.S. It does not contain aprotinin, which has been associated with adverse health effects.

**Contraindications:** Evicel is not indicated for patients known to have anaphylactic or severe systemic reactions to human blood products. As with other plasma-derived products, the risk of transmitting infectious agents cannot be completely eliminated.

**Benefit:** The sealant is easy to use and readily available for time-sensitive needs in the operating room. The success of a surgical procedure sometimes depends on the surgeon’s ability to control blood

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loss quickly. Evicel has become important in hemostasis during liver and vascular procedures. The expansion of this indication to general surgery will bring the benefits of this product to more surgeons and their patients.

Sources: www.pharmacyonesource.com; www.fda.gov; www.lifesciencesworld.com/news/views/58194

Public Health Notification: Stent Graft Monitoring

Patients receiving endovascular grafts need continual surveillance. The notification focuses on the mortality risks associated with the AneuRx Stent Graft System, which is used to prevent abdominal aortic aneurysm (AAA) rupture. This is the only marketed device with long-term clinical follow-up of a significant number of patients at five years.

Recommendations:

1. Clinicians should consider the information in the product labels and in the yearly clinical updates from Medtronic and other graft manufacturers when selecting treatments for patients with AAAs and in following previously treated patients. The clinical updates for three of the currently marketed AAA endovascular grafts can be found at these Web sites: www.endologix.com, www.goremedical.com, and www.medtronic.com.

2. Patients should be encouraged to comply with the follow-up recommendations in the product labeling.

3. The graft should be used only for patients who can be treated in accordance with the instructions and who meet the appropriate risk–benefit profile. Among the factors to consider are:

- the patient’s long-term AAA-related mortality, especially with AAA rupture. The risk of late AAA-related mortality associated with the AneuRx graft exceeds that associated with open surgery.
- the experience of the institution or the physician. If open or endovascular surgery is performed in institutions or by physicians with little experience with this type of AAA repair, the mortality rate may be higher than average.
- surgical risk factors. Elderly patients and those with cardiac, renal, pulmonary comorbidities may experience a higher-than-average mortality rate with open AAA resection. The rate can range from 2% in those with no risk factors to above 40% in those with several comorbidities.
- the patient’s willingness to comply with the follow-up schedule for the graft.

Source: www.fda.gov