NEW DRUGS

Protein C (Ceprotin): Orphan Drug For Clotting Disorder

The U.S. Food and Drug Administration (FDA) has licensed protein C concentrate (Ceprotin, Baxter Healthcare), the first biologic treatment for a potentially life-threatening clotting disorder.

Made from the plasma of healthy human blood donors, Ceprotin is a concentrated form of protein C, which is normally manufactured in the liver and circulates in the plasma in very small amounts. It helps prevent the formation and growth of blood clots.

Severe congenital protein C deficiency is a rare genetic defect, affecting one to two newborns for every million births. Patients with insufficient levels of protein C experience abnormally high numbers of blood clots. A complete absence of the protein is fatal.

The FDA granted Ceprotin orphan drug status.

For more information on protein C concentrate, see the Pharmaceutical Approval Update column in this issue of P&T on page 290.

(Source: FDA, March 30, 2007.)

Retapamulin (Altabax) Ointment for Impetigo

Retapamulin ointment (Altabax, GlaxoSmithKline) has been approved for the topical treatment of impetigo caused by susceptible strains of Staphylococcus aureus or Streptococcus pyogenes, the two most common types of bacteria in this kind of infection.

Impetigo is considered a contagious infection of the skin’s top layers. It is most common among infants and children two to six years of age.

Altabax represents the first new class of prescription topical antibacterial agents (called pleuromutilins) to be approved by the FDA in nearly two decades. It is indicated for use twice daily for a five-day period in patients nine months of age and older; other prescription topical antibacterials may need to be used as much as three times daily for up to 12 days.

In vitro, this new topical antibiotic is considered to have a low potential for the development of resistance.

To reduce the development of drug-resistant bacteria and to maintain the effectiveness of Altabax and other antibacterial drugs, this product should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

(Source: FDA, April 12, 2007; GlaxoSmithKline, www.gsk.com.)

Sitagliptin/Metformin (Janumet) for Type-2 Diabetes

Merck has announced the approval of sitagliptin plus metformin (Janumet), the first tablet to combine a dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of type-2 diabetes. Sitagliptin (Januvia, Merck) was approved for patients with type-2 diabetes in the U.S. in 2006 either as monotherapy or as combination therapy when added to either metformin (Glucophage, Bristol-Myers Squibb), a glucose-lowering agent, or a thiazolidinedione such as rosiglitazone maleate (Avandia, GlaxoSmithKline) or pioglitazone (Actos, Takeda/Eli Lilly).

Janumet is approved as an adjunct to diet and exercise to improve glycemic control in adult patients with type-2 diabetes whose glucose levels are not adequately controlled with metformin or sitagliptin alone or for those who are using sitagliptin and metformin. It is not indicated for type-1 diabetes or diabetic ketoacidosis.

The combination tablet targets diminished insulin release, uncontrolled production of glucose, and insulin resistance. The drug’s labeling contains a boxed warning about the risk of lactic acidosis.

More information on Janumet is presented in this month’s Pharmaceutical Approval Update column on page 290.

(Source: Merck, April 2, 2007.)

First Avian Flu Vaccine

The FDA has approved the first vaccine in the U.S. for humans against the H5N1 influenza virus, commonly known as avian flu or bird flu.

The vaccine, made by Sanofi-Pasteur, could be used if the current H5N1 avian virus were to develop the capability to spread among humans. If such an influenza pandemic emerges, the vaccine may provide early limited protection in the months before a vaccine tailored to the pandemic strain of the virus could be produced.

The H5N1 virus is one version of the influenza A virus commonly found in birds. Unlike seasonal influenza, the disease caused by H5N1 is more severe and occurs quickly. Pneumonia and multi-organ failure are commonly seen.

Almost 300 people worldwide have been infected with this virus since 2003; more than half of them have died.

The vaccine, obtained from a human strain, is intended for people 18 through 64 years of age. Two intramuscular injections are given approximately one month apart.

Sanofi-Pasteur does not plan to sell the vaccine commercially. The federal government has purchased it to be included within the U.S. Strategic National Stockpile for distribution by public health officials if needed.

In a study, 45% of people who received the 90-mcg, two-dose regimen developed antibodies at a level expected to reduce the risk of influenza.

(Sources: FDA, April 17, 2007; www.pandemicflu.gov.)
Injectable Zoledronic Acid For Paget’s Disease

Reclast (zoledronic acid) injection (Novartis) has been approved as the first new treatment in nearly a decade for patients with Paget’s disease. It is given as a single 5-mg, 15-minute infusion; current oral therapies must be taken daily for up to six months.

Paget’s disease is a chronic, often painful bone disorder that causes abnormal bone growth and weak and brittle bones. Reclast attaches to bone and blocks excessive bone breakdown and rebalances the natural bone-remodeling process.

Reclast has been found to be more effective and faster-working than risdroronate sodium (Actonel, Procter & Gamble), the current standard therapy for patients with Paget’s disease, and it offers a longer period of remission.

The injection has been approved in more than 50 countries as Aclasta, and it is being reviewed for the treatment of postmenopausal osteoporosis.

Zoledronic acid is also marketed as Zometa for use in oncology.

(Source: Novartis, April 17, 2007; www.paget.org.)

Generic Approvals

Generic Corzide for Hypertension

Impax Laboratories has announced the FDA’s final approval of its Abbreviated New Drug Applications (ANDAs) for nadolol/bendroflumethiazide 40 mg/5 mg and 80 mg/5 mg. The product is a generic formulation of Corzide for the treatment of high blood pressure.

Nadolol, a nonselective beta blocker, decreases the force and rate of heart contractions; bendroflumethiazide is a diuretic.

Corzide is marketed by Monarch Pharmaceuticals, a subsidiary of King Pharmaceuticals, Inc.


Generic Zantac Syrup For Reflux Disease and Ulcers

The Actavis Group has received approval to market ranitidine oral solution USP in the 15-mg/mL strength. This product is the generic equivalent of GlaxoSmithKline’s Zantac Syrup. Ranitidine is indicated for the treatment and prevention of ulcers and gastroesophageal reflux disease (GERD) and for the treatment of conditions caused by high acid secretion.

(Source: Actavis, March 1, 2007.)

Generic Ambien for Insomnia

The first generic versions of zolpidem tartrate (Ambien, Sanofi-Aventis) immediate-release tablets have been approved. This sedative–hypnotic drug is indicated for the short-term treatment of insomnia.

The tablets are available in formulations of 5 and 10 mg.

Sanofi-Aventis’ patent for zolpidem tartrate expired on April 21, 2007.

(Sources: FDA, April 24, 2007, www.fda.gov/cder/consumerinfo/generic_equivalence.htm.)

Full Approval: Cytarabine (DepoCyt) Injection For Lymphomatous Meningitis

The FDA has granted full approval for cytarabine liposome injection (DepoCyt, Enzon) for patients with lymphomatous meningitis, a life-threatening complication of lymphoma.

DepoCyt was originally approved under the Accelerated Approval regulations of Subpart H of the Food, Drug and Cosmetic Act.

Lymphomatous meningitis is characterized by the spread of the cancer to the central nervous system and the formation of secondary tumors within the thin membranes surrounding the brain. Symptoms can include numbness or weakness in the extremities, pain, sensory loss, double vision or loss of vision, hearings problems, and headaches.

DepoCyt is a sustained-release formulation of cytarabine. Lymphomatous meningitis can be controlled with cytarabine, but because of the drug’s short half-life, a spinal injection is required twice per week, whereas DepoCyt is given once every two weeks. Cytarabine is gradually released into the cerebrospinal fluid, resulting in an extended half-life, prolonged exposure to the therapy, and a more uniform distribution.

Patients receiving DepoCyt should be treated concurrently with dexamethasone to mitigate the symptoms of chemical arachnoiditis.

(Source: Enzon, April 20, 2007.)

NEW INDICATIONS

Immune Globulin (Rhophylac) for Immune Thrombocytopenic Purpura

The FDA has approved an additional indication for human immune globulin IV (Rhophylac Rh0[D], CSL Behring) for the treatment of immune thrombocytopenic purpura (ITP). This product helps raise platelet counts in Rh0(D)-positive, non-splenectomized adults with chronic ITP.

This sterilized solution, obtained from pooled human plasma, was approved in 2004 for suppressing Rh isoimmunization in pregnancy and obstetric conditions and following an incompatible transfusion. It is used to prevent an immune response to Rh-positive blood in people with an Rh-negative blood type.

ITP is an autoimmune disease in which the immune system destroys the body’s platelets. Purple bruises on the skin (purpura) signify bleeding in small blood vessels under the skin, and small red splotches may be present on the skin.

continued on page 265
Rhophylac has also been used to prevent hemolytic disease of the newborn—which can affect an infant born as a result of an Rh-incompatible pregnancy—and to treat Rh-negative individuals in the event of an incompatible blood transfusion.

(Source: CSL Behring, April 2, 2007; www.Rhophylac4ITP.com; Platelet Disorders Support Association, www.pdsa.org.)

**Immune Globulin (HepaGam B) To Prevent Hepatitis B Re-infection**

HepaGam B (Cangene, Canada) has been approved for the prevention of hepatitis B re-infection in certain liver transplant recipients. HepaGam B is made from human plasma from healthy donors in the U.S.

Liver transplant patients who have previously been exposed to the hepatitis B virus (HBV) are at an increased risk of re-infection because they have weakened immune systems.

HepaGam B provides an immediate immune response to the virus. This immunity protects patients previously exposed to HBV. Patients must receive injections at the time of transplantation and throughout their lives.

In January 2006, FDA licensed HepaGam B to prevent infection with HBV after acute exposure to blood or certain body fluids containing HBV; after perinatal exposure of infants to mothers previously exposed to HBV; after sexual exposure to persons previously exposed to HBV; and after household exposure to persons with acute HBV infection.

(Source: FDA, April 6, 2007.)

**NEW FORMULATIONS**

**Morphine Sulfate (Kadian) for Pain**

Alpharma’s morphine sulfate extended-release capsule (Kadian) has been approved in a new dosage strength of 200 mg. Kadian is currently available in strengths of 20 mg, 30 mg, 50 mg, 60 mg, 80 mg and 100 mg.

The capsules are indicated for the management of moderate-to-severe chronic pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. They can be taken once daily every 24 hours or twice daily every 12 hours to provide up to 24 hours of pain relief.

The 100-mg and 200-mg doses are indicated for opioid-tolerant patients only.

The capsules contain an opioid agonist, which is a Schedule II controlled substance.

(Source: Alpharma, March 1, 2007; www.kadian.com.)

**Coated Niacin (Niaspan) Tablets For Lipid Disorders**

The FDA has approved coated niacin (Niaspan, Abbott/Kos) extended-release tablets. Available since 1997, the product is indicated for boosting high-density lipoprotein-cholesterol (HDL-C) levels.

Three major clinical studies showed an average increase of 22% in HDL-C for patients receiving 2,000 mg of the product at bedtime.

Niacin has several indications, including reducing levels of total cholesterol, triglycerides, and apolipoprotein B; promoting the regression of coronary atherosclerosis; and reducing the risk of recurrent myocardial infarction.

(Source: Abbott, April 6, 2007.)

**FDA Rejects Etoricoxib (Arcoxia) for Osteoarthritis**

The FDA has issued a nonapprovable letter for Merck’s etoricoxib (Arcoxia), an osteoarthritis medication, because of concerns that it might carry cardiovascular risks similar to those associated with the company’s rofecoxib (Vioxx). Rofecoxib was withdrawn from the market in 2004.

The FDA stated that Merck needed to provide more data in support of the benefit-to-risk profile for the proposed doses of Arcoxia in order to gain approval. The FDA’s decision was anticipated after an FDA advisory panel voted 20-1 against the approval in April.

Arcoxia is a pain reliever in the same class of drugs known as COX-2 inhib-
NEW DRUGS

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Editors. It has been sold for the past five years in 63 other countries.

Merck had been awaiting approval of Arcoxia since December 2003 and had asked the FDA to approve 30-mg and 60-mg doses.

(Source: The Philadelphia Inquirer, April 28, 2007.)

New Dosing Schedule for Twinrix Hepatitis Vaccine

The FDA has approved an accelerated dosing schedule for an inactivated hepatitis A vaccine and recombinant hepatitis B vaccine (Twinrix, GlaxoSmithKline): three doses given within three weeks, followed by a booster dose at 12 months.

As the only hepatitis A and hepatitis B combination vaccine available in the U.S., Twinrix will now be given at zero, seven, and 21 to 30 days, followed by the booster dose at one year.

The vaccine was first approved for adults older than 18 years of age in May 2001 on a dosing schedule of zero, one, and six months.

Hepatitis A, which can be fatal, is spread by close personal contact and by eating food or drinking water contaminated with the hepatitis A virus. Hepatitis B is transmitted through infected blood or body fluids.

(Source: GlaxoSmithKline, www.gskvaccines.com, April 2, 2007.)

Off the Market

Tegaserod (Zelnorm) For Bowel Disorders

Novartis is suspending the marketing and sales of tegaserod maleate (Zelnorm) in the U.S. This medication is indicated for patients with irritable bowel syndrome (IBS) plus constipation and for those with chronic constipation, including symptoms such as abdominal pain and bloating.

When tegaserod was approved in 2002, a statistically nonsignificant imbalance in cases of angina pectoris was recorded and included in the U.S. label. A more recent analysis revealed a statistically significant imbalance in the incidence of cardiovascular ischemic events in patients taking the drug compared with those taking placebo. These events included myocardial infarction, stroke, and unstable angina pectoris.

All of the affected patients had pre-existing cardiovascular disease or cardiovascular risk factors. Multiple studies do not suggest any constrictive effects of the drug on coronary arteries.

Novartis is meeting with health authorities in other countries where the product is sold to determine the next steps.

(Source: Novartis, March 30, 2007.)

Pergolide (Permax) For Parkinson’s Disease

Manufacturers of pergolides, which are used to treat Parkinson’s disease, have volunteered to remove these drug products from the market because of the risk of serious damage to the heart valves.

The products being withdrawn are Permax (Valent), which was developed by Eli Lilly & Co, and two generic versions, made by Par and Teva.

Pergolide, a dopamine agonist, is used with levodopa and carbidopa to manage the tremors and slowness of movement in patients with Parkinson’s disease.

Valvular heart disease was first described in association with pergolide in 2002. In 2003, the FDA asked Eli Lilly to add valvulopathy to the warnings section of Permax labeling. In 2006, this warning was upgraded to a black-box warning.

Patients taking pergolide should contact their doctors to discuss alternative treatments, and they should not stop taking the medication abruptly.

The removal of pergolide products is not expected to adversely affect patient care, because safer alternative therapies are available.

The FDA is working with manufacturers to determine whether it might be possible, after pergolide is withdrawn from the market, to make it available under an Investigational New Drug Application (INDA) for the few patients who cannot be successfully converted to other available treatments.


Non–FDA-Approved Anti-nausea Suppositories

Companies have been ordered to stop manufacturing and distributing suppositories containing trimethobenzamide HCl because they lack effectiveness. Used to treat nausea and vomiting in adults and children, they have not been FDA-approved.

The affected products include Tigan (King), Tebamide, T-Gen, Trimazide, and Trimethobenz. Several oral capsules and injectable products containing trimethobenzamide have been approved by the FDA and are not affected by this action.

The move was part of a campaign by the agency to re-evaluate drugs approved before 1962, the year drug makers had to start proving that their products worked. Before 1962, they had to prove only that they caused no harm.

Many alternative products are available as tablets, capsules, solutions, injectables, and suppositories.

A small quantity of these products will still be available in pharmacies until supplies are exhausted. Five manufacturers and six distributors make these suppositories. Drug companies wishing to market a trimethobenzamide product in suppository form must now obtain an approved New Drug Application prior to...
marketing.

(Sources: FDA, April 6, 2007; The New York Times, April 7, 2007; Bloomberg News.)

**Lithium Builds Gray Matter In Patients with Bipolar Disorder**

Lithium, considered the standard therapy for bipolar disorder for at least 50 years, has been found to increase the amount of gray matter in the brains of patients with the illness.

Neuroscientists at the University of California, Los Angeles, used high-resolution, three-dimensional magnetic resonance imaging (MRI) to map the entire surface of the brain. They compared the brains of bipolar patients taking lithium with those of patients without the disorder and those of bipolar patients not taking lithium. The volume of gray matter in the brains of those taking lithium was as much as 15% higher in areas that regulate attention, motivation, and emotions, although the total volume of white matter did not differ between the groups.

Bipolar disorder is characterized by a wide range of emotions between mania and depression, but it is not clear how lithium helps in controlling severe mood swings. These new findings indicate that lithium might work by increasing the amount of gray matter in certain brain areas; this suggests that existing gray matter in these regions of bipolar brains might be underused or dysfunctional.

It was not clear whether the increase in gray matter would persist if lithium treatment were discontinued.

(Sources: Biol Psychiatry, January 18, 2007 online; images at www.loni.ucla.edu.)

**A Rapid Case of Acute Bacterial Cholangitis**

Clinicians at Charité University Hospital in Berlin reported on an alarmingly swift case of secondary sclerosing cholangitis. The natural course of secondary sclerosing cholangitis is a slow progression over a period of years; in their own patient, it took less than two months to develop.

This is the first reported case of sclerosing cholangitis caused by vancomycin-resistant enterococci. An 82-year-old woman was admitted to the hospital with acute cholangitis, among other problems. In the intensive-care unit, septicemia rapidly progressed to septic shock along with transient acute renal failure.

Antibiotic therapy was started, and emergency endoscopic retrograde cholangiography with endoscopic sphincterotomy was performed on the second day.

Endoscopic nasobiliary drainage was also started, but six days later, the biliary stent became occluded and portal vein thrombosis developed. The stent became occluded again six days later, and drainage was performed again.

Ten days after admission, *Enterococcus faecium* and *Enterococcus faecalis* organisms were isolated, and vancomycin (Vancocin, Viro Pharma) was added to the antibiotic regimen.

The patient’s clinical situation deteriorated, and vancomycin and gentamicin (Garamycin, Schering) were discontinued on day 21. New treatment with linezolid (Zyvox, Pfizer) and imipenem/cilastatin (Primaxin, Merck) led to significant clinical improvement.

Approximately 52 days after admission, however, secondary sclerosing cholangitis was diagnosed. Vancomycin-resistant enterococci (VRE) were isolated from the bile on day 69 and from blood on days 74 and 78.

Linezolid and IV teicoplanin (Targocid, Sanofi-Aventis) therapy for another four weeks led to clinical improvement and sterile blood cultures. The patient was discharged, but she died two weeks later at home from unknown causes.

The researchers say that patients with VRE bacteremias are more likely to die but that linezolid is generally effective because of its excellent tissue penetration, even into inflamed tissues.

(Source: J Infect 2007;54:e65–e68.)

**Esmolol (Brevibloc) Eases Intubation for Smokers**

Laryngoscopy and tracheal intubation can be risky for smokers who, with their predisposition to atherosclerosis, hypertension, and bronchospasm, may have a more intense hemodynamic response to the procedure.

Researchers from Greece theorized that esmolol HCl (Brevibloc, Bedford Labs), a beta-adrenergic blocker with a rapid onset and short duration of action, might help control that cardiovascular response. Esmolol provides temporary control of heart rate and blood pressure and helps to reduce the workload on the heart.

Patients who were heavy smokers (defined as 20 to 30 cigarettes per day for more than 10 years) were divided into three groups: 53 received placebo; 54 received esmolol 1 mg/kg; and 55 received esmolol 2 mg/kg.

Because nicotine in the systemic circulation can increase the heart rate, all patients had abstained from cigarettes for at least eight hours before being anesthetized.

Anesthesia was induced with propofol (Diprivan, AstraZeneca) and remifentanil HCl (Ultiva, GlaxoSmithKline). IV rocuronium bromide (Zemuron, Orga-

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n) was administered, and IV esmolol was then given slowly for two minutes before tracheal intubation.

The smokers in the placebo group showed increases in systolic and diastolic blood pressure, as well as heart rate, for
three minutes after intubation. Those who received esmolol 1 mg/kg had a milder response in systolic blood pressure and heart rate but not in diastolic blood pressure. The 2-mg/kg dose appeared to provide the most hemodynamic stability.

Although esmolol can cause bronchospasm, only one patient in the lower-dose group, one patient in the placebo group, and none of the patients in the higher-dose group experienced this reaction.


**Identifying Patients At Risk for Heparin-Induced Thrombocytopenia**

One in 13 patients presenting to an emergency department (ED) with chest pain or symptoms of thrombosis may be at risk for heparin-induced thrombocytopenia (HIT), according to a study from the University of Texas School of Medicine at Houston.

The researchers tested admission samples from 324 ED patients for heparin-PF4 antibodies and, if these were positive, for platelet-activating antibodies. Twenty-four patients (7.4%) were found to have the antibodies.

Of the 196 patients hospitalized within the previous six months, 18 (9%) were seropositive, compared with six (5%) of 128 who had not been recently hospitalized. Sixteen of 231 patients with chest pain who received esmolol 1 mg/kg had a milder response in systolic blood pressure, compared with the placebo group.

Although assessment of the platelet count is important for identifying patients with HIT, in this study, it was not generally helpful in determining who might have heparin-PF4 antibodies. The researchers suggested that the patient history is an alternative means of quickly identifying at-risk patients. They reasoned that because heparin is used so commonly in hospital patients, anyone who had been hospitalized in the previous six months (the amount of time during which antibodies are typically circulating) might have a higher risk. Sure enough, of the eight patients with the most reactive (i.e., platelet-activating) antibodies, seven had been hospitalized within the previous six months and one patient had been in the hospital within the previous year.

It is unlikely that the seropositive patients with symptoms of thrombosis had delayed-onset HIT, because 22 of 24 of them were not thrombocytopenic on admission. However, it was also possible that a relative drop in the platelet count might have occurred.

Heparin-PF4 antibodies, even if they do not induce HIT, are clinically significant. Seropositivity without thrombocytopenia is associated with higher rates of myocardial infarction and thrombotic outcomes in at-risk patients. Those patients, they suggest, might benefit from more aggressive antithrombotic therapies. In the meantime, the researchers advise that non-heparin anticoagulation would be prudent.


**Possible Progesterone Benefits In Traumatic Brain Injury**

For patients with traumatic brain injury, there are no proven neuroprotective drugs, although progesterone treatment offers some faint hope.

In a phase 2 study at Grady Memorial Hospital in Atlanta, Georgia, progesterone caused no discernible harm and showed possible signs of benefit. Seventy-seven adult trauma patients were randomly assigned to receive intravenous (IV) progesterone and 23 were assigned to placebo.

Throughout the three-day infusion interval, the progesterone group experienced a lower increase in mean temperature, compared with the placebo group. The researchers say that this is important, because the endogenous release of progesterone is associated with an increase of 1 degree Fahrenheit in core temperature, and elevated temperatures have been posited to adversely affect neurological outcomes.

Seven placebo patients and 10 progesterone patients died within 30 days; the progesterone group had a strong trend toward fewer deaths from neurological causes. Mortality differed by severity of injury. Six of 15 patients with an index Glasgow Coma Scale score of 4 to 8 who received placebo died, as did seven of 53 patients (13%) taking progesterone. One patient of seven in the placebo group who had Glasgow Coma Scale scores of 9 to 12 died, as did three of 18 patients in the progesterone group.

The researchers noted that the survival benefit seemed highest in patients with severe traumatic brain injury. If, as the findings suggest, a higher proportion of severely injured patients treated with progesterone survived, this might explain why members of this group were comatose longer and were less likely to have moderate to good Glasgow Outcome Scale–Extended (GOS–E) scores. Patients with severe injury (index scores of 4 to 8) who received progesterone remained in a coma more than twice as long as placebo patients (mean, 10 days vs. 4 days).

Thirty days after their injury, most survivors with scores of 4 to 8 were functioning at a “relatively poor” level, regardless of treatment. Only four of 15 placebo patients had GOS-E scores compatible with moderate or good recovery, compared with 11 of 52 in the progesterone group. Among patients enrolled with an index score of 9 to 12 on the Glasgow Coma Scale, none of the seven placebo patients had moderate-to-good recovery, compared with 10 of the 18
patients receiving progesterone.

A similar relationship was seen in disability ratings. Survivors with severe injury who received placebo were slightly less disabled than those treated with progesterone. But in those with moderate traumatic brain injury, the progesterone-treated patients were significantly less disabled. (Source: Ann Emerg Med 2007;49:391–402.)

**USP Drug-Quality Program**

Dr. Reddy’s Laboratories, a generic drug manufacturer in Hyderabad, India, has signed on as the first participant in the U.S. Pharmacopeia’s Pharmaceutical Ingredient Verification Program.

The USP created the program in response to increasing concerns throughout the drug industry about the quality and consistency of pharmaceutical ingredients. The program enables manufacturers to show the quality and integrity of their ingredients with a recognizable “USP Verified” mark.

The company will submit ingredients to the USP’s verification process, which includes the following steps:

- evaluating the quality systems of ingredient manufacturers through an audit for compliance with Good Manufacturing Practices
- reviewing manufacturing and quality-control documents for the ingredients
- laboratory testing of ingredient samples from USP-selected lots to ensure compliance with the USP’s FDA-enforceable standards for purity, potency, and quality
- surveillance testing of ingredients bearing the USP Verified mark after the verification process

After each ingredient or excipient is verified, Dr. Reddy’s will receive a Certificate of Standards Compliance. The company may then post the Verified mark on the shipping container and the certificate of analysis demonstrating that it has met the USP’s quality standards.

The USP is named in U.S. federal law, and compliance with its standards is enforceable for drugs and dietary supplements marketed in the U.S. USP standards are also recognized worldwide. (Source: U.S. Pharmacopeia, April 17, 2007, www.usp.org.)

**Banana Vaccine for Hepatitis B Virus**

Bananas may be the next candidate to deliver a bite-sized vaccine for hepatitis B virus (HBV) in developing countries.

In the forthcoming June 1 issue of Biotechnology Progress, co-published by the American Chemical Society and the American Institute of Chemical Engineers, researchers in India review the efforts to genetically engineer plants as biofactories for vaccine production and focus on transferring genes to produce HBV vaccine.

There are already 350 million carriers of hepatitis B worldwide, with one million new cases diagnosed each year.

Plant-based production of an oral hepatitis B vaccine has advantages over the injectable vaccine. Bananas, potatoes, lettuce, carrots, and tobacco have been successfully engineered to produce HBV vaccines.

(Source: American Chemical Society Press, April 25, 2007.)

**Drug Safety News on Audio**

Health care professionals and consumers can now hear FDA broadcasts on drug safety. The podcasts can be transmitted to personal computers and personal audio players. The broadcasts are free to everyone at www.fda.gov/cder/drug/podcast/default.htm.

The service was launched in February 2007 as an addition to the FDA’s print-based and Web-based public health advisories. (Source: FDA, April 23, 2007.)

**NEW MEDICAL DEVICES**

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

**Name:** TephaFLEX Absorbable Sutures

**Manufacturer:** Tepha, Inc., Cambridge, MA

**Approval Date:** February 21, 2007

**Use Classification:** This is the first absorbable polymer suture made from material that has been isolated from bacteria and modified by recombinant DNA technology. The material’s properties are uniquely suited for implantable medical devices (e.g., artificial cardiac valves and vascular grafts).

**Description:** Recombinant DNA technology allows materials to be engineered for tissue repair and replacement. After the repair process, the biopolymers degrade in the body to natural metabolites in a biocompatible, cell-friendly manner within a short period of time.

The polymers can be softened with heat and hardened with cooling. Compared with synthetic polymers (polylactic acid and polyglycolic acid), the material is tougher and more flexible.

Unlike other biopolymers (e.g., collagen and hyaluronate), this polymer can be fabricated into virtually any shape or form.

**Purpose:** The sutures are used for tissue repair and replacement in implantable devices.

**Benefit:** These sutures are engineered to be one of the strongest absorbable fibers known. They are up to 50% greater in tensile strength than monofilament absorbable sutures. They also offer surgeons improved flexibility, good knot security, and prolonged strength retention when they are implanted. Inside the body, the sutures are
non-inflammatory and biocompatible. 

**Precautions:** This product is contraindicated in patients who are allergic to the cells or to the growth media used to produce the absorbable polymeric material.

**Source:** FDA news, April 9, 2007; www.fda.gov; Medgadget online, February 13, 2007.

**Name:** Temporary Limb Salvage Shunt

**Manufacturer:** Vascutek Ltd., Renfrew, Scotland

**Approval Date:** February 9, 2007

**Use Classification:** The vascular shunt is used to help save the arms and legs of soldiers critically injured in combat as well as individuals in other trauma settings and emergency situations.

**Description:** The shunt is a tube formed from two layers of plastic. Several features optimize its use in a trauma situation, including (1) a self-sealing elastomer membrane that permits drugs to be injected directly into the shunt without loss of blood; (2) beveled ends that facilitate quick and effective placement of the device within the severed blood vessel; (3) graduated markings that provide visual confirmation of proper device placement; and (4) extra reinforcement in the center of the device so that it can be cut to a shorter length if needed.

**Purpose:** The device works by connecting together the ends of a severed blood vessel, providing a bridge or shunt around the damaged area and restoring blood flow to the injured limb. It can be implanted on the battlefield and in other remote areas to bypass damaged blood vessels and temporarily maintain blood flow to the injured limb until the patient can be transported to a surgical facility.

**Benefit:** The device provides surgeons with a new tool to help their patients avoid the need for limb amputation following traumatic injury.

**Sources:** FDA news, www.fda.gov/bbs/topics/news/2007/new01559.html

**Name:** ExAblate 2000 Incisionless Surgery System

**Manufacturer:** InSightec Ltd., Haifa, Israel

**Approval Date:** March 1, 2007

**Use Classification:** This surgical method is used to detect uterine fibroids in association with General Electric Healthcare’s 3 Tesla Magnetic Resonance Imaging (MRI) systems and Kalma Zoo Neurology Imaging (KNI). The system combines MRI with focused ultrasound waves to destroy tumors noninvasively. It was previously approved for use with the 1.5 Tesla magnet.

**Description:** This is the first FDA-approved system to use the breakthrough technique combining MRI to visualize tissues in the body, plan treatment, and monitor real-time treatment outcomes along with high-intensity focused ultrasound to thermally ablate uterine fibroid tissue.

**Purpose:** This noninvasive, outpatient procedure is used to treat symptomatic uterine fibroids. More than 2,500 patients have been treated worldwide.

**Benefits:** Real-time magnetic resonance thermal feedback allows physicians to ensure that the targeted tumor is fully treated and that the surrounding tissue is spared. Physicians can use ExAblate with either a 1.5- or a 3-Tesla MRI scanner, allowing busy MRI centers greater flexibility in scheduling and allowing women greater access to this noninvasive procedure.

**Sources:** www.insightec.com; www.prnewswire.com, March 1, 2007

**Asthma Device Alert**

The Institute for Safe Medication Practices (ISMP) has alerted health care professionals about a potential problem with Twisthalers. Each Twisthaler contains multiple metered doses of mometasone furoate (Asmanex, Schering), a corticosteroid inhalation powder used to treat asthma in patients 12 years of age or older. It is also approved for patients using bronchodilators alone or who require oral corticosteroid therapy.

Under certain circumstances, the dose counter of an empty Twisthaler can indicate that the product still contains medication. This might cause patients to try to administer the drug from an empty container.

To prepare a dose, the patient twists the white cap counterclockwise and removes it while holding the inhaler upright. This action loads a single dose, ready for inhalation, and it decreases the dosage counter by one.

After the dose is inhaled, the patient replaces the cap and turns it clockwise until it clicks. The click indicates that the device is ready for the next dose to be loaded.

When the dose counter reaches 00, the Twisthaler locks shut to prevent the patient from using an empty device.

The problem can occur if the patient twists the cap forcefully after the dosage counter reaches 00. This action can reset the counter to show some remaining doses, even though the device cannot deliver them.

Before Asmanex is prescribed, dispensed, or administered, patients should be shown the dosage counter window, located under the indented arrow on the white part of the cylinder. They should be reminded to refill the prescription when the dosage counter reaches 10 and to discard the Twisthaler when the dosage counter reaches 00. They should not keep the product more than 45 days after the pouch has been opened, regardless of the number of remaining doses.


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