NEW DRUGS

Decitabine for Myelodysplastic Syndromes

Decitabine injection (Dacogen, MGI Pharma, Inc./SuperGen, Inc.) has been approved by the U.S. Food and Drug Administration (FDA) for patients with myelodysplastic syndromes (MDS). MDS comprises a group of bone marrow diseases characterized by the production of poorly functioning and immature blood cells. Over time, MDS can progress to acute leukemia.

A phase 3 clinical trial showed an overall response rate of 21% in decitabine-treated patients with MDS who received at least two cycles of treatment, compared with 0% in the patients receiving supportive care. All patients who responded to the treatment became or remained transfusion-independent during the time of the response.

It is recommended that decitabine be used for a minimum of four cycles. Treatment may continue as long as the patient benefits from it.


Rasagiline for Parkinson’s Disease

The FDA has approved the molecular entity rasagiline (Agisilec, Azilect, Teva Pharmaceuticals, Israel) for the treatment of Parkinson’s disease. The drug is a monoamine oxidase type-B inhibitor that blocks the breakdown of dopamine. Dopamine sends information to the parts of the brain that control movement and coordination.

Parkinson’s disease is caused by the destruction of the brain cells that produce dopamine. As dopamine levels decline, patients become incapable of initiating and controlling movements.

Rasagiline may be associated with hypertensive crisis if patients also consume tyramine-rich foods or beverages (e.g., cheese, red wine) or dietary supplements or amines contained in many cough and cold medications.

(Source: FDA, May 18, 2006.)

Antiemetic Nabilone Capsules

Marketing approval has been granted for nabilone oral capsules (Cesamet, Valeant) for treating nausea and vomiting associated with cancer chemotherapy in patients who have not responded to conventional antiemetic treatments.

Nabilone is similar to the active ingredient occurring naturally in marijuana. The drug is a synthetic cannabinoid, and its mechanism of action differs from that of conventional anti-emetics. It has a long duration of action, which allows for less frequent dosing, typically twice daily.

The drug should not be taken with alcohol, sedatives, hypnotics, or other psychoactive substances. It should be used with caution in patients with a history of psychiatric disorders, alcohol abuse, or marijuana use.

(Source: Valeant, May 16, 2006.)

Varenicline for Smoking Cessation

Varenicline tartrate tablets (Chantix, Pfizer) have been approved to help cigarette smokers stop smoking. The active ingredient is a new molecular entity that received a priority FDA review.

The drug acts at sites in the brain affected by nicotine by providing some nicotine effects to ease withdrawal symptoms; it also blocks the effects of nicotine if the person resumes smoking.

In clinical trials, varenicline was superior to placebo. Treated patients were also more successful in giving up smoking than patients treated with bupropion (Zyban, GlaxoSmithKline).

(Source: FDA, May 11, 2006.)

First Shingles Vaccine

Merck has received approval for its Zostavax vaccine to prevent shingles, a varicella infection, in people 60 years of age or older.

Shingles is caused by the chickenpox virus. It usually affects older adults who contracted chickenpox earlier in their lives. It occurs when the virus lying dormant in the cells “wakes up” in older people and in others with health problems. The vaccine is a boosted dose of the chickenpox vaccine currently given to children.

In addition to triggering painful rashes, shingles can also cause painful nerve damage. About one million Americans become ill with shingles every year.

Up to 10% of older patients won’t be candidates for the vaccine because of weakened immune systems caused by cancer therapy, AIDS, or organ transplantation.

(Sources: WebMD, May 25, 2006; Market Watch, May 26, 2006.)

NEW INDICATIONS

Thalidomide for Multiple Myeloma

The FDA has granted accelerated approval to Celgene’s supplemental New Drug Application for thalidomide (Thalomid). The drug is used in combination with dexamethasone to treat newly diagnosed multiple myeloma, a cancer of the bone in which malignant plasma cells are overproduced in the bone marrow. Multiple myeloma is the second most common blood cancer in the U.S.

The agent’s effectiveness is based upon response rates; no controlled trials have shown a clinical benefit, such as improved survival.

Thalidomide is available through a special education and prescribing safety system. Common adverse effects include constipation, sensory neuropathy, confusion, hypocalcemia, edema, dyspnea, thrombosis or embolism, and rash or desquamation; these events occurred in
20% of patients with a frequency less than or equal to 10% in patients treated with thalidomide/dexamethasone compared with dexamethasone alone.

The risk of venous thromboembolic events is increased risk when thalidomide is used in combination with standard chemotherapeutic agents, including dexamethasone.

Thalidomide was approved in 1998 for the treatment of cutaneous manifestations of moderate-to-severe erythema nodosum leprosum and as maintenance therapy to prevent and suppress cutaneous manifestations of recurrence.

The capsules are available in strengths of 50, 100, and 200 mg.

(Source: Celgene, May 25, 2006.)

**Three Approvals for Children: Esomeprazole for Reflux**

AstraZeneca has announced the FDA’s approval of esomeprazole magnesium (Nexium) delayed-release capsules in children 12 to 17 years of age with gastroesophageal reflux disease (GERD).

GERD affects approximately 8% of adolescents in the U.S. Children with GERD commonly experience vomiting or regurgitation as well as decreased appetite or refusal to eat. Asthma also may be a sign of the disease.

Families are encouraged to try lifestyle or dietary changes, such as smaller, more frequent meals. If these initial methods fail, physicians may recommend over-the-counter antacids or medications that suppress acid. Most erosions heal in four to eight weeks.

(Source: AstraZeneca, May 1, 2006, www.nexium-us.com.)

**Growth Hormone For Short Stature**

The FDA has approved a supplemental New Drug Application for somatropin (of rDNA origin for injection) (Genotropin) to treat growth failure associated with Turner syndrome in patients whose bones are still capable of growing.

The approval was based on two randomized, open-label, clinical trials in 38 children of short stature with Turner syndrome. Both studies demonstrated statistically significant growth increases from baseline height, and growth responses were greater in the study in which patients received a larger dose.

Turner syndrome is an “orphan disease” that affects an estimated 60,000 girls and women in the U.S. Relatively few people are affected, but treatment is essential for better outcomes. Blood tests can determine whether one of the two X chromosomes normally found in females is missing or incomplete.

Genotropin has orphan drug status for other growth-related conditions (“small-for-gestational-age” and Prader-Willi syndromes). It is also indicated for growth failure in children with an inadequate secretion of endogenous growth hormone.

(Source: Pfizer, May 4, 2006.)

**Infliximab for Children with Crohn’s Disease**

Infliximab (Remicade, Centocor) has been approved for children with active Crohn’s disease, a chronic, inflammatory bowel condition.

This genetically engineered monoclonal antibody reduces inflammation by blocking the action of tumor necrosis factor-alpha (TNF-α). The agent was initially approved in 1998 to treat Crohn’s disease in adults.

The drug’s safety and effectiveness were assessed in a randomized study of 112 children, 6 to 17 years of age, who had not responded adequately to conventional therapies. The proportion of patients achieving clinical responses compared favorably with that of adults in an earlier study. The pediatric trial showed no new safety concerns not already expressed in the product’s current label.

(Sources: JAMA, May 17, 2006; FDA, May 19, 2006.)

**NEW FORMULATIONS**

**Higher-Dose Valsartan Combination for Hypertension**

Two new higher-dose formulations are now available for patients with hypertension: valsartan/hydrochlorothiazide (Diovan HCT) 320/12.5 and 320/25 mg. The tablets are already available in combinations of 80/12.5, 160/12.5, and 160/25 mg. Diovan HCT contains the angiotensin receptor blocker valsartan and the diuretic hydrochlorothiazide (HCTZ).

Many patients need a combination of two therapies to achieve blood pressure (BP) goals.

The higher doses provided significantly greater reductions in BP compared with either agent alone. Giving the combination also reduced the incidence of low blood potassium, which is associated with HCTZ.

(Source: Novartis, May 1, 2006, www.pharma.us.novartis.com.)

**Ultra-High-Dose Anti-hemophilia Drug**

The FDA has approved a 2,000- IU (5-ml) ultra-high dosage of recombinant anti-hemophilic factor (Advate, Baxter Healthcare Corporation). This is the only therapy free of blood-based additives, including human albumin or other plasma proteins, for preventing and controlling bleeding episodes in patients with classical hemophilia (hemophilia A).

These patients do not produce adequate amounts of factor VIII, which is necessary for blood to clot. If severe hemophilia A remains untreated, the patient’s life expectancy is reduced.
Infused directly into the bloodstream, Advate temporarily raises factor VIII levels, thus enabling the body’s blood-clotting process to function properly.

Advate is available in five strengths: low (250 IU), medium (500 IU), high (1,000 IU), super-high (1,500 IU) and ultra-high (2,000 IU). It was approved in 2003.

Advate is not indicated for patients with von Willebrand’s disease.

(Sources: Baxter, May 9, 2006; www.advate.com)

**DRUG NEWS**

**Costly Whooping Cough Outbreak Spurs Vaccinations**

The recent rise in pertussis (whooping cough) cases in the U.S. poses a threat to hospital safety and resources. A single case of pertussis can easily spread to many health care workers, leaving the hospital responsible for containment costs.

The tetanus–diphtheria–acellular pertussis (Tdap) vaccine may be a cost-effective and responsible measure that hospitals should consider. A pertussis outbreak cost one hospital $74,870—2.38 times the dollar amount needed to vaccinate its health care workers.

An outbreak reported at the Dartmouth–Hitchcock Medical Center in New Hampshire resulted in 62 cases of pertussis; 34 employees were affected. This followed a 2003 outbreak in the same facility.

The risk of pertussis among health care workers is 1.7 times higher than that in the general adult population. To help prevent future outbreaks, the medical center launched a vaccination campaign for the 6,100 hospital employees.

Pertussis is caused by infection with the bacterium Bordetella pertussis. Widespread use of vaccines has led to a decline in pertussis cases, but the disease has made a comeback in recent years. Two brands of Tdap vaccine were licensed last year: one for children and adolescents 10 to 18 years of age (Boostrix, GlaxoSmithKline), and one for adolescents and adults 11 to 64 years of age (Adacel, Sanofi-Pasteur).

The Advisory Committee on Immunization Practices at the Centers for Disease Control and Prevention (CDC) recommends that adults receive a booster vaccination to prevent pertussis and that the Tdap combination vaccine be given in place of the tetanus–diphtheria (Td) booster that is given every 10 years.


**Potential Alzheimer’s Vaccine Effective in Mice**

A vaccine for Alzheimer’s disease appears to improve learning and memory deficits in mice. Findings from Brigham and Women’s Hospital and Harvard University have shown promise for a potentially safer and more effective Alzheimer’s vaccine in humans.

One theory is that amyloid-beta plaques (clumps of protein) build up between nerve cells in the brain and contribute to cognitive and behavioral deficits. Scientists have developed a vaccine using a special type of amyloid-beta substance that can trigger the immune system to produce antibodies that reduce the buildup of plaques in the brains of mice.

The vaccine, given by nose drops, targets only the region of the amyloid-beta protein involved in generating antibodies against amyloid-beta, and it avoids the immune response in mice that had been thought to cause brain inflammation, observed with an earlier vaccine in humans. The new vaccine still produced antibodies that cleared the brain of amyloid deposits.

(Source: J Neurosci May 3, 2006.)

**Paroxetine and Suicide Risk**

GlaxoSmithKline and the FDA have warned doctors that the antidepressant paroxetine (Paxil) may raise the risk of suicidal behavior in young adults. The letter was accompanied by changes to the labeling of both Paxil and controlled-release Paxil.

A recent analysis of data on nearly 15,000 patients revealed a higher frequency of suicidal behavior in young adults who used the drug. The FDA reported 11 suicide attempts—none resulting in death—among the patients in the trials. Only one patient receiving placebo attempted suicide.

Given that small number, the results “should be interpreted with caution,” the FDA said. In eight of the 11 attempts, the patients were between 18 and 30 years of age. All of the patients in the trial had psychiatric disorders, including major depression.

All patients who use paroxetine, especially young adults and those whose symptoms are improving, should be carefully monitored.

(Sources: Associated Press, May 12, 2006; FDA, www.fda.gov/medwatch/safety/2006/safety06.htm{PI:EF}paxil.)

**If SSRIs Don’t Work, Don’t Tweak—Switch**

When one selective serotonin re-uptake inhibitor (SSRI) does not seem effective for depression, substituting a different antidepressant has led to a remission of symptoms for almost 25% of patients.

In a multicenter study, 727 outpatients with a nonpsychotic major depressive disorder who were still symptomatic or who could not tolerate the SSRI citalopram (Celexa, Forest) were switched to sustained-release bupropion (Wellbutrin, GlaxoSmithKline), sertraline (Zoloft, Pfizer), or extended-release venlafaxine (Effexor XR, Wyeth) for up to 14 weeks.
At the end of the study, it seemed clear that any one of these three agents was a "reasonable second-step choice," the researchers say. Remission rates ranged from 18% to 28%.

Contrary to the belief that intolerance of one SSRI predicts intolerance of another, sertraline was tolerated as well as sustained-release bupropion, even though 56% of patients could not tolerate citalopram. Thus, both within-class and out-of-class medication switches should be considered.


**Aggressive Statin Therapy May Reverse Atherosclerosis**

Traditional thinking has viewed atherosclerosis as "inexorably progressive," say researchers who offer a more optimistic outlook: that aggressive treatment can actually reverse the atherosclerotic disease process.

They conducted a multinational study of very high-intensity rosuvastatin calcium (Crestor, AstraZeneca) at a dose of 40 mg/day in 349 patients at 53 community and tertiary-care centers.

The treatment halved low-density lipoprotein (LDL)-cholesterol levels, from a mean of 130.4 to 60.8 mg/dl. Mean high-density lipoprotein (HDL) cholesterol increased 14.7%, from 43.1 mg/dl at the baseline evaluation to 49 mg/dl. The total atheroma volume declined by a median of 6.8%. The average change in the percentage of atheroma volume in the most diseased subsegment was –6.1 mm³.

Rosuvastatin 40 mg/day was well tolerated, with no cases of rhabdomyolysis.

(Source: JAMA 2006;295:1556–1565.)

**Reducing Warfarin Interactions**

It’s not uncommon for patients who take warfarin to be taking other drugs—or for those drugs to have a significant potential for interaction.

Researchers from Kaiser Permanente and Northwest Permanente in Portland, Oregon, and from Harvard University in Boston evaluated the effectiveness of electronic medical record alerts. In one retrospective review, they found 65% of patients taking warfarin received a concurrent prescription for at least one interacting drug that increased the risk of bleeding.

Their study involved 239 primary care providers at 15 clinics and 9,910 patients. The clinics received the alerts for the co-prescription of warfarin and five interacting medications: acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), fluconazole, metronidazole, and sulfamethoxazole. All of the alerts were clearly identified as safety alerts; they included a short description of the clinical issue or risk and recommended medication alternatives.

At the baseline evaluation, nearly one third of the patients had one of the interacting study medications. The most common co-prescription was for warfarin and acetaminophen. The researchers also noted an immediate and continued decline in the prescribing of medications interacting with warfarin, for a 15% relative reduction by the 12th month.

Co-prescribing warfarin and potentially interacting medications is not necessarily contraindicated in all situations, the researchers acknowledge. In fact, they say, acetaminophen alone or in combination with narcotics is sometimes the best pain medication for patients taking warfarin. Similarly, the antibiotics targeted in their study might be the best or only choice. The coadministration of warfarin and acetaminophen remains an area of controversy, however.

They add that their definition of co-prescribing was conservative; that is, they counted a prescription overlap of even a single day.

(Source: Arch Intern Med 2006;166:1009–1015.)

**Low Estradiol + Low Testosterone = Fracture Risk**

Serum estradiol and testosterone together may be useful clues as to whether older men are at risk for hip fractures.

Researchers from Boston University, Boston Veterans Affairs Medical Center, and Harvard University observed 793 men from the Framingham Heart Study for up to 18 years. The men with both low estradiol and low testosterone levels had the greatest risk.

Of the 793 men in the study, 173 had low testosterone (below 3.85 ng/ml), 281 had mid-level testosterone (3.85–5.29 ng/ml), and 338 had high testosterone (5.30 ng/ml or more). During the follow-up period, 40 men experienced a hip fracture; 39 of these were atraumatic.

The higher risk was observed in men with serum estradiol below 20 ng/ml.

It is difficult to determine whether the major hormonal influence on hip fracture risk was testosterone or estradiol, but results suggest a synergistic effect.


**Natalizumab Cleared for MS**

Natalizumab (Tysabri, Biogen Idec/Elan), a once-monthly IV drug for multiple sclerosis, will be available again under a restricted distribution program. It was pulled from the market last year because of a life-threatening side effect.

Approved in November 2004, the drug was voluntarily withdrawn in February 2005 after two patients in clinical trials died of progressive multifocal leukoencephalopathy, a rare brain infection.

This drug is to be used alone in patients who have not responded adequately to, or who cannot tolerate, other MS drugs.

(Source: Associated Press, June 5, 2006.)
NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

**Name:** STS Continuous Glucose Monitoring System

**Manufacturer:** DexCom, San Diego, CA

**Approval Date:** April 24, 2006

**Use Classification:** The system provides continuous monitoring of glucose levels in diabetic patients.

**Description:** The patient inserts a tiny wire-like sensor just under the skin of the abdomen. The sensor, held in place by an adhesive, measures glucose levels, which are transmitted wirelessly to the “cell phone”-like STS receiver. The receiver displays the current glucose level as well as one-hour, three-hour, and nine-hour trends. The receiver sounds an alert when very high or low glucose levels are detected.

**Purpose:** To help patients manage glucose levels effectively.

**Benefit:** This technology is expected to improve the quality of life for patients with diabetes mellitus. With the push of a button, the hand-held receiver provides real-time glucose measurements and alerts patients to wide upward or downward deviations in glucose levels.

**Precautions:** This prescription-only device is an adjunct to a blood glucose meter but does not replace it. The system must be removed before magnetic resonance imaging. The use of acetaminophen may affect the performance of the device. The calibration should be updated every 12 hours at a minimum.

**Sources:** www.pharmacyonesource.com; www.dexcom.com

**Name:** Powerlink-120 Endoluminal Stent Graft

**Manufacturer:** Endologix, Irvine, CA

**Approval Date:** April 25, 2006

**Use Classification:** The stent graft is used to treat abdominal aortic aneurysms (AAAs). An AAA is a weakening of the wall of the aorta, resulting in a balloon-like enlargement. After an AAA develops, it continues to enlarge. If left untreated, it is susceptible to rupture. The overall mortality rate for a ruptured AAA is approximately 75%, making it the 13th leading cause of death in the U.S.

**Description:** This is a new short-body and short-limb variant of the Powerlink System endoluminal stent graft for the minimally invasive treatment of AAAs.

**Purpose:** To treat AAAs. The two Powerlink-120 models can be used for the 5% to 10% of patients who might be excluded from treatment because of anatomical characteristics. Endoluminal repair may emerge as an interventional strategy to treat AAAs, especially if surgery poses a high risk for patients.

**Benefit:** Stents and stent–graft prostheses provide a less invasive alternative to major abdominal surgery.

**Source:** www.pharmacyonesource.com

**Name:** Exponent RX Self-Expanding Carotid Stent

**Manufacturer:** Medtronic, Minneapolis, MN

**Approval Date:** April 27, 2006

**Use Classification:** The stent/filter system offers a minimally invasive option to prevent stroke in patients with carotid artery disease. Medtronic has received the CE Mark (Conformité Européenne) of approval certifying that the product has met all health and safety requirements for use in Europe.

**Description:** The tiny stent restores adequate blood flow in blocked arteries. A filter, a miniature mesh basket, enables blood to flow normally while it traps loose particles in the bloodstream, preventing them from reaching the brain and causing a stroke during surgery.

**Purpose:** To prevent stroke in patients with blocked carotid arteries.

**Benefit:** Carotid stenting has become an alternative to carotid endarterectomy, in which physicians surgically open the carotid artery and remove the fatty buildup of plaque to restore blood flow. With stenting, which is less invasive, the physician inserts a catheter into a small incision or puncture made in the arm or groin. The catheter is guided to the area of blockage in the carotid artery, and the stent is opened in position.

**Sources:** www.pharmacyonesource.com; Web Wire, April 27, 2006.

**Safety Alert: Colleague Infusion Pumps**

The FDA suggests that all health care providers take precautions when using Baxter Healthcare’s Colleague Volume Infusion Pump. The pump has had problems, including underinfusion, battery and alarm failures, and false alarms. Over the past year, Baxter has issued four urgent safety notices and recalls.

The company and the FDA recommend that the pump not be used if delaying or interrupting therapy in order to reprogram or replace a malfunctioning pump might be life-threatening. A back-up pump should be available in case infusion therapy is disrupted. Patients should be monitored frequently, and pumps should be checked often.


**Recall: Contact Lens Solution**

Bausch & Lomb has proposed that unique characteristics of its formulation of ReNu with MoistureLoc contact lens solution in certain unusual circumstances may increase the risk of Fusarium infection. The company has decided to remove this product from the market worldwide. No problems have been observed with ReNu MultiPlus or ReNu Multi-Purpose solutions or with other generic cleaning solutions.

(Source: FDA, May 15 and 16, 2006.)