NEW DRUGS

Mycophenolic Acid to Prevent Organ Rejection

The Food and Drug Administration (FDA) has approved the use of enteric-coated, delayed-release mycophenolic acid (MPA) tablets (Myfortic®, Novartis) in combination with cyclosporine (Neoral®, Novartis) and corticosteroids to prevent organ rejection in kidney transplant recipients.

On February 7, 2004, the drug successfully completed the European Mutual Recognition Procedure and was approved to prevent acute rejection in kidney allografts in adults. It was first approved in Switzerland in 2002.


Cinacalcet for Chronic Kidney Disease

Patients with the debilitating consequence of chronic kidney disease now have a new treatment option. The FDA has approved cinacalcet HCl tablets (Sensipar™, Amgen) to treat secondary hyperparathyroidism in dialysis patients.

Cinacalcet is the first drug in the class of compounds known as calcimimetics to be approved. Elevated levels of parathyroid hormone (PTH), the hallmark of secondary hyperparathyroidism, are associated with altered metabolism of calcium and phosphorus, bone pain, fractures, and an increased risk of cardiovascular death. Cinacalcet lowers serum levels of PTH as well as calcium x phosphorus product (a measure of the amount of serum calcium and phosphorus). When this value is elevated, harmful deposits of calcium occur.

Cinacalcet was also granted an orphan designation to treat hypercalcemia associated with parathyroid carcinoma, a rare cancer that raises serum calcium levels. Elevated calcium levels of serum calcium can cause mental confusion, lethargy, dehydration, nausea, vomiting, constipation, and kidney damage.

Cinacalcet therapy should not begin if calcium levels are below 8.4 mg/dl.

(Sources: FDA, March 9, 2004; www.amgen.com.)

DRUG NEWS

Caution Urged with SSRI Antidepressants in Adults, Children

The FDA has issued a Public Health Advisory for physicians, their patients, and families and caregivers of patients about the need to monitor adults and children with depression, especially at the beginning of treatment with selective serotonin reuptake inhibitors (SSRIs) or when doses are increased or decreased.

The FDA has been reviewing the results of studies in children since June 2003, after an initial report on studies of paroxetine (Paxil®, GlaxoSmithKline) and subsequent reports on studies of other drugs appeared to suggest an increased risk of suicidal thoughts and actions in children taking antidepressants. There were no suicides in any of the trials. It was unknown whether certain behaviors reported in these studies represented actual suicide attempts or other self-injurious behavior that was not suicide-related.

It is not clear whether the drugs contribute to the emergence of suicidal thinking and behavior, but patients should be observed for behaviors known to be associated with these drugs (e.g., anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, severe restlessness, hypomania, and mania). Physicians have been asked to be especially vigilant with patients who have bipolar disorder.

The FDA has asked manufacturers to change the labels of 10 drugs to include stronger cautions about the need to monitor patients for worsening depression and the emergence of suicidal ideation, regardless of the cause.

The drugs under review are bupropion (Wellbutrin®, GlaxoSmithKline) citalopram hydrobromide (Celexa™, Forest), fluoxetine (Prozac®, Eli Lilly), fluvoxamine maleate (Luvox®, Solvay), mirtazapine (Remeron®, Organon), nefazodone (Serzone®, Bristol-Myers Squibb), paroxetine, sertraline (Zoloft®, Pfizer), escitalopram oxalate (Lexapro™, Forest), and venlafaxine (Effexor®, Wyeth).

(Source: FDA, March 22, 2004.)

Long-Acting Venlafaxine Superior for Depression?

Prescribing extended-release venlafaxine rather than fluoxetine for depression might be more beneficial to patients in the long term. Researchers from Prescriptions Solutions in Costa Mesa, California, and Wyeth Research in St. Davids, Pennsylvania, found that patients taking venlafaxine XR were at least three times more likely to be treated adequately through the crucial first eight months.

The researchers evaluated pharmacy refill claims, which reflect the patients’ actual behavior in filling prescriptions, not necessarily the physicians’ actual treatment regimen.

(Source: Pharmacotherapy 2004;24: 33–40.)

LMWHs Preferred for Pulmonary Embolism

Low-molecular-weight heparins (LMWHs) have advantages over unfractionated heparin: they are more convenient, they carry a lower risk of allergic reactions and thrombocytopenia, and they seem to be effective for treating nonmassive pulmonary embolism (PE).

In a meta-analysis of 12 trials involving 2,051 patients, researchers from King’s College Hospital in London, United Kingdom, and the University of Western Australia, Perth, found that LMWHs reduced
recurrent symptomatic events at the end of treatment. Results were similar for patients with or without symptoms of PE.

Among the 1,023 patients who received LMWHs, the incidence of major bleeding was 1.4%, compared with 2.3% among the 298 patients who received unfractionated heparin.

Many clinicians continue to use unfractionated heparin as first-line therapy for the initial management of PE because of a lack of evidence for the effectiveness of LMWHs, the researchers note. They believe, however, that the fact that deep venous thrombosis and PE are different facets of the same underlying disease process suggests that they should respond similarly to the same treatment.

(Source: Ann Intern Med 2004;140:175–183.)

More Intense Statin Therapy May Avert Heart Disease

Lowering cholesterol far below the level now considered adequate appears to substantially reduce patients’ risk of death from heart attacks. These findings from the “Prove It” Study (Pravastatin or Atorvastatin Evaluation and Infection Therapy) may change the way heart disease is treated. The study compared high doses of a powerful statin, or cholesterol-lowering drug, atorvastatin calcium (Lipitor®, Pfizer), with a less potent statin, pravastatin sodium (Pravachol®, Bristol-Myers Squibb). The patients taking Lipitor® were much less likely to have heart attacks or to need bypass surgery or angioplasty.

National guidelines currently call for levels of low-density lipoprotein (LDL) cholesterol, which carries cholesterol to arteries, to be below 100 mg/dl in high-risk patients.

In an earlier study, Lipitor® halted plaque growth and Pravachol® slowed but did not stop it. The current study suggests that for patients with recent acute coronary syndrome, an intensive lipid-lowering statin regimen might provide greater protection against death or major cardiovascular events than a standard regimen and that patients would benefit from early reduction of LDL cholesterol to below present target levels.


Is “Good” Cholesterol Really “Good”?

For years, doctors thought that to prevent heart disease, patients should pay attention to both the low-density lipoprotein (LDL, or “bad”) cholesterol and the high-density lipoprotein (HDL, or “good”) cholesterol. The good, they assumed, could counteract the bad. Some experts are now questioning whether high levels of the “good” cholesterol are always healthy.

An LDL level below 100 is optimal, 100 to 129 is near or above optimal, and above 130 is high (even these standards are becoming stricter). The average HDL level for men is 40 to 50 mg/dl and for women 50 to 60 mg/dl. Even when HDL levels are much higher, the LDL can overpower the HDL. Some experts have concluded that HDL levels should play a minor role in decisions as to whether to prescribe cholesterol-lowering drugs.

A high HDL level might not create a total immunity to heart disease. Some people have high levels of HDL, but it does not function properly; these patients may be vulnerable to heart disease. In summary, no one should ignore high levels of LDL.


Opening Arteries Might Not Prevent Heart Attacks

It may turn out that increasingly popular aggressive treatments, such as bypass surgery and stents, may be doing little to prevent heart attacks. Although these measures alleviate chest pain and stents can also eliminate an obstruction and hold a closed artery open, a new model of heart disease suggests that most heart attacks do not originate with obstructions that narrow the arteries.

Although the new stents are coated with drugs to prevent scar tissue from growing back in the immediate area, there is no evidence that they change the course of heart disease. Stenting can actually cause minor heart attacks in about 4% of patients. The true purpose of the procedure is more likely symptom relief to enhance quality of life.

Systemic statin or antiplatelet therapy might be more helpful than bypass surgery or stenting. It may take a while for cardiologists to agree, however.


NEW MEDICAL DEVICES

By Marvin M. Goldenberg, PhD, RPh, MS

Name: COBAS AmpliScreen HIV-1 Test v.1.5

Manufacturer: Roche Diagnostics, Basel, Switzerland

Approval Date: March 2, 2004

Use Classification: Qualitative in vitro testing to detect human immunodeficiency virus type 1 (HIV-1) in both source plasma and organ donors.

Description: Roche’s patented polymerase chain reaction (PCR) technology enables direct detection of the genetic material of HIV-1 earlier in the infection cycle, often before any symptoms of disease are manifested. It replaces the traditional HIV-1 p24 antigen testing, which detects an HIV-1–associated protein that appears in the body later in the infection cycle.

Purpose: This is the first licensed nucleic acid screening test available for
manufacturers of plasma-based therapeutics to use in their own laboratories.

**Benefits:** The test demonstrates reliably quantitation of low HIV-1 viral load levels with a detection rate of greater than 95% at 50 copies/ml. With an assay specificity of 100%, the test monitors provide laboratories with an unmatched level of assurance, reducing the need for time-consuming, expensive repeated tests and false-positive results that could trigger unnecessary treatment changes and compromise long-term therapeutic management.

**Source:** Roche Diagnostics Division, www.roche-diagnostics.com.

**Name:** MDP-25 Diagnostic Agent  
**Manufacturer:** DRAXIS Health, Draximage, Inc., Mississauga, Ontario, Canada  
**Approval Date:** March 1, 2004  
**Use Classification:** Formulation of a diagnostic product to prepare a skeletal imaging agent used to demonstrate areas of altered osteogenesis or bone growth.

**Description:** The newly formulated product is a kit for preparing technetium Tc 99m medronate injection (99mTc-Methylene Diphosphonic Acid Kit). Each vial of MDP-25 contains lyophilized (freeze-dried) powder that is reconstituted immediately before use with radioactive sodium pertechnetate solution. The resulting active labeling agent remains stable throughout its 12-hour life.

**Purpose:** MDP-25 is used to detect metastatic bone disease, Paget’s disease, arthritic disease, and osteomyelitis. Following injection, the agent is accumulated and retained by the patient’s skeleton so that a gamma camera can be used to obtain an image of the bone anatomy. Areas of abnormal osteogenesis show altered uptake, making it possible to visualize a variety of bone lesions.

**Benefit:** MDP-25 offers enhanced imaging of the extremities, particularly the hands and feet, thereby resulting in improved whole-body skeletal imaging.

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

**Name:** BreastScan Infrared™ System  
**Manufacturer:** Infrared Sciences Corporation, Hauppauge, New York  
**Approval Date:** February 26, 2004  
**Use Classification:** Digital infrared imaging for the early detection of breast cancer.

**Description:** The procedure takes approximately 10 minutes, and results are available immediately. Patients are not exposed to any radiation, and compression and contact with the breasts are not required.

The patient sits in a chair facing an infrared camera while a nurse performs the procedure. This unique evaluation provides physiological data, which can indicate indirect areas of concern; by comparison, mammography, ultrasound, and magnetic resonance imaging provide anatomical data, which requires that anomalies be sufficiently developed to be physically detectable. This means that the best indication of an abnormality is through corroboration of different tests.

The scan method pinpoints areas that might not have been detected by standard mammograms, including areas beneath dense breast tissue. The system can also localize areas to be investigated further by ultrasound. For younger women, the system can track breast health and provide baseline data.

**Purpose:** An automated, real-time report can be used as an adjunctive test along with mammography, ultrasound, or clinical examination. The scan does not replace mammography or ultrasound, and it does not stand alone as a single test that can determine overall breast health.

**Benefit:** This painless, noninvasive procedure measures various temperature parameters in the breast. No data must be “interpreted”; all findings are quantified by the system’s computer and provided to the physician in a format that clearly indicates any areas of concern.

**Source:** www.pharmacyonesource.com.

**Name:** Peg-Intron Redipen™  
**Manufacturer:** Schering-Plough Corporation, Kenilworth, New Jersey  
**Approval Date:** February 17, 2004  
**Use Classification:** Easy-to-use pen that provides Peg-Intron® (peginterferon alfa-2b) Powder for Injection

**Description:** The Redipen™ is the first and only pen-delivery system approved for administering pegylated interferon therapy for patients with chronic hepatitis C. The pen is a disposable, one-time-use, precision dosing system that allows patients to administer the powder in three easy steps: “mix, dial, and deliver.” Patients simply push down on the pen to combine the powder with sterile water, which are both stored in the body of the pen; dialing allows patients to select a preset dose; and delivery allows patients to inject this dose.

**Purpose:** The pen is designed to help patients feel confident that they are receiving an accurate dose of pegylated therapy.

**Benefit:** This system offers an easy-to-read dial-up dosing button for precise, individualized weight-based administration, a self-priming action that removes air bubbles from the pen before patient self-administration, and a small needle size (30-gauge) to minimize discomfort. The system offers an alternative for patients who might be intimidated by a traditional needle-and-syringe system. Doses are available in four strengths (50, 80, 120, and 150 mcg), and each is indicated by a color-coded button.

**Source:** Schering-Plough Corporation, www.sch-plough.com.