**NEW DRUGS**

**Abarelix Approved for Advanced Prostate Cancer**

The Food and Drug Administration (FDA) has approved the New Drug Application to permit the marketing of abarelix (Plenaxis™, Praecis). This drug is indicated for patients with advanced prostate cancer who have no alternative therapy because of an increased risk of serious and potentially life-threatening allergic reactions to other available medications.

The drug is to be marketed under a voluntary risk-management program. Approximately 5% to 10% of these patients have the type of advanced, symptomatic disease that would make them candidates for Plenaxis™.

Plenaxis™ is a gonadotropin-releasing hormone (GnRH) antagonist that lowers levels of testosterone, a key factor that is involved in most prostate cancer growth. A study of 81 men showed that they could avoid surgical castration by undergoing at least 12 weeks of treatment. Some of the men also experienced other benefits, including decreased pain and relief from urinary problems. However, three of the 81 patients in the clinical trial experienced serious allergic reactions, including loss of consciousness.

Because of the risk of low blood pressure and fainting as part of the allergic reaction to Plenaxis™, patients are to be monitored for at least 30 minutes after receiving a dose of the drug in their health care provider’s office.

Plenaxis™, which is injected into the muscles of the buttocks every two weeks for the first month of therapy and once every four weeks thereafter. Because the drug may stop working in certain patients, physicians should perform blood tests about every two months to make sure that it is still effective in keeping testosterone levels low.

Side effects included hot flashes, sleep disturbances, generalized pain, back pain, breast enlargement or pain, and constipation.

The risk-management program is designed to ensure that patients and physicians are fully informed of the advantages and disadvantages of Plenaxis™ before using it. The company also plans to collect and report adverse events to the FDA.

(Source: FDA Talk Paper, November 26, 2003.)

**DRUG NEWS**

**Study Finds Inadequate Treatment of Early-Stage Breast Cancer**

Data from a new study point to an alarming pattern in breast cancer treatment: more than 50% of women with early-stage breast cancer have not received their full, recommended dose of potentially life-saving chemotherapy.

A comprehensive retrospective analysis showed that 56% of the almost 20,800 women who were being treated for cancer in 1,243 community-based oncology practices in the U.S. received less than 85% of their recommended dose intensity, as prescribed in the optimal treatment plan, because of delays of at least one week (in 25% of patients) or dose reductions (in 37%). Earlier studies have indicated that receiving less than 85% of the recommended dose intensity can result in lower survival rates for patients.

The primary reason for the chemotherapy delays is the presence of neutropenia, a deficiency of white blood cells, which fight infection and which are destroyed by the effects of the chemotherapy. If the white blood cell count falls too low, patients are at increased risk for infection and, consequently, chemotherapy must be delayed until the cells are replenished.

Although white blood cell “boosters,” known as colony-stimulating factors, are available for the treatment of neutropenia, only 25% of patients received them during chemotherapy.

The researchers noted that these results are particularly disturbing because earlier studies have underscored the importance of maintaining full chemotherapy dose intensity, especially in responsive and potentially curable malignancies, such as early-stage breast cancer. The study also disclosed a tendency of oncologists to lower dose intensity in order to reduce side effects.

Almost two-thirds of patients older than age 65 were less likely to receive the recommended doses, even though studies have shown that elderly patients can benefit from chemotherapy as much as younger patients. African-American women were also more likely to experience delays in treatment because of lower white blood cell counts.

The women in the study ranged in age from 11 to 90, with a mean age of 52.


**Drug Aids Survival in Early Breast Cancer**

A chemotherapy cocktail that contains docetaxel (Taxotere®, Aventis) has shown promise in improving survival rates for women with early-stage breast cancer while reducing the likelihood of recurrence.

Researchers presented their findings at the San Antonio Breast Cancer Symposium, held from December 2–6, 2003. In a study of almost 1,500 women, 87% of those who were taking the drug were alive 55 months later, compared with 81% of women taking 5-fluorouracil, a commonly used therapy. In addition, 75% remained disease-free, compared with 68% receiving the standard treatment.
The researchers suggested that if all patients with newly diagnosed disease received the new regimen, almost 18,000 women would still be living five years after their diagnosis.

Taxotere® was approved in 1996 for women with advanced breast cancer.

(Source: Wall Street Journal, December 8, 2003.)

**Combination Therapy for Enlarged Prostate: Better Than Each Drug Alone**

Two drugs that are often used to treat prostate gland enlargement (benign prostatic hypertrophy) have been found to be more effective in alleviating symptoms and slowing the progression of disease when used in combination than when used individually.

Doxazosin (Cardura®, Pfizer) relieves some symptoms quickly by relaxing bladder and prostate muscles, although it does not reduce the gland’s size. Finasteride (Proscar®, Merck) shrinks the gland but works more slowly and might reduce the need for prostate surgery.

The researchers observed 3,047 men with urinary-tract symptoms for an average of four and one-half years. Compared with patients taking placebo, patients receiving both medications experienced a smaller risk of a worsening condition, a reduced risk of urinary retention, and a reduced need for surgery.

The best candidates for the combination treatment appear to be men with significant prostate enlargement and urinary-tract symptoms.


**Tolerability of Rofecoxib and Naproxen for Osteoarthritis**

Rofecoxib (Vioxx®, Merck) works as well as naproxen (e.g., Naprosyn®, Roche) at controlling the symptoms of osteoarthritis and is also effective at a much lower dose and with less severe adverse gastrointestinal (GI) effects. The ADVANTAGE (Assessment of Differences between Vioxx And Naproxen To Ascertain Gastrointestinal tolerability and Effectiveness) Study Group compared the use of rofecoxib 25 mg/day with that of naproxen 500 mg twice daily in 5,557 older patients with osteoarthritis. This is thought to be the largest trial to compare GI symptoms that prompt patients to discontinue treatment.

Overall, a statistically significant lower number of patients stopped taking rofecoxib (5.9%) because of GI adverse drug events (ADEs) compared with the naproxen group (8.1%). A similar risk of ending treatment was noted among subgroups of patients using low-dose aspirin and among those who had previously ceased to use their arthritis medication because of GI symptoms. Improved GI tolerability was confirmed by the decreased use of gastroprotective medications and by a reduced incidence of serious GI events, such as perforations, ulcers, and bleeding. No significant differences were observed in general, cardiovascular, or hypertension-related ADEs.

(Source: Ann Intern Med 2003;139: 539–546.)

**COX-2 Inhibitors Do Not Prevent Alzheimer’s Disease**

Although scientists had hoped that the painkiller rofecoxib (Vioxx®, Merck) would help to prevent Alzheimer’s disease (AD), an earlier study this year found that this drug, along with naproxen (e.g., Aleve®, Naprosyn®, Roche) did not benefit patients who already had AD.

The findings were revealed at the annual meeting of the American College of Neuropsychopharmacology in San Juan, Puerto Rico. The study had enrolled 1,457 older patients with mild cognitive impairment, a group with risk factors for the development of AD. After half of the patients received rofecoxib therapy and the other half were given a placebo, it was found that AD developed in 6.4% of the rofecoxib group and in 4.5% of the placebo group. The study was discontinued after 189 cases of AD were observed.

On the surface, it appears that rofecoxib caused AD in these patients, but an analysis of the patients’ cognitive abilities showed that the risk associated with the drug was similar to that for the placebo.

COX-2 inhibitors attack inflammation, and it had been thought that these drugs would be able to prevent AD by inhibiting inflammation of the neurons in the brain.


**HIV Drug Cost Rises by 400%**

Abbott Laboratories has notified physicians, pharmacists, and organizations of a price increase for its protease inhibitor ritonavir (Norvir®). The drug is taken in small doses to enhance the efficacy of combination-drug therapies used to treat acquired immunodeficiency syndrome (AIDS).

The price increase does not affect drugs that are bought by government programs such as Medicaid or AIDS Drug Assistant Programs. State-run programs such as Medicaid or AIDS Drug Assistant Programs. State-run programs have negotiated discounts for Norvir® and other AIDS drugs through the end of 2005.

Norvir® was the second protease inhibitor to be approved in 1996 and the first one to show that it increased survival rates. At that time, it cost $20.52 per day for 1,200 mg. However, after the drug was found to be associated with severe adverse effects, it was discovered that a lower dose could be effective and could boost the potency of other protease in-
hibitors.

Until recently, the drug cost $1.75 per day and most patients were taking a dose of 100 mg. The wholesale price for a month’s treatment is expected to increase from $54 to $265.


**Timing Statins Just Right**

When is the best time to take a statin? The findings from several studies have been conflicting, although most statin manufacturers say that nighttime is ideal because most cholesterol is synthesized when dietary intake is low.

Researchers from the University of Sunderland in Tyne, Great Britain, randomly assigned 60 patients to take simvastatin (Zocor®, Merck) in the morning or evening for eight weeks. Patients who switched from evening to morning had statistically significantly higher total cholesterol and low-density lipoprotein-cholesterol (LDL, or “bad,” cholesterol) levels. From the baseline evaluation to week eight, total cholesterol values rose by an average of 0.38 mmol/liter and LDL-cholesterol levels rose by an average of 0.25 mmol/liter.

In a study of atorvastatin (Lipitor®, Pfizer), no significant difference in cholesterol concentrations was observed between evening and morning, but the researchers note that this drug’s longer elimination half-life might be the explanation.

(Source: BMJ 2003;327:788.)

**Growth Hormone and Short-Bowel Syndrome**

The FDA’s Office of Orphan Products Development has granted an orphan drug designation for Serono’s Zorbtive™ (Somatropin [rDNA origin] for injection), a recombinant human growth hormone, for use in the treatment of short-bowel syndrome (SBS).

SBS is a rare and potentially life-threatening condition that follows extensive surgical removal of portions of the small intestine as a treatment for acute or chronic disorders of the intestine. Removal of a large portion of the bowel results in impaired absorption of nutrients. The standard treatment for SBS involves careful management of dietary intake and hydration or, when appropriate, total parenteral nutrition (TPN), in which patients are fed through an intravenous (IV) tube. On rare occasions, surgical transplantation of the intestine may also be performed for this condition. Approximately 10,000 to 20,000 patients in the U.S. are receiving TPN for SBS.

In a randomized double-blind, controlled, parallel-group phase III clinical study, Serono’s recombinant human growth hormone, administered with specialized nutritional support, was shown to significantly reduce patient dependence on TPN, as measured by total volume, total calories, and frequency of infusion.

Common adverse events associated with growth hormone therapy are mild to moderate muscle and joint pain and swelling or edema, which occur in a dose-related manner and often subside with continued treatment or dose reduction. Cases of new-onset impaired glucose intolerance, new-onset type-2 diabetes mellitus, and exacerbation of pre-existing diabetes mellitus have been reported.

Diabetic ketoacidosis and diabetic coma may occur, and for some patients taking growth hormone therapy, anti-diabetic treatment must be initiated or adjusted. Patients with a history of hyperglycemia or other risk factors for glucose intolerance should be monitored closely. Temporary increases in glucose levels occur early in treatment and should be monitored.

The use of growth hormone is contraindicated in patients who are in intensive-care units because of complications following open-heart surgery or abdominal surgery, trauma, or acute respiratory failure; patients with active neoplasia; and patients with known hypersensitivity to growth hormone.

(Source: Serono news, December 2, 2003; www.serono.com.)

**Eight Is Enough**

Eight days of antibiotic therapy is sufficient for patients with ventilator-associated pneumonia (VAP), according to the PneumA Trial Group in France. The researchers compared eight-day and 15-day treatments in 401 patients in 51 intensive-care units. Primary outcome measures (e.g., death, recurrent pulmonary infection, and antibiotic-free days) were assessed 28 days after the onset of VAP and were analyzed on an intent-to-treat basis.

Mortality rates were similar in both groups of patients; 37 of 197 in the eight-day treatment group died, and 35 of 204 in the 15-day treatment group died. Both groups also experienced similar rates of recurrent infections (28.9% vs. 26%) as well as similar times to recurrence, time to relapse, and time to the development of superinfection.

On average, the eight-day group had 50% more antibiotic-free days. That finding alone could mean a shorter treatment time, the researchers suggest. Also, the fact that the multiresistant pathogens emerged more frequently in the 15-day group (62.3% vs. 42.1%), underscores the importance of discouraging the indiscriminate use of antibiotics.

(Source: JAMA 2003;290:2588–2598.)

**Healing Pressure Ulcers with Nerve Growth Factor**

Pressure ulcers seem to heal faster with a daily topical solution of nerve growth factor, according to a study conducted at a teaching nursing home in Fontecchio,
Antidepressants and the Need for Blood Transfusions

Patients who take serotonergic antidepressants might be at higher risk for bleeding during orthopedic surgery, say researchers at St. Elisabeth Hospital in Tilburg, the Netherlands. The number of blood transfusions almost quadrupled for those patients, compared with patients who were not taking antidepressants.

Of 520 patients, 26 (5%) used serotonergic antidepressants before surgery. Of those, six (23%) received perioperative blood transfusions. Antidepressant use was significantly associated with increased blood loss during surgery (1,109 ml for users, 582 ml for nonusers).

Serotonergic antidepressants had already been associated with bleeding disorders, and reports have raised concerns about the safety of these drugs for older patients. The researchers cite earlier studies that found possible links to bleeding-related problems. One, for instance, found a threefold increase in the risk of gastrointestinal (GI) bleeding in primary care patients; another estimated an absolute risk of eight new serotonergic antidepressant–induced GI hemorrhages per 1,000 persons per year in elderly patients.

The researchers explain that the main mechanism for the increased risk might occur via reduced intraplatelet serotonin concentrations, which then affect platelet aggregation.

Lower platelet serotonin levels and a concurrent rise in plasma serotonin levels have also been associated with surgical procedures. Thus, patients experiencing stress from surgery may be at higher risk for bleeding complications because of platelet impairment. The combination of those two effects may act synergistically and negatively on hemostasis.

Recombinant human erythropoietin has the potential to reduce the need for allogeneic blood transfusions, the researchers suggest, thus avoiding or minimizing transfusion-related complications.

(Source: Arch Intern Med 2003;163: 2354–2358.)

Inhaled Insulin: A Better Choice for Some

Adding inhaled insulin to the treatment regimens of diabetic patients may help improve glycemic control when treatment with oral hypoglycemic agents alone has failed. In a study of 68 patients with inadequately controlled type-2 (“adult-onset,” or non–insulin-dependent) diabetes, researchers from San Diego Endocrine and Medical Clinic, Yale University, and Pfizer, Inc., demonstrated that inhaled insulin before meals reduced the glucose burden after meals and helped to dispose of meal-related glucose. Inhaled insulin also lowered fasting glucose substantially, they say.

The inhaled insulin was well tolerated and was associated with no greater risk of hypoglycemia than were combined oral hypoglycemic agents and subcutaneous insulin. It also improved triglyceride levels, possibly because of the restoration of insulin regulation of lipolysis. Patients did gain weight, but that effect might be related to improved glycemic control, with fewer calories lost through urinary glucose.

For patients who have trouble injecting insulin, the inhaled version provides a bonus. After the study, 97% of patients who received the inhaled form opted to continue in a one-year extension of the therapy.

(Source: Arch Intern Med 2003;163: 2277–2282.)

FDA Update on Drug-Coated Stents

The FDA has clarified information about adverse events associated with Cordis
Corporation’s Cypher Coronary Stent. The agency emphasized that it considers the drug-eluting stents safe and effective when label directions are followed, particularly in terms of patient selection and the appropriate use of the medication.

Numerous patients have been successfully treated with the stent, which was approved in April 2003 for patients undergoing angioplasty procedures to open clogged coronary arteries. In October, however, the FDA notified physicians about reports of thrombosis and clotting occurring within 30 days after the device was implanted and of possible hypersensitivity reactions. The agency asked physicians and patients to report any adverse effects associated with the stents.

To date, the rate of thrombosis has remained within the expected range for any stent. As of November 21, 75 additional (more than 360 total) cases of thrombosis have been reported, including 10 additional deaths (more than 70 in all).

In most cases, hypersensitivity reactions were minor (e.g., skin rashes and itching that cleared up within a few days), but some reactions were severe (e.g., anaphylaxis). Although some of the reactions remain unexplained, many of them are believed to be related to standard drug therapy associated with the procedure.

The update is available at www.fda.gov/cdrh/safety/cypher2.html.

(Source: FDA Talk Paper, November 25, 2003.)

**Benefits of Costly Schizophrenia Drug Questioned**

A study at 17 Veterans Affairs (VA) hospitals comparing an older, pennies-a-day schizophrenia drug with a newer, far more expensive one found little advantage to the high-ticket drug. The researchers say that this is the first long-term, rigorously designed experimental study of the newer drug, which boasts U.S. sales of $2 billion annually.

The researchers compared haloperidol decanoate (Haldol®, Ortho-McNeil), from an earlier class of schizophrenia drugs called typical antipsychotic agents, with olanzapine (Zyprexa®, Eli Lilly), the most expensive among the newer atypical antipsychotics. Used alone, the older medications are more likely to cause troubling side effects such as tremors and twitching.

In this study, physicians prescribed haloperidol as they would have in actual practice, that is, accompanied from the outset by another drug, benzotropine mesylate (Cogentin®, Merck), to minimize side effects.

After one year, the randomized, double-blind study found no differences between the drugs in reducing schizophrenia symptoms or in improving quality of life. Olanzapine tended to cause weight gain but resulted in slightly less restlessness and in somewhat better cognitive status; however, it was not enough to improve patients’ quality of life or overall functioning.

Although the drugs produced similar results in general, they come with a whopping difference in price: olanzapine costs more than $8/day per patient; haloperidol costs only about 6 cents/day. The higher-priced drug did not lead to any significant reduction in hospital or outpatient costs.

The researchers did not think that the study would prompt a return to the older class of schizophrenia drugs.

Typical antipsychotic drugs such as haloperidol are recommended only when patients do not respond to the standard first-line regimen. However, physicians are urged to use their discretion and to take into account the needs of their individual patients.

Eli Lilly supplied the drugs and placebo for this study, but the analysis was conducted with complete independence on the part of the VA.

(Sources: *JAMA* 2003;290(20):2693–2702; VA Northeast Program Evaluation Center, West Haven, CT, November 25, 2003.)

**Oral Cephalosporin Antibiotic Available in U.S.**

Purdue Pharmaceutical Products L.P. has begun shipping cefditoren pivoxil tablets (Spectracef®) to drug wholesale and pharmacy customers in the U.S. This product is a leading oral cephalosporin antibiotic in Japan. In May 2003, Purdue announced its exclusive licensing agreement with Meiji Seika Kaisha, Ltd., of Japan to market Spectracef® in the U.S. and Puerto Rico. Purdue has also acquired the Canadian rights to Specttracef®.

The FDA first approved this drug in 2001, and it was originally marketed in the U.S. by TAP Pharmaceutical Products, Inc.

Spectracef® 200 mg twice daily is indicated for the treatment of mild to moderate infections in adults and adolescents 12 years of age and older from pharyngitis and tonsillitis caused by susceptible strains of *Streptococcus pyogenes* (S. pyogenes) and uncomplicated skin and skin structure infections caused by susceptible strains of *Staphylococcus aureus* or S. pyogenes. A dosage of 400 mg twice a day is recommended for the treatment of community-acquired pneumonia (CAP) and acute bacterial exacerbations of chronic bronchitis caused by susceptible strains of *Haemophilus influenzae* (H. influenzae), *H. parainfluenzae*, *S. pneumoniae* (penicillin-susceptible strains only), or *Moraxella catarrhalis*.

Side effects are generally mild and self-limiting. The most commonly reported adverse events in clinical trials were diarrhea, nausea, vaginal yeast infections, headache, abdominal pain, dys-
Darbepoetin alfa for Anemia of Cancer

Interim data from a randomized, multicenter study indicate that darbepoetin alfa (Aranesp®, Amgen) is beneficial in correcting anemia in cancer patients who are not undergoing chemotherapy. The results were presented at the 45th annual meeting of the American Society of Hematology, from December 6–9, 2003 (Abstract No. 1816).

The hemoglobin counts at the baseline examination were 10.1 g/dl in the Aranesp® group and 10.4 g/dl in the control group. After 12 weeks of treatment, the mean change in hemoglobin was 1.9 g/dl for the Aranesp® group and 0.2 g/dl in the controls, who received standard care.

Patients in the Aranesp® group received 3 mcg/kg every other week for 21 weeks; the controls were observed for 12 weeks, then received nine weeks of Aranesp® therapy. The Kaplan-Meier estimates (95%) of hematopoietic response were 81% for the Aranesp® group and 26% for the controls.

Although anemia is recognized as a common problem in cancer patients receiving chemotherapy, other patients may have anemia because of the cancer itself; the anemia is unrelated to chemotherapy. Common symptoms of anemia of cancer include physical and mental fatigue.

In July 2002, the FDA approved Aranesp® to treat chemotherapy-induced anemia in patients with nonmyeloid malignancies. In September 2001, Aranesp® was approved for the treatment of anemia associated with chronic renal failure (chronic kidney disease) in both dialysis and non-dialysis patients.

Aranesp® is a recombinant erythropoietic protein that stimulates production of oxygen-carrying red blood cells. Compared with earlier products, it offers more activity with the added benefit of less frequent administration.

This medication is contraindicated in patients with uncontrolled hypertension. Erythropoietic therapies may increase the risk of thrombotic and other serious events; the dose should be reduced if the hemoglobin increase exceeds 1.0 g/dl in any two-week period.

Commonly reported side effects in trials were fatigue, edema, nausea, vomiting, diarrhea, fever, and dyspnea.

(Sources: Amgen news release, December 6, 2003; www.hematology.org; www.abstracts2view.com.)

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS
Source: ww.fda.gov/cdrh/newpg.html

Name: ALLEGRETTO WAVE™ Excimer Laser System

Manufacturer: Lumenis/Wavelight Laser Technologie AG, Erlangen, Germany

Approval Date: October 7, 2003

Use Classification: LASIK surgery

Description: The refractive excimer laser system uses invisible ultraviolet (UV) light pulses to remove precise amounts of corneal tissue from the eye in patients with nearsightedness and astigmatism. An eye tracker detects the position of the eye and aligns the laser pulse with the cornea. The surgical procedure is known as laser-assisted in situ keratomileusis (LASIK).

Purpose: To treat nearsightedness. The surgeon uses the excimer laser system to remove tissue from the center of the cornea to flatten it and treats astigmatism by flattening the central cornea by different amounts and at different orientations to correct for an uneven focus. The device is indicated for patients with nearsightedness up to −12 diopters (D) and astigmatism up to −6 D. Patients should be 18 years of age or older, and their eyesight should have been stable (.50 D or less) for the year before the pre-operative examination.

Precautions: Side effects include glare from bright lights and from lights and headlights at night, halos (rings around lights), light sensitivity, and visual fluctuations. After surgery, patients sometimes need reading glasses at earlier ages than usual.

The system should not be used for patients who are pregnant or nursing; those who have a collagen-vascular, autoimmune or immunodeficiency disease; those with signs of keratoconus (thinning of the cornea with resulting blurred or distorted images); or those who are taking medications that are associated with ocular side effects, such as isotretinoin (Accutane®, Roche) and amiodarone (Cordarone®, Wyeth).
Potential adverse effects associated with LASIK surgery include loss of best-spectacle corrected visual acuity; overcorrection; an increased refractory cylinder; worsening of double vision or glare; sensitivity to bright lights; increased difficulty with night vision; fluctuations in visual acuity; increased intraocular pressure; corneal haze; corneal infections, ulcers, or infiltrates; corneal decompensation or edema; the need for secondary surgical intervention; problems associated with the flap, including a lost, misplaced, or misaligned flap; retinal detachment; and retinal vascular accidents.

**Name:** S.M.A.R.T.™ Nitinol Stent System and S.M.A.R.T.™ Control™ Nitinol Stent System

**Manufacturer:** Cordis Corporation, Miami Lakes, FL

**Approval Date:** August 12, 2003

**Use Classification:** Stents

**Description:** A small, thin, flexible, metal mesh tube (stent) and a long flexible tube (catheter) are used to deliver the stent to a specific area inside the iliac artery, which courses through the pelvic area. The stent is mounted on the end of the delivery catheter in a compressed state. The delivery catheter and stent are inserted into an artery in the leg and moved through the artery to the blocked area of the iliac artery. The compressed stent is then released from the delivery catheter in the artery. By expanding and pushing the area with plaque outward against the walls of the artery, the stent opens the iliac artery to aid in the normal flow of blood. The delivery catheter is then removed, and the stent is left within the patient’s artery.

**Purpose:** To treat atherosclerotic disease of the iliac arteries. The disease results in the buildup of plaque in the artery wall, causing the opening in the artery to close down and slow the normal flow of blood. The improved convenience of rapid-exchange delivery systems, also known as single-operator systems, offers important advantages compared with standard over-the-wire delivery technology, including the use of shorter guide wires, which makes stent placement faster and easier to control.

**Precautions:** These stents should not be used in patients with a history of sensitivity to x-ray contrast medium or to nickel. Major adverse effects have included death (1%), myocardial infarction (1%), amputation of the target limb (1%), revascularization of the target vessel (2%), and stent thrombosis (1%).

**Name:** INDEPENDENCE™ iBOT™ 3000 Mobility System

**Manufacturer:** Johnson & Johnson/Independence Technology

**Approval Date:** August 13, 2003

**Use Classification:** Wheelchairs

**Description:** The iBOT™ 3000 Mobility System is an indoor/outdoor powered mobility device that can rise to eye level, drive over uneven surfaces, climb curbs, and go up or down stairs. Because of its unique balancing mechanism, it remains stable and the seat stays level under most conditions.

The iBOT™ has five operating functions:

- Standard (for moving indoors and across smooth surfaces)
- Four-wheel drive (for traveling over uneven surfaces such as curbs, grass, or gravel)
- Balance (for rising to eye level or reaching objects at an elevated height)
- Stair (for climbing up and down steps)
- Remote (for transporting the device while unoccupied)

**Purpose:** To help people with disabilities to gain improved mobility. With the standard setting, the iBOT™ works like other powered wheelchairs. In the other settings, computers, gyroscopes, and electric motors provide stability and balance. The gyroscopes constantly measure stability; when they sense movement, they signal the computer. The computer then drives the motors to move the wheels so that the iBOT™ remains upright and stable. The device has two pairs of rear drive wheels.

With the four-wheel drive, the wheelchair can move over obstacles, uneven terrain, and other soft surfaces. Patients can remain seated at an elevated height and can ascend and descend stairs with or without assistance.

With the balance function, one pair of wheels can be lifted off the ground and the remaining pair of wheels can be balanced.

With the stair function, the drive wheels rotate up and over each other to climb up or down, one stair at a time.

With the remote function, the device can be transported while it is unoccupied.

The iBOT™ can be used indoors or outdoors by people with impaired mobility and who have the use of at least one upper extremity. The device is available only by prescription from specially trained health care professionals. This system provides mobility on smooth surfaces and inclines at home and in the community.

**Precautions:** The iBOT™ should be used only after patients have completed a training program. It should not be used by people who weigh more than 250 pounds, who cannot use at least one hand, who cannot bend their knees enough to use standard foot rests, who need tilting or reclining seating systems, who require mechanical ventilators, or who have conditions that increase their risk of bone fracture, such as severe osteoporosis, osteogenesis imperfecta, or metastatic bone cancer.

*continued on page 32*
Do Antiretroviral Agents Raise the Risk of Myocardial Infarction?

Although combination antiretroviral therapy has helped to prolong the lives of patients with human immunodeficiency virus (HIV) infection, it may also be contributing to an increased risk of myocardial infarction (MI).

After collecting follow-up data on 23,468 patients from 11 previously established cohorts, researchers from Hvidovre University Hospital in Denmark found a 26% relative increase in the number of MIs per year of exposure to antiretroviral agents during the first four to six years of use.

That being said, the researchers emphasized that the absolute risk of MI was low and “must be balanced against the marked benefits from antiretroviral treatment.”

To more truly reflect the diverse composition of the HIV-infected population, the researchers enrolled participants from various geographic locations and included substantial numbers of women and minority groups. This prospective study, in contrast to other previous studies, allowed the researchers to document all MIs according to predefined standards.

The median known duration of HIV-1 infection was 3.5 years, and 26.2% of the patients had previously been found to have acquired immunodeficiency syndrome (AIDS). At the baseline evaluation, 81% of the patients had received at least one antiretroviral drug and 75% had received combination antiretroviral therapy. Because of the different dates on which various drugs were first marketed, patients were more likely to have taken protease inhibitors (PIs) than non-nucleoside reverse transcriptase inhibitors (NNRTIs).

Because the patients were relatively young, with a median age of 39 years, the prevalence of previous cardiovascular disease was low (only 1.5%). However, many of the patients had cardiovascular risk factors, such as smoking, dyslipidemia, hypertension, or diabetes.

During the follow-up (i.e., 36,199 person-years), 126 patients had MIs. The incidence of MIs increased with increasing exposure to combination antiretroviral therapy. Other factors that independently predicted MI were smoking, previous cardiovascular disease, and male sex.

The researchers say that the relationship between the antiretroviral therapy and MI is plausible, because combination antiretroviral therapy can cause adverse metabolic changes that are known risk factors for cardiovascular disease. Randomized trials are needed to determine whether the observed association reflects a cause-and-effect relationship.

Before the advent of combination antiretroviral therapy, the annual mortality rate among patients with HIV-1 infection exceeded 20%, in contrast to less than 2% in this study. Moreover, among the patients who died in their study, only 6.4% died as a result of MIs. The progression of HIV-related disease was the leading cause of death. The annual rate of MI, even among patients who had been taking the antiretroviral treatment for four to six years, was less than 0.6%. In the end, only a portion of the apparent excess risk could be attributed to combination antiretroviral therapy.