**NEW DRUGS**

**First Angiogenesis Inhibitor for Colorectal Cancer**

The U.S. Food and Drug Administration (FDA) has approved bevacizumab (Avastin™, Genentech) as a first-line treatment for patients with metastatic colorectal cancer. A monoclonal antibody, it is the first FDA-approved product that prevents the formation of new blood vessels, a process known as angiogenesis. Avastin™ extended patients’ lives by about five months when it was given intravenously as a combination treatment with standard chemotherapy drugs for colon cancer in a regimen consisting of irinotecan, 5-fluorouracil (5-FU), and leucovorin (IFL).

Avastin™ is a genetically engineered version of a mouse antibody that contains both human and mouse components. Special technology allows it to be produced in large quantities in the laboratory.

This product targets and inhibits a natural protein, called vascular endothelial growth factor (VEGF), which stimulates new blood vessel formation. When VEGF is bound to Avastin™, tumors are denied blood, oxygen, and other nutrients needed for their growth.

Colorectal cancer is the third most common cancer affecting men and women in the U.S. and the second leading cause of cancer-related deaths.

A clinical trial of more than 800 patients with metastatic colorectal cancer was designed to determine whether Avastin™ extended the lives of patients. Roughly half the patients received IFL, the standard chemotherapy combination, and the other half received Avastin™ once every two weeks in addition to IFL. Overall, patients given Avastin™ with IFL survived about five months longer, and the average time before tumors started regrowing or new tumors appeared was four months longer than patients receiving IFL alone. The overall response rates were 45% for the treated patients and 35% for the controls.

Serious but uncommon side effects include gastrointestinal perforation, impaired wound healing, and pulmonary or internal bleeding. Other more common effects are hypertension, fatigue, blood clots, diarrhea, decreased white blood cells, headache, appetite loss, and mouth sores.

(Source: FDA News, February 26, 2004; www.fda.gov.)

**Liquid Rh\(0(D)\) Human IVIG for Hemolytic Disease in Newborns**

Rhophylac® is the first FDA-approved liquid Rh\(0(D)\) immune globulin (human) that can be administered intramuscularly (IM) or intravenously (IV) for sale in the U.S. Used to prevent hemolytic disease of the fetus and newborn (HDN), Rhophylac® provides a choice for physicians and patients who are concerned about the pain associated with IM administration, especially when multiple injections are required.

HDN is a serious and sometimes fatal disorder in which antibodies produced by a pregnant Rh-negative woman attack the red blood cells of her Rh-positive fetus. Although HDN has no adverse effect on the mother, its consequences to the child can range from reversible (jaundice, anemia) to severe (brain damage, heart failure, death).

The rhesus (Rh) factor is a protein on the surface of the red blood cells; people with the Rh factor are considered Rh-positive, and people without it are Rh-negative.

Without treatment, if blood from an Rh-positive fetus “leaks” into the bloodstream of an Rh-negative mother, she can have a reaction to the Rh factor and antibodies may develop. These leaks, called fetomaternal hemorrhages, can occur naturally, such as during birth or miscarriage, or through a medical procedure, such as an amniocentesis. Serious trauma, such as a car accident or fall, can also cause hemorrhages that affect mother and child.

Rhophylac®, a highly purified, plasma-derived product, is indicated to prevent formation of Rh antibodies (known as Rh sensitization) after transfusion of Rh-positive blood to Rh-negative patients. Although Rh sensitization has no immediate consequences, the antibodies may attack the blood of the fetus in subsequent pregnancies, causing HDN.

Approximately 10% of all pregnancies in North America involve Rh-negative mothers. To prevent Rh sensitization, a dose of Rhophylac® is given to Rh-negative women between 28 and 30 weeks of pregnancy. A second dose is given within 72 hours after delivery if the baby is Rh-positive. Additional treatments may be necessary if a large fetomaternal hemorrhage is suspected.

Rhophylac® is free of mercury-containing thimerosal and other preservatives, and a latex-free syringe is used to eliminate the risk of reactions.

The product will be available in ready-to-use, prefilled syringes containing 300 mcg of Rh\(0(D)\) immune globulin in 2 ml. It is expected to be available in the U.S. this month; it has been marketed in Switzerland since 1996 and in other European markets since 2002.

(Source: ZLB Bioplasma, February 17, 2004; www.zlbusa.com.)

**NEW INDICATION**

**Dalteparin Sodium Anticoagulant Therapy for Prevention of DVT**

The FDA has granted approval for Pfizer to market dalteparin sodium injection (Fragmin®), a low-molecular-weight (LMW) heparin, to prevent deep vein thrombosis (DVT) or pulmonary embol-
ism (PE) in acutely ill patients with severely restricted mobility.

Fragmin® was initially approved by the FDA in 1996. In the U.S., it is also used as prophylaxis for ischemic complications of unstable angina and certain heart attacks, when used with aspirin, and for DVT or PE in patients undergoing hip replacement surgery or abdominal surgery (including cancer patients).

DVT is a potentially life-threatening condition that is caused by blood clots in the large veins if the clots break away and travel to the lungs to cause PE. Patients with illnesses such as cancer, certain types of congestive heart failure, acute respiratory failure, or acute infection often require a hospital stay of at least four days and are at high risk for DVT or PE. Additional risk factors include age over 75 years, a previous DVT, varicose veins, and obesity.

In the U.S., approximately 450,000 patients have DVT, and approximately 240,000 die each year as a result of PE.

In the recently completed Prospective Evaluation of Dalteparin Efficacy in Immobilized Patients Trial (PREVENT), 3,681 seriously ill hospitalized patients received 5,000 International Units of Fragmin® once daily for 14 days. Compared with patients receiving placebo, they experienced a 45% reduction in DVT or PE by the 21st day. This benefit was maintained for the entire 90 days. They also experienced a low incidence of bleeding and thrombocytopenia, an abnormal decrease in the number of platelets.

Fragmin® cannot be used interchangeably (unit for unit) with unfractionated heparin or other LMW heparins. It is contraindicated in patients with active major bleeding or with known hypersensitivity to the drug, to heparin, or to pork products. It should be used with extreme caution in patients with a history of heparin-induced thrombocytopenia.

(Source: Pfizer, January 30, 2004.)

**Modafinil for Apnea and Sleep Disorders in Night Shift Workers**

Cephalon, Inc., has received approval to market modafinil (Provigil®) tablets to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome and “shift work sleep disorder.”

In 1998, modafinil became the first in a new class of wake-promoting agents for patients with narcolepsy.

In preclinical studies, the drug promoted wakefulness without causing generalized stimulation in the brain. It seems to work selectively through the sleep–wake centers to activate the brain cortex. Activation of the cortex is essential for wakefulness.

The safety of modafinil was shown in clinical trials that enrolled more than 3,500 patients. The drug does not affect the ability to sleep when sleep is desired.

(Source: Cephalon, January 26, 2004; www.provigil.com.)

**Letrozole: A Promising Option for Endometriosis**

Letrozole (Femara®, Novartis Oncology), an aromatase inhibitor that is used to prevent breast cancer recurrence in postmenopausal women, shows promise in the treatment of endometriosis.

Endometriosis, which affects 10% to 15% of women of childbearing age, results when tissue that is similar to the uterine lining grows elsewhere in the body. It causes chronic pelvic pain and is a risk factor for infertility.

Researchers at Northwestern Memorial Hospital in Chicago evaluated 10 patients with moderate-to-severe endometriosis. All of the women had been treated both medically and surgically with unsatisfactory results. The patients took letrozole plus progestin for six months along with calcium citrate and vitamin D to reduce the risk of bone loss. The side effects of occasional irregular bleeding and mild hot flashes were well tolerated.

Laparoscopy was used to evaluate the pelvic structures at the beginning and end of the study. In all patients, a second laparoscopic examination showed that endometriosis had either disappeared or was significantly reduced.

Until now, the most commonly used therapies for endometriosis have been gonadotropin-releasing hormone analogues, but they produce unpleasant side effects and can only be used for a short time. Even with surgery, symptoms of endometriosis return rapidly in more than 50% of surgical patients.


**Topical Vancomycin after Cranioplasty**

From an experimental procedure, physicians learned that vancomycin, a glycopeptide antibiotic, could be used topically rather than systemically, over several years, in a poorly vascularized area.

A patient underwent evacuation of a subdural hematoma that was complicated by subarachnoid hemorrhage. A subsequent craniotomy for decompression of a neck aneurysm was followed by cranioplasty (a procedure to correct a skull defect) using an autologous bone graft. The graft became infected with methicillin-resistant *Staphylococcus aureus* (MRSA), which responded to intra-venous (IV) vancomycin (Vancocin®, Eli Lilly Japan). The graft was then replaced with a ceramic artificial bone implant, but the implant site became
re-infected with MRSA.

This time, a vancomycin infusion was not successful. The physicians suggested to the patient that the infected ceramic implant be removed, but because of her fear of neurological complications as well as cosmetic concerns, she did not agree. Stymied, the doctors then took the unusual step of applying the medication as an ointment.

The ointment was applied daily into the cavity under the ceramic bone. Two days after the topical treatment began, microbiological examinations showed negative results for the presence of MRSA. Even while blood concentrations of MRSA remained below detectable levels, the patient was consistently afebrile.

After four months, the clinicians substituted topical bucladesine sodium, a nucleotide derivative that mimics the action of cyclic adenosine monophosphate (cAMP), to encourage the formation of granulation tissue. However, the MRSA infection was again detected, and vancomycin treatment was resumed. A subsequent infection at the gastrostomy tube site was also treated with the vancomycin ointment.

Several years later, the patient became unconscious and her husband consented to have the ceramic implant removed. The aperture in the left frontal portion closed after about one month, and no MRSA infection was detected.

(Source: Ann Pharmacother 2004;38:70–72.)

Antibiotic Therapy and Tremors

Patients receiving high-dose trimethoprim–sulfamethoxazole (TMP–SMX, Bactrim®, Women First; Septra®, Monarch) appear to be at higher risk for abnormal muscle contractions such as myoclonus and asterixis. In fact, these side effects might not be as rare as once thought.

A 63-year-old woman with a history of non-Hodgkin’s lymphoma, hypertension, hypercholesterolemia, and transient ischemic attack had recently been in remission for acute myelogenous leukemia. Admitted to the hospital with a Nocardia asteroides infection, she began a regimen of trimethoprim 20 mg/kg per day and sulfamethoxazole 100 mg/kg per day, given intravenously in two doses, along with 2 g of ceftriaxone sodium (Rocephin®, Roche), given twice daily.

Her fever abated, but she began to experience progressively worsening involuntary movements involving her head and her extremities. Neurological examination revealed diffuse, multifocal myoclonus and bilateral asterixis but no other abnormalities. The TMP–SMX therapy was stopped, and the involuntary movements decreased markedly the next day. By the fourth day, they disappeared.

The physicians knew of only one report describing tremors in an immunocompetent patient.

The complication of tremors is dose-related, not immunological. The physicians suggest that the “rare” effect might actually be underdiagnosed, and they advise stopping TMP–SMX treatment before ordering a costly neurological evaluation.


Alendronate for Bone Disease in Cystic Fibrosis

Thanks to some treatment advances, patients with cystic fibrosis (CF) are living much longer; however, with longer lives have come more health problems. Bone disease, for instance, is now a major concern for these patients; it can lead to pathological fractures and kyphosis and might even prevent them from being considered suitable candidates for lung transplantation.

The cause of bone disease in patients with CF is not clear, but delayed pubertal maturation, malabsorption of vitamin D, poor nutritional status, physical inactivity, hypogonadism, and glucocorticoid therapy are possible factors. A study of the bisphosphonate alendronate sodium (Fosamax®, Merck) in these patients suggests that chronic pulmonary infection might be even more important because it increases bone resorption and suppresses bone formation through the activity of inflammatory cytokines.

In short, the chronic inflammation associated with CF puts stress on the bones; adults with CF lose bone mineral density (BMD) three to five times faster than do healthy adults. Increased bone resorption occurs even when the lung disease is quiescent, and it escalates during periods of lung infection.

It was discovered in 1979 that patients with CF are likely to have low BMD, and there have been only a few therapeutic trials. Researchers decided to test the effectiveness of alendronate in adults with CF, and so they compared the effects of oral alendronate 10 mg/day in 24 patients with those of placebo in 24 patients for one year. All of the patients received 800 International Units of cholecalciferol (vitamin D3) and 1,000 mg of calcium carbonate.

At one year, 100% of the patients taking alendronate showed an increase in spinal BMD and 78% had increased femoral BMD; 50% of the patients taking placebo showed increased spinal BMD, and 35% of them experienced increased femoral BMD. The alendronate patients gained a mean of 4.9% in spinal BMD and 2.8% in femoral BMD. In contrast, the placebo patients lost 1.8% in spinal BMD and 0.7% in femoral BMD.

Patients with a lower T score (a number that indicates whether bone loss has occurred), a low body mass index, or decreased lung function at the baseline...
evaluation responded better to treatment. The alendronate group also showed lower levels of urinary markers of bone resorption.

Because less than 1% of alendronate is absorbed in healthy adults, its bioavailability was a concern. However, its long half-life, which had a cumulative protective effect on BMD, mitigated the absorption problems.

The researchers strongly suggest that bone disease in CF patients, despite intestinal malabsorption, is treatable. They advise clinicians to be aware that the problem starts when patients are young and emphasize the importance of screening for low BMD and for treating it before bones begin to break.

(Source: Am J Respir Crit Care Med 2004;169:77–82.)

When Warfarin Can Be Dangerous

For patients with heparin-induced thrombocytopenia (HIT), treatment with warfarin sodium (Coumadin®, Bristol-Myers Squibb) can be very risky at times.

Researchers reported on six patients with severe warfarin-related complications. In all six patients, the difficulties emerged after two to seven days of use. Five patients had warfarin-induced skin necrosis, two had venous limb gangrene, and one patient had both. In four patients, the complications occurred with the use of unopposed warfarin; in two patients, they resulted when a direct thrombin inhibitor was withdrawn.

All of the patients had higher-than-therapeutic International Normalized Ratios (INRs). Lesions progressed rapidly in one woman; four days after she received warfarin for postoperative atrial fibrillation, pain and discoloration developed in her left breast, right leg, and left foot. A mastectomy was required, her right leg was amputated below the knee, and her left foot was amputated. Nonetheless, five weeks later, she was readmitted to the hospital with upper-extremity swelling. Another patient died of septicemia even after warfarin was discontinued.

These patients “illustrate a gamut of HIT clinical scenarios,” the researchers say. In three patients, heparin therapy was stopped because of acute HIT, after which unopposed warfarin was started or continued. HIT was initially unrecognized in one patient. In two patients, HIT had a delayed-onset component, and both patients experienced warfarin-related complications that emerged during overlap with lepirudin (recombinant DNA) (Refludan®, Berlex) therapy.

Although the researchers cite other reports that link venous limb gangrene and HIT with warfarin use, they believe that they are the first to report on the potential danger for patients with HIT during the transition period of switching from a direct thrombin inhibitor to warfarin. They emphasize that warfarin-induced skin necrosis or worsening venous thrombosis should alert clinicians to the possibility of underlying HIT.

To help minimize the risks of warfarin therapy, the investigators recommend that clinicians:

• wait for the platelet count to rise to near normal as the HIT is “cooled.”
• start with modest doses so as not to exceed the targeted INR.
• avoid unopposed warfarin therapy and ensure adequate levels of an alternative anticoagulant during the transition period.

For patients with HIT who are new to warfarin treatment, initial doses of 5 mg/day or lower are recommended.

(Source: Arch Intern Med 2004;164:66–70.)

Fast Relief for Intractable Pain

When opioid therapy does not relieve pain or when it leaves patients with intolerable side effects, a new option might be ziconotide (SNX-111, Pfizer/Elan/Warner-Lambert/Partner Medtronic).

In experimental studies, the fact that intrathecal ziconotide cleared rapidly suggested that it would also metabolize through the cerebrospinal fluid rapidly. One study involved 24 patients who had chronic pain from cancer, acquired immunodeficiency syndrome (AIDS), and other conditions and who experienced pain control with opioids, even when they were given intrathecally. Of those 24 patients, 19 rated their pain on the Visual Analogue Scale of Pain Intensity as 43% lower in degree and 15 patients were able to reduce their concomitant use of opioids by at least 50%. Central nervous system effects were diminished or resolved when the infusion rate was reduced or stopped.

Encouraged by these preliminary findings, researchers conducted a double-blind, placebo-controlled trial of 111 patients at 32 study centers in the U.S., Australia, and the Netherlands. Intrathecal ziconotide was titrated over five to six days, followed by a five-day maintenance phase for responders. Non-responders could cross over to the opposite treatment group.

For patients without previously implanted medication pumps, the researchers implanted an intrathecal catheter and used an external infusion system. Because of the known risk of infection with external systems, they limited the total time frame for drug infusion to two weeks. Even so, meningitis developed in seven patients, which the researchers attributed to poor physiological status and an external catheter, not to the drug.

Mean scores on the Visual Analogue
Do Antibiotics Raise Breast Cancer Risk?

A study linking antibiotics with breast cancer does not prove that they cause the disease, but it should prompt women to make sure that they are not using the drugs inappropriately, researchers say.

In a study of more than 10,000 women, those who used the most antibiotics—with more than 25 prescriptions, or antibiotic use for at least 501 days—faced double the risk of breast cancer over an average of about 17 years, compared with women who did not use the drugs.

The study compared 2,266 women 20 years of age and older with invasive breast cancer with 7,953 women who did not have breast cancer. An increased breast cancer risk was found with the greater use of antibiotics, with the highest increased risk in women who took the drugs for at least 501 days. Even the figure of 25 prescriptions over 17 years was associated with an increased risk—a breast cancer rate that was almost 1.5 times higher than that of nonusers.

The study authors suggested that it might have been the diseases that women used antibiotics to treat—rather than the drugs—that resulted in an increased risk of breast cancer.

Because antibiotics are widely used to treat various common infections caused by bacteria, it might be that women who never took the drugs were unusually healthy and therefore were somehow resistant to cancer, the researchers said. They emphasized that it was premature for people to stop taking antibiotics when they are needed. It was also suggested that their effects on the intestinal bacteria might change the body’s immune system or the way in which the body metabolizes foods that protect against cancer.

Women should use antibiotics only after they have discussed their ailments with their doctors to see whether these drugs are the most appropriate treatment.

(Courtesy: JAMA 2004;291:63–70.)

Cefdinir Recommended for Acute Bacterial Sinusitis

New treatment guidelines published by the Sinus & Allergy Health Partnership have identified cefdinir (Omnicef®, Abbott) as one of the primary treatment options for acute bacterial sinusitis. Omnicef® is the only extended-spectrum cephalosporin included in the guidelines, which were developed as an educational tool for health care providers who treat acute bacterial rhinosinusitis (ARBS) in children and adults. ARBS is the leading respiratory illness in the U.S. This is the first update for the guidelines, which were originally published in 1999.

Omnicef® is contraindicated in those patients with allergies to cephalosporin antibiotics. Its safety and efficacy in have not been established in neonates and infants younger than six months of age.

(References: Abbott Laboratories, February 26, 2004; Sinus & Allergy Health Partnership, www.sahp.org.)

Experimental Vaccine Prevents Return of Lung Cancer

Scientists have developed an experimental vaccine that might be used to block the progress of lung cancer. A small study suggests that it might delay the recurrence of tumors in patients with non–small cell lung cancer, the most common form.

Doctors called the research encouraging because treatment options for patients with this type of lung cancer are limited. Non–small cell lung cancer is the nation’s leading cause of deaths from cancer; more than 150,000 patients die of this disease each year. It is related to smoking and is often difficult to treat. Treatment usually involves chemotherapy, removal of the tumor, or both.

The researchers, from Baylor Medical Center in Dallas, Texas, monitored 43 patients, 10 with early-stage disease and 33 with advanced-stage cancer. After surgeons removed the tumors, the patients received a vaccine (GVAX, Cell Genesys) that included cells from the tumors and a gene that changed the surface of the cells to help the body identify them as cancerous. The body’s immune cells then began to recognize, attack, and destroy the cancerous cells in the lungs.

The patients then received the vaccine every two weeks for three months. A few patients were still free of cancer three years after vaccination. In other patients, the vaccine appeared to delay the recurrence of cancer for several months.

The researchers hope to apply for FDA approval in three years.

Warning: Olanzapine Risky in Older Adults?

Olanzapine (Zyprexa®, Eli Lilly), an antipsychotic agent that is often used to calm elderly people with dementia, may increase the risk of strokes and death in those patients, according to a letter sent by Eli Lilly & Co. to physicians on January 15, 2004.

The letter mentioned a “significantly higher” incidence of stroke among these patients and a higher rate of deaths of all types (3.5%) compared with a rate of 1.5% in patients receiving placebo.

Although this drug is not approved for use in elderly patients with dementia (it is indicated for people with schizophrenia and bipolar disorder), over time, olanzapine and drugs like it have become widely used in nursing homes and hospitals to treat verbal outbursts and behavior problems in older patients.

A Lilly spokesperson cautioned that the elderly patients in whom the increased risks were seen often had other serious medical problems, and it was not clear whether olanzapine actually played a role in the higher death rates.


New Requirements for Bar Codes and Drugs

The FDA is issuing a final rule requiring linear bar codes on labels of thousands of drugs and biological products in an effort to protect patients from preventable medication errors, to reduce health care costs, and to promote quality care. Each bar code will contain, at a minimum, the drug’s National Drug Code number. Machine-readable information on container labels of blood and blood components intended for transfusion will also be required.

(Source: FDA, Department of Health and Human Services, February 25, 2004.)

NEW MEDICAL DEVICES

By Marvin M. Goldenberg, PhD, RPh, MS

Name: Guardian™ Continuous Glucose Monitoring System
Approval Date: January 2004
Manufacturer: Medtronic MiniMed, Northridge, CA
Use Classification: Continuous monitoring of glucose in diabetic patients
Description: The monitoring system consists of three components:

- A sensor is inserted just under the skin to record glucose levels using interstitial fluid from the layer of fat between the skin and muscle. After the sensor is inserted, it is virtually painless and easy to wear, even for children. Patients can wear the sensor up to three days. To calibrate the sensor, patients enter their glucose readings from a traditional (finger-stick) monitor at least twice each day.
- A transmitter receives blood glucose readings from the sensor, then uses radio waves to relay this information to a monitor. Patients can wear the transmitter discreetly under their clothing; it is not implanted into the body.
- The monitor can be worn on the patient’s belt or can be placed in a pocket or a purse, as long as it is within six feet of the transmitter to receive signals. Approximately the size of a pager, the monitor records glucose readings received from the sensor via the transmitter.

Software and hardware allow patients to download all of the glucose values that have been stored in the monitor to a personal computer. The software then graphs these values so that patients can view trends in blood glucose control and make informed decisions about therapy.

Purpose: The system alerts patients that blood glucose levels are not within desirable ranges. If glucose readings fall out of range, the monitor sounds an alarm. Patients or their health care providers can preset the monitor with the desired glucose ranges before use. For example, if a low target of 70 mg/dl and a high target of 200 mg/dl are set, the monitor is designed to alert patients when it detects a reading outside these low and high values.

Precautions: None listed

Name: Nociceptive Trigeminal Tension Suppression System
Approval Date: January 2004
Manufacturer: NTI-TSS, Mishawake, IN
Use Classification: Prevention of medically diagnosed migraine pain, tension-type headache, and jaw disorders (temporomandibular joint syndrome), without drugs or surgery, by reducing trigeminally innervated muscular activity.
Description: The NTI system is a prefabricated matrix that is customized by a dentist to snap into place and fit over the upper front teeth; sometimes it can be adapted to fit over the lower front teeth. It is worn during sleep and prevents the intensity of muscular parafunction.

The practitioner must relieve the internal pressures to provide for a snap-in fit without placing strain or pressure on the teeth. Patients must make a dedicated effort to remove the device. If they can remove the apparatus without using their hands, it should be relined or made to fit additional lateral teeth for added retention.

For migraine patients, a more discreet version is available for daytime use. For best results, the daytime version should usually be worn, in addition to the nighttime device, for six to eight weeks.
**Purpose:** The NTI-tss device prevents the intensity of muscular parafunction during sleep. Chronic, intense nighttime muscular clenching has a considerable influence on the triggering of migraine. In clinical trials, 82% of patients with medically diagnosed migraine experienced a 77% reduction in migraine episodes within the first eight weeks of wearing the device. Thus, during the night it prevents occlusion of the canine and molar teeth (which is required to generate significant muscle contraction intensity and jaw joint strain), and reduces the muscular triggering component of migraine, chronic headache, and jaw disorders.

**Precautions:** Patients should not wear the device while they are chewing food. For patients who experience intense grinding of the teeth, a divot (cavity) may develop over time in the Discluding Element of the NTI-tss. In such an event, the practitioner must periodically fill and smooth the divot.


**Name:** Ariol™ HerSight™ Immunohistochemistry

**Approval Date:** January 2004

**Manufacturer:** Applied Imaging Corporation, Santa Clara, CA

**Use Classification:** The Ariol™ HER-2/NEU Immunohistochemistry (IHC) application aids in detecting overexpression of the HER-2 protein in patients with breast cancer.

**Description:** The Ariol™ System assists in the analysis of a complex test in the evaluation and selection of certain breast cancer patients to receive trastuzumab (Herceptin®) therapy. Herceptin® is a targeted therapeutic treatment that is indicated for women with metastatic breast cancer with tumors that overexpress the HER-2 protein.

**Purpose:** When used in conjunction with the Dako Hercep Test®, the Ariol™ System is indicated for assessing breast cancer patients when Herceptin® therapy is being considered. It is designed to bring out proprietary quantitative immunomicroscopy technologies to help physicians in meeting the needs for targeted therapeutics.

**Precautions:** None listed


**Name:** Pandin Continuous Nerve-Stimulating Catheter

**Approval Date:** January 2004

**Manufacturer:** HDC Corporation, Milpitas, CA

**Use Classification:** The Pandin Catheter is now available in the U.S. and worldwide, allows placement of a catheter next to the nerves and the nerve plexus for continuous nerve block anesthesia or analgesia and enables physicians to confirm a catheter’s location in relation to the nerve after removal of a Tuohy needle from a patient.

**Description:** The Pandin Catheter is an accessory set that facilitates continuous local anesthesia. It is constructed with a braided conductive wire with a rounded, nontraumatizing stainless steel ball tip that provides excellent stimulating properties.

**Purpose:** The catheter is used for continuous regional anesthesia procedures that use nerve-stimulating devices (e.g., Neurotrace II and III nerve locators and stimulators). It has been used in outpatient, orthopedic, and pain clinics.

**Precautions:** None listed


**Name:** TriActive™ Laser Dermatology System

**Manufacturer:** Cynosure, Inc., Chelmsford, MA

**Approval Date:** January 2004

**Use Classification:** A deep laser action from six near-infrared diode lasers enhances microcirculation. This system offers deep massage, localized cooling, and stimulating action on the subcutaneous tissue, which results in a tighter appearance in the treated areas. When used in a series of sessions, this system appears to be effective in enhancing overall body contouring and in reducing the appearance of “cellulite” (primarily caused by a prolonged inflammatory response and insufficient circulation).

**Description:** The triple-action methodology is intended to restore a normal balance to the skin and outer layers, including smoothing and tightening.

**Purpose:** The laser system is intended as anti-cellulite therapy for patients undergoing liposuction and for nonsurgical patients. The laser is used before liposuction. Anesthesia is more evenly distributed in this system and the laser component appears to break up the fat. The system targets the midriff; larger areas prone to cellulite, such as the thighs and buttocks; small areas such as the face and neck; and the hips, abdomen, upper arms, and neck.

The procedure is painless and less strenuous than traditional massage. Patients may need a series of 10 to 15 treatments as often as three times a week or perhaps only once a week.

**Precautions:** None listed


continued on page 167
Drug-Coated Stents in the “Real World”

So far, clinical studies have found that drug-coated coronary stents, which can be implanted in patients with blocked arteries, are safe and effective—but what about in the “real world”? Patients who need stents are typically older or sicker than patients who are selected for clinical trials. That’s why the one-year findings from a study at Erasmus Medical Center in Rotterdam, The Netherlands, might be reassuring. Sirolimus-eluting stents were compared with uncoated (bare metal) stents in an unselected population.

Sirolimus (rapamycin [Rapamune®], Wyeth), an immunosuppressant, has recently been discovered to block cell growth that produces scarring, to inhibit the proliferation of vascular smooth muscle, and to reduce cell wall thickening in injured vessels. In 2003, the FDA approved the use of rapamycin-coated stents to prevent restenosis, a vexing problem after percutaneous intervention.

The study involved 508 patients who had de novo lesions that had been treated with the Cypher (Johnson & Johnson) stents and 450 patients who had received bare stents just before the study. Sixty-eight percent of the patients did not meet the selection criteria for the clinical trials. Approximately 50% of the patients in both groups had acute coronary syndrome, and 16% in each group also had diabetes. Patients receiving coated stents were more likely to have multivessel disease and to require more stents than patients who received uncoated stents. Only 3.7% of the patients with the coated stents needed repeated procedures to unblock reclogged vessels, compared with 10.9% of the patients with the bare stents. At one year, 9.7% of patients with coated stents had experienced a major adverse cardiac event (myocardial infarction, target vessel revascularization, or death), compared with 14.8% of patients with uncoated stents. Treatment effects were similar across all the subgroups, the researchers say, for long and short lesions, for small vessels, and in “all kinds of anatomic settings.”


MS Linked to Lack of Sunlight-Generated Vitamin D

Two recent studies have linked a lack of exposure to vitamin D, which is created naturally by sunshine or artificial ultraviolet (UV) light, to the development of multiple sclerosis (MS), an often debilitating disease that affects 250,000 to 350,000 Americans.

The body makes vitamin D through exposure to sunlight’s UV-B ultraviolet rays. The exact causes of MS remain unknown, but MS becomes more prevalent in people living farther away from the Equator. It is thought that a minimum level of UV exposure throughout the year might be important in conferring protection by influencing the immune system response, possibly through changes in the production of vitamin D and melanin, the substance involved in acquiring a tan.

A major hindrance to generating sufficient vitamin D is living at high latitudes, where exposure to natural sunlight may be insufficient. Some research, including these two new studies, has shown a correlation between high latitudes and increases in diseases linked to vitamin D deficiency.

In the National Institutes of Health study of more than 185,000 women, MS was 40% less likely to develop in women who maintained recommended levels of vitamin D than in women who were otherwise deficient in vitamin D.

(Sources: Neurology 2004;62:60–65; Wolff Systems Technology, Atlanta, February 23, 2004.)