NEW DRUGS

Darifenacin for Overactive Bladder

The U.S. Food and Drug Administration (FDA) has approved darifenacin (Enablex®, Novartis) extended-release tablets (7.5 and 15 mg) for the treatment of overactive bladder accompanied by symptoms of urge urinary incontinence. The product, which is taken once a day, is a potent muscarinic receptor agonist that helps to increase the amount of urine that the bladder can hold and decreases the pressure associated with the urge to urinate.


Generic Provigil® Approved

The FDA has tentatively approved Mylan’s Abbreviated New Drug Application for modafinil tablets, 100 and 200 mg. This is the generic version of Cephalon’s Provigil® Tablets, indicated for promoting wakefulness.

(Source: Mylan, February 10, 2005.)

Generic Celexa® Available

Mylan has announced the FDA’s final approval of its Abbreviated New Drug Application for citalopram hydrobromide tablets, 10, 20, and 40 mg. This is the generic version of Forest Laboratories’ Celexa®, an antidepressant medication.

(Source: Mylan, February 4, 2005.)

Doxorubicin Injection For Ovarian Cancer

The FDA has approved doxorubicin HCl liposome injection (Doxil®, Tibotec) for women with ovarian cancer whose disease has progressed or recurred after platinum-based chemotherapy. The agent originally received accelerated approval for refractory ovarian cancer in June 1999. The product label has been updated to include data on survival, time to disease progression, and tumor response rates from a randomized phase 3 clinical study.

Under the accelerated approval, the drug was indicated for metastatic ovarian cancer that was refractory to both paclitaxel- and platinum-based chemotherapy regimens.

Doxil® is indicated for patients with a history of cardiovascular disease only when the benefits outweigh the risks. Acute infusion-associated reactions have occurred in up to 10% of patients receiving Doxil®. Serious allergic and anaphylactoid infusion reactions have also been reported. Medications and emergency equipment should be available for immediate use to treat reactions. Severe myelosuppression sometimes occurs. The dosage should be reduced in patients with impaired hepatic function. Accidental substitution of Doxil® for doxorubicin HCl has resulted in adverse side effects.

(Sources: Tiobec, February 7, 2005; www.tibotectherapeutics.com; www.doxil.com; www.jnjpharmarnd.com; www.alza.com.)

Easy-Delivery Growth Hormone

Somatropin (recombinant DNA) injection (Novo Nordisk), a prefilled, multidose, liquid growth hormone (Norditropin® in a disposable pen (NordiFlex®) is now available in the U.S. The medication is indicated for the long-term treatment of children with growth failure resulting from inadequate secretion of endogenous growth hormone and for adults with growth hormone deficiency.

NordiFlex® was approved in October 2004. Norditropin® was approved for children in 1997 and for adults in November 2004. The product is convenient to use; no loading or mixing is required. Fine dosing increments, starting from 0.025 mg, allow patients to set a precise dose to avoid wasting the hormone. A demonstration kit will also be available for health care professionals to teach patients how to administer the injections themselves.


DRUG NEWS

Tigecycline Granted Priority Review Status For Intra-abdominal and Skin Infections

The FDA has granted priority review status to Wyeth’s New Drug Application for the investigational intravenous (IV) antibiotic tigecycline (Tygacil™). As the first in a new class of antibiotics, called glycylcyclines, to be submitted for regulatory approval, this agent was designed to circumvent two major resistance mechanisms that have limited the use of many antibiotics: efflux pumps and ribosomal protection.

Wyeth is seeking market approval for this drug as a single-agent therapy to treat complicated intra-abdominal infections and complicated skin and skin structure infections caused by gram-negative and gram-positive pathogens, anaerobes, and methicillin-susceptible and methicillin-resistant strains of Staphylococcus aureus.

Antibiotic resistance results in increased mortality and morbidity and generates a minimum of $4 billion to $5 billion in costs to the U.S. society annually.

(Source: Wyeth, January 28, 2005.)

Duloxetine NDA Withdrawn For Stress Urinary Incontinence

Eli Lilly and Boehringer Ingelheim have announced that Lilly has withdrawn its New Drug Application for duloxetine HCl for the treatment of stress urinary incontinence (SUI). The decision was based on discussions with the FDA, suggesting that the agency was not prepared to grant approval based on the data pack-
Do aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) cause false-positive results in fecal occult blood tests?

Apparently not, according to a study at the Roudebush Veterans Affairs Medical Center in Indianapolis, Indiana. Of 193 patients referred for colonoscopy after a positive fecal occult blood result, 135 used aspirin or NSAIDs regularly (at least one daily dose for at least three days a week). The researchers found no difference between regular aspirin or NSAID users and patients who did not use the drugs in terms of the prevalence of colonoscopic findings that would potentially explain a positive result.

Twenty-nine patients (21%) had findings that could explain the positive result, compared with 11 (19%) of 58 patients who did not use the drugs. Among regular aspirin users, there was no relationship between the dose of aspirin and the likelihood of explanatory colonic findings. The lack of association held, even after adjustment for factors such as age, body mass index, a family history of colorectal cancer, and the use of proton-pump inhibitors or histamine-2 receptor antagonists.

Do Beta Blockers Help Prevent Heart Failure in Dialysis Patients?

Heart failure (HF) is more common and at least as lethal as ischemic coronary heart disease (CHD) in patients with severe chronic kidney disease, including those on long-term dialysis. HF also differs from CHD, and different therapy is needed. Preload reduction and blood pressure control aren’t enough: neurohormonal blockade with beta blockers and angiotensin-converting enzyme (ACE)–inhibitors is also essential, say researchers from Walter Reed Army Medical Center, the Uniformed Services University of the Health Sciences, the Madigan Army Medical Center, the National Institutes of Health, and Rush–Presbyterian Medical Center.

Given the overactivity of the sympathetic nervous system in renal parenchymal disease, they theorized, beta blockers ought to be the ideal antihypertensive agents for dialysis patients.

To test this theory, the researchers conducted a retrospective study of 2,550 patients enrolled in the U.S. Renal Data System. Among those patients, 20% with known HF were using beta blockers, as were 19% of those without known HF.

The use of beta blockers was independently associated with a lower risk of de novo HF, a composite outcome of HF and cardiovascular death, and all-cause death, even in models limited to patients taking beta blockers. Beta-blocker use remained statistically significant even when the researchers adjusted for diabetes, CHD, or hemodialysis or peritoneal dialysis.

The use of ACE-inhibitors was not associated with de novo HF, cardiovascular death, or all-cause death in dialysis patients who did not have known HF. Aspirin use increased the risk of recurrent HF, as did the use of beta blockers and aspirin together.

Although the use of cardioselective beta blockers was statistically significant, the use of noncardioselective beta blockers, also used much less frequently, was not. (Cardioselective beta blockers are less prone to causing peripheral vasoconstriction and are associated with a lower risk of hyperkalemia than noncardioselective beta blockers. This might partly explain why they were used more often.)

The study revealed a lack of benefit from beta blockers in patients with established HF, but the researchers suggest that it would be premature for clinicians to withhold beta blockers from patients with end-stage renal disease and a history of HF.

As many as 70% of high-risk patients can tolerate beta blockers; thus, their use in dialysis patients seems far lower than is appropriate.

(Source: Arch Intern Med 2004;164: 2465–2471.)

Pioglitazone and Edema

Because thiazolidinediones are known to induce pulmonary edema in patients... continued on page 152
with left ventricular dysfunction, they are contraindicated in patients with New York Heart Association class III and IV heart failure (HF).

Thiazolidinedione-induced HF in patients with normal left ventricular systolic and diastolic function has not been widely reported. However, physicians from Stanford University Medical Center in California reported findings in two patients who developed dangerous edema within one month of starting pioglitazone (Actos®, Takeda/Eli Lilly), although they had no history of HF.

The first patient, 77 years of age, had diabetes, chronic obstructive pulmonary disease, hypertension, and chronic renal insufficiency. He began taking 15 mg daily, then 45 mg daily over three weeks. During that period, peripheral edema and paroxysmal nocturnal dyspnea developed. The patient also gained 20 pounds; however, he was not taking any drugs that were associated with thiazolidinedione fluid retention.

Physical examination revealed bibasilar rales and bilateral mild (2+) pitting edema extending to his knees. The creatinine level was 1.7 mg/dl. A chest radiograph showed interstitial edema, but an echocardiogram showed normal left ventricular function and no valvular abnormalities.

The pioglitazone was discontinued, and the patient underwent a six-liter diuresis with furosemide. Upon discharge, she had lost 10 pounds and the pulmonary edema had resolved. At six months, no HF was present.

These two case histories suggest a broader population at risk for thiazolidinedione-associated adverse effects. The physicians advise monitoring patients closely, especially if other risk factors for thiazolidinedione fluid retention are present, such as the use of other medications, older age, and chronic renal insufficiency.

(Source: Am J Med 2004;117:973–974, letter to editor.)

Aprepitant for Chemotherapy-Related Vomiting

Aprepitant (Emend®, Merck), a new neurokinin-1 (NK-1) antagonist, can help delay and prevent chemotherapy-related nausea and vomiting. Researchers from Medical University of South Carolina in Charleston observed that aprepitant significantly augmented the effects of corticosteroids and serotonin type 3 (5-HT₂) antagonists when given before highly emetogenic chemotherapy, including cisplatin.

This agent seems to work better on vomiting than on nausea by blocking the emetic effects of substance P, a mediator of vomiting.

Aprepitant should not be used routinely as a first-line therapy in patients receiving moderately or mildly emetogenic chemotherapy, the researchers say. Although aprepitant is well tolerated with minimal adverse effects, there are many potential drug interactions. Patients should be carefully monitored.

(Source: Ann Pharmacother 2005;39: 77–85.)

A New Alternative For Crohn’s Disease

Although infliximab (Remicade®, Centocor) is quite effective in treating Crohn’s disease, some patients stop responding to it over time. Fortunately, another drug is waiting in the wings: adalimumab (D2E7/Humira®, Abbott), a recombinant humanized monoclonal immunoglobulin G (IgG₁) antibody. Its mechanism of action appears to be similar to that of infliximab.

In a study from Cedars–Sinai Medical Center in Los Angeles, California, 15 patients with active Crohn’s disease whose response to infliximab had begun to weaken were given adalimumab over six months.

Of the 13 patients who had follow-up evaluations, seven (54%) had a complete response and four (31%) had a partial response. Two patients were non-responders. Eight of 11 patients who were taking corticosteroids concurrently were able to stop or reduce the steroid dosage. The mean time to response was five weeks. Adalimumab was well tolerated, although two patients experienced injection-site reactions.

(Source: Am J Gastroenterol 2005;100: 75–79.)

“Not Approvable” Letter for Vincristine in Lymphoma

An FDA action letter states that the anticancer drug vincristine sulfate liposome injection (Marqibo™, Inex) is not approvable for treating relapsed aggressive non-Hodgkin’s lymphoma under the agency’s accelerated approval regulations, based on the phase 2 clinical trial data submitted.

The letter listed deficiencies in the chemistry, manufacturing, and control relating to the packaging, labeling, and product specifications. The FDA recommended additional studies to compare the product with other chemotherapy
regimens.
(Source: Inex, January 19, 2005.)

**New AIDS Strain Worrisome**

Health officials in New York City have discovered a new strain of the human immunodeficiency virus (HIV) that is drug-resistant and that causes a quick onset of the acquired immunodeficiency syndrome (AIDS). The patient, a man in his mid-40s, had had unprotected sex with other men, often while using crystal methamphetamine, an addictive stimulant. The strain was diagnosed in December 2004.

The patient appeared to have fallen ill with AIDS within two or three months, and at most 20 months, after infection. The virus did not respond to three of four types of antiviral drugs most commonly prescribed. He is receiving a fourth regimen of treatment.

Although drug resistance is increasingly common among HIV patients, even among those who had never been treated before, such a rapid progression to AIDS is unusual.

The Centers for Disease Control and Prevention said that it is unaware of any other case like this in the U.S. or anywhere else in the world. Some health care professionals do not see cause for alarm, but the city’s health commissioner considers this a wake-up-call to anyone who engages in unprotected sex and other high-risk behaviors.


**New Guidelines for HIV Therapies**

The Centers for Disease Control and Prevention (CDC) has announced new federal guidelines for the use of antiretroviral drugs to prevent HIV infection after exposure to the virus through sexual intercourse, sexual assault, injection drug use, or accidents.

“Non-occupational post-exposure prophylaxis” (NPEP) is recommended only for patients who seek treatment no more than 72 hours after a high-risk exposure with a person known to have HIV infection. Treatment should begin as soon as possible after exposure and must continue for 28 days.

The guidelines update the guidance of the Department of Health and Human Services (DHHS) issued in 1998. Some recommendations for physicians include the following:

- When potentially exposed persons seek care within 72 hours of exposure but do not know the HIV status of the person who was the possible source, clinicians should evaluate the risks and benefits on a case-by-case basis.
- When a person seeks care more than 72 hours after exposure or when HIV exposure risk is low, NPEP is not recommended.
- Use of the antiretroviral drugs is not recommended for people whose behaviors result in frequent, recurrent exposures to HIV.
- People who are frequently at risk of exposure to HIV would benefit more from intensive risk-reduction interventions than from NPEP.
- Post-exposure prophylaxis has been recommended for health workers exposed to HIV since 1996 and has been associated with an 80% reduced risk of infection.
- Antiretroviral regimens given to HIV-infected women around the time of labor may cut the risk of mother-to-child transmission by about 50%.
- Any three-drug combination of antiretroviral medications recommended by the DHHS may be used as NPEP, except those containing nevirapine (Viramune®, Boehringer Ingelheim). When used under conditions similar to the NPEP approach, nevirapine has been associated with severe reactions and liver damage.
- Women who are pregnant or of childbearing age should not receive regimens containing efavirenz (Sustiva®, Bristol-Myers Squibb).

(Source: CDC, January 21, 2005, www.cdc.gov/mmwr/mmwr_rr.html.)

**Prostate Cancer Vaccine Shows Promise**

An experimental treatment called Provenge® has been shown to triple the survival rate of men with advanced prostate cancer. Developed by Dendreon, the treatment is considered a vaccine—not because it prevents disease but because it tries to harness the body’s own immune system to fight cancer after the disease has developed. Until now, many such cancer “vaccines” have been unsuccessful in trials. This treatment seems to have a chance of winning approval from the FDA, especially if another trial, expected to be completed by the end of the year, confirms the results.

Provenge® improved survival for all patients, not just those with less aggressive cancers. The lead investigator said that the treatment was much less toxic than chemotherapy.

During the treatment, the patient’s blood is run through a machine for two or three hours to extract certain immune system cells. The cells are then mixed with a protein (prostatic acid phosphatase), which is present on most prostate cancers. The lead investigator said the treatment was considered a prostate cancer. Developed by Dendreon, the treatment is considered a vaccine—not because it prevents disease but because it tries to harness the body’s own immune system to fight cancer after the disease has developed. Until now, many such cancer “vaccines” have been unsuccessful in trials. This treatment seems to have a chance of winning approval from the FDA, especially if another trial, expected to be completed by the end of the year, confirms the results.

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During the treatment, the patient’s blood is run through a machine for two or three hours to extract certain immune system cells. The cells are then mixed with a protein (prostatic acid phosphatase), which is present on most prostate tumors. The mixture is then returned to the patient in a one-hour infusion.

The process is repeated three times within a single month to alert the immune system that cells containing prostatic acid phosphatase, namely tumor cells, are invaders to be attacked.
ADHD Drug Pulled from Canada After 20 Deaths

Health Canada has ordered that a drug for attention deficit hyperactivity disorder (ADHD) be removed for sale after learning that it has been linked to 20 sudden deaths and 12 strokes in the U.S.

Adderall XR® (Shire), an amphetamine stimulant, was approved for sale in Canada just over a year ago.

Shire maintains that the drug is safe. Health Canada’s decision to suspend sales is at odds with the FDA in the U.S., where the drug remains on the market with a revised warning label stating that it should not be used in patients with heart problems.

It is not clear whether the adverse reactions resulted from the drug’s use. Of the 20 cases of sudden death linked to the drug, 14 occurred in children. Two of the 12 strokes were suffered by children taking the drug.

Most of the patients had had no history of previous cardiac problems. The patients had been taking the prescription as directed.

The immediate-release form of the drug is available in the U.S. but has never been approved for sale in Canada.

(Sources: www/consumeraffairs.com; www.ctv.ca; © 2005 Bell Globemedia Inc.; www.AdderallXR.com.)

Can Minor Heart Defect Surgery Prevent Migraine?

Researchers are exploring whether a 45-minute outpatient procedure used to treat a heart problem in stroke victims might help millions of patients experiencing migraine headaches.

The debilitating headaches have unexpectedly disappeared in some stroke patients who have undergone the procedure intended to prevent another stroke. Researchers think some types of strokes and some migraines might be linked to a minor heart defect that affects nearly 25% of the human population.

The defect, a small hole called a patent foramen ovale, allows blood to travel from the right upper chamber of the heart to the upper left side. Inside a mother’s womb, this pathway permits oxygenated blood to pass through the fetus. It closes in most people within a year after birth. When it remains open, researchers speculate, it may allow tiny blood clots or chemicals to bypass the natural filter of the lungs and enter the brain, triggering strokes or migraines.

Tests are under way to learn whether repairing the defect eliminates or reduces migraines that are accompanied by an aura, which can consist of flashing lights, vision loss, and other temporary neurological changes.

The closure repair, which involves placing a tiny device in the heart to seal the opening, has been performed on a small number of U.S. stroke patients during the past several years under an unusual FDA authorization, called a Humanitarian Device Exemption.

(Sources: J Am Coll Cardiol 2005;45: 496–498; The Wall Street Journal, February 15, 2005.)

Antidepressant Found “Not Guilty” in Murder Case

A teenage who killed his grandparents when he was 12 years old was convicted of two counts of murder by jurors who rejected his claim that an antidepressant made him unable to discern right from wrong. The defendant, now 15 years old, was sentenced to 30 years in prison.

Some relatives claimed that the child had not been “himself” the night of the crime. They were referring to the effects of the drug sertraline (Zoloft®, Pfizer) on the boy.

The jurors believed that the defendant exhibited side effects from the antidepressant, but they did not feel that these were severe enough to let him escape criminal responsibility.

They also heard that the antidepressant and others in its class have been linked to increased suicidal ideation, agitation, restlessness, and other abnormal behavior in adolescents. Prosecutors called the “Zoloft® defense” a smoke screen during closing arguments.

In the end, the jury decided that the child knew right from wrong and was not a victim of antidepressant use.

(Source: CNN Law Center, February 16, 2005; www.cnn.com.)
Do Flu Shots Help the Elderly?
A new study based on more than three decades of data suggests that giving influenza vaccine to older adults might not have saved any lives. Instead, the authors say, the government should consider extending vaccination to school-aged children, the most frequent spreaders of the virus.

The study, led by researchers from the National Institutes of Health, challenges standard government dogma. Yearly flu shots have been recommended for people 65 years of age or older since the 1960s and for those aged 50 or older since 2000. The study found that vaccination rates had risen among the elderly to 65% in 2001 from 20% before 1980. However, the researchers could find no corresponding decrease in death rates.

Although the study examined data from the whole elderly population over time, it did not directly compare elderly people who have been vaccinated with those who have not. Previous studies that made that comparison found a decreased rate of winter deaths from all causes among those who had been vaccinated.

Responding to the latest study, the Centers for Disease Control and Prevention said it planned no changes in its position on who should receive flu vaccine.


New FDA Chief Named
President George W. Bush has announced that he will nominate the acting commissioner of the FDA, Dr. Lester M. Crawford, as the permanent head of the agency. The move comes amid a Congressional investigation of the agency and widespread calls that it strengthen oversight of drug safety.

Dr. Crawford, whom Mr. Bush considered and rejected for the post in 2001, has made the following initiatives top priorities: speeding crucial drug approvals, protecting drugs and food from terrorist attacks, and improving the manufacture and safety of medications. He has opposed legalizing drug imports.

(Source: The New York Times, February 14, 2005.)

FDA: Monitoring Drug Safety
DHHS Secretary Michael Leavitt and Acting FDA Commissioner Lester M. Crawford unveiled a new vision for the FDA that they hope will promote a culture of openness and enhanced oversight within the agency.

The agency plans to create a new independent Drug Safety Oversight Board (DSB) to review the management of drug safety issues within the Center for Drug Evaluation and to provide emerging information to health providers and patients about the risks and benefits of medications. (See Dr. Stefanacci’s commentary on page 176.)

As the FDA develops new communications formats, it will be soliciting public input on how it should manage potential concerns associated with disseminating emerging information prior to regulatory action. The agency will issue draft guidance on procedures and criteria for identifying drugs and information for its Drug Watch Web page.

(Source: FDA, February 15, 2005.)

Vioxx® May Return
An expert advisory panel of the FDA has narrowly voted in favor of allowing celecoxib (Celebrex®, Pfizer) and other drugs in the class of cyclo-oxygenase-2 (COX-2) inhibitors to remain available. However, a majority of the 32-member panel recommended steps to significantly restrict the use of these agents and recommended extensive new testing of similar new or existing arthritis drugs.

The proposed restrictions included (1) a ban on direct-to-consumer advertising, (2) a strong “black box” warning on the label, and (3) a requirement that patients be given a written warning that the drugs increase the risk of heart attacks and strokes. Some members also said that the drugs should be used only when other medications have been unsuccessful.

Celebrex® and Vioxx® were approved in the late 1990s and were aggressively advertised as breakthrough treatments for arthritis. Millions of patients began taking them, although studies have shown that many patients were not at risk for the gastrointestinal problems sometimes caused by older pain relievers. The newer drugs were designed to prevent such problems.

(Source: The Washington Post, February 19, 2005.)

Protease Inhibitors and Heart Problems
A widely used class of drugs known as HIV protease inhibitors, which keep HIV infection from progressing to AIDS, may cause serious and potentially lethal heart rhythm disturbances in some patients, according to Mayo Clinic findings.

Some have hypothesized that protease inhibitors might relate to the development of heart rhythm problems by blocking a channel. These drugs include lopinavir (Kaletra®), nelfinavir (Viracept®), indinavir (Crixivan®), ritonavir (Norvir®), and saquinavir (Fortovase®).

The researchers emphasize that the
New Guidelines For Asthma in Pregnancy

The National Asthma Education and Prevention Program is issuing new treatment guidelines for managing asthma during pregnancy. Poorly controlled asthma can lead to serious problems for pregnant women and their fetuses.

Medication can be increased, if needed, or decreased, when possible; it might be safer to take medications than to experience asthma exacerbations. If the mother has trouble breathing, the fetus will also have trouble getting oxygen.

Maternal asthma is associated with an increased risk of infant death, pre-eclampsia, premature birth, and low birth weight.

Pregnant patients with persistent asthma should be checked at least monthly. Albuterol (e.g., Proventil®, Schering) should be available to provide quick relief of symptoms.

Women should limit their exposure to irritants (e.g., dust mites, tobacco smoke).

(Source: J Allergy Clin Immunol, January 2005; National Institutes of Health/National Heart, Lung, and Blood Institute, January 11, 2005.)

Severe Hypotension from Lisinopril plus Tizanidine

“Dramatic” hypotension in a patient who was taking lisinopril (Zestril®, AstraZeneca), an ACE-inhibitor, might have been caused by an interaction with tizanidine (Zanaflex®, Elan), a muscle relaxant, say physicians from Taipei Veterans General Hospital in Taiwan.

A 48-year-old woman was admitted to the hospital with a cerebral hemorrhage. Five days after the onset of stroke, her abnormal body posture improved but her blood pressure was still fairly high (160/100 mm Hg). The medical team started antihypertensive therapy, including lisinopril. Three weeks later, they added tizanidine in hopes of improving the patient’s rigidity and still-high blood pressure by reducing muscle tone. Her blood pressure plummeted within two hours, from 130/85 to 66/42 mm Hg.

The physicians did not find any newly developed focal deficits or worsening systemic infection. Because of the acute hypotension and deterioration in consciousness, they started dopamine therapy to maintain blood pressure. They withdrew tizanidine and all antihypertensive agents.

Within five hours, the patient’s blood pressure increased to 120/50 mm Hg. Dopamine was stopped 20 hours later. The alpha-beta blocker labetolol (e.g., Trandate®, Prometheus), the calcium-channel blocker amlodipine besylate (e.g., Norvasc®, Pfizer), the cerebral artery spasm inhibitor nimodipine (e.g., Nimotop®, Bayer), and tizanidine were successively resumed 42 hours later when her blood pressure reached 152/85 mm Hg, but they did not produce similar results.

Tizanidine is an alpha2-adrenergic agonist much like clonidine (Catapres®, Boehringer Ingelheim) but with less severe side effects. Because clonidine can depress blood pressure through volume depletion and an ACE-inhibitor may further compromise the renin–angiotensin system, the authors theorize that tizanidine might provoke the same response.

The authors concede that the drastic decrease in blood pressure might have been an idiosyncratic reaction. The use of ACE-inhibitors in post-stroke patients is not rare, and tizanidine is increasingly chosen for its antispastic effect with few hemodynamic influences. However, they add, significant hypotensive events are seldom reported.

(Source: Ann Pharmacother 2004;38:1840–1843.)

Postop Therapy Offers Hope Against Deadly Lung Cancer

Non–small cell lung cancer (NSCLC) is the most common form of lung cancer in the world. New trials have confirmed the effectiveness of adjuvant (post-operative) therapy, which is expected to rapidly become the standard treatment for NSCLC.

A plateau has been reached in terms of the efficacy of first-line, platinum-based chemotherapy regimens for NSCLC. Surgery is the best option for cure in early-stage (1 and 2) disease. However, NSCLC is seldom detected early; even after surgery, the chances of a recurrence remain high.

After surgery, oncologists often administer adjuvant chemotherapy to patients to eliminate any potential cancer cells that might not have been removed. Until recently, the benefits of adjuvant therapy have been inconclusive because of negative results and because the non-randomized trials in the past have been small. However, two recent clinical trials from 2004 suggested the potential effectiveness of adjuvant NSCLC therapy.

The use of adjuvant therapy in the United Kingdom is slightly more complicated; surgery is not performed there

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as often. Thus, chemotherapy for early- stage disease is not necessarily adjuvant chemotherapy. The National Institute of Clinical Excellence (NICE) in the U.K. is drawing up guidelines for the diagnosis and treatment of NSCLC, but some authorities worry that adjuvant therapy will not be included in the guidelines. (Source: www.datamonitor.com.)

Genotyping Test Screens For Drug Effectiveness

A new laboratory test system allows physicians to consider unique genetic information from patients when it comes to selecting medications and doses for many conditions such as cardiac disease, psychiatric disorders, and cancer.

The AmpliChip Cytochrome P450 Genotyping Test (Roche) was cleared for use with the GeneChip Microarray Instrumentation System (Affymetrix). The FDA granted clearance for the Affymetrix GeneChip System 3000Dx, an instrumentation system to analyze in vitro diagnostic microarrays.

(Sources: FDA; BioWorld Online, December 29, 2004, www.bioworld.com.)

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS
Name: UroVysion™ DNA Probe Assay
Manufacturer: Abbott Laboratories, Chicago IL
Approval Date: February 1, 2005
Use Classification: The assay is used as an aid in the diagnosis of bladder cancer in patients with hematuria.

Description: The assay is used in conjunction with cystoscopy. It represents the first gene-based test available for both diagnosis and monitoring of bladder cancer recurrence. In one clinical study, a comparison of UroVysion™, performed on urine samples with cystoscopy and histology testing methods, demonstrated a clinical sensitivity of 68.8% and a clinical specificity of 77.7%. Urine cytology demonstrated a relative sensitivity of 39.2% and a relative specificity of 91.5%.

Source: www.pharmacyonesource.com

Name: Procedur™-10, Procedur™-SF Syringes
Supplier: Avanca Medical Devices, Albuquerque, NM
Approval Date: January 27, 2005
Use Classification: This family of syringes allows health care providers to inject and aspirate with one hand while maintaining unprecedented needle stability.

Description: Having one hand free allows medical professionals to perform an injection or withdraw fluids more efficiently, compared with conventional syringes, and can help reduce the chances of injury or complications arising from the procedures.

Purpose: These syringes offer extensive applications in medical and surgical procedures. The patented reciprocal technology allows injection and withdrawal of fluids or tissues simultaneously.

Benefits: Clinical trials have demonstrated decreased patient pain, reduced procedure time, and improved satisfaction for health care providers. The syringes have been successfully used in a number of procedures, including arthrocentesis, local anesthesia, and joint injections.

Source: www.pharmacyonesource.com

Name: TonoPach™
Manufacturer: RetinaPharma Technologies, Inc., Jenkintown, PA
Approval Date: January 6, 2005
Use Classification: This device is used for the simultaneous determination of intraocular pressure (IOP) and central corneal thickness at the same location on the cornea.

Description: The patented technology combines central corneal thickness and IOP in a single, inexpensive, easy-to-use instrument.

Purpose: It is estimated that millions of patients are not receiving correct diagnoses for glaucoma and ocular hypertension, which are leading causes of preventable blindness in adults. TonoPach™ is intended to enable more accurate diagnoses by allowing ophthalmologists to adjust the IOP for corneal thickness at the exact point of measurement.

Benefits: Central corneal thickness is an important risk assessment parameter for glaucoma or ocular hypertension. A combined measure of this thickness and the IOP is significantly predictive of visual field damage. The TonoPach™ may be especially beneficial in evaluating patients with corneas that have been thinned by excimer laser corrective surgery or disease, because thinned corneas can alter IOP readings and mask underlying glaucoma.

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**NEW DRUGS**

**DRUG NEWS**

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**Name:** OpusDuo™ Laser (Erbium: Yttrium Aluminum Garnet and Carbon Dioxide) System

**Manufacturer:** Lumenis® Ltd., Lume.Pk, and OpusDent™ Ltd., Dental Division, Santa Clara, CA

**Approval Date:** January 3, 2005

**Use Classification:** This laser system incorporates the Er:YAG and CO₂ lasers in a single device for contact bone removal during oral surgical and periodontal procedures.

**Description:** The OpusDuo™ combines two wavelengths. The Er:YAG laser is used for hard-tissue drilling. The CO₂ laser, considered the gold standard instrument for surgical procedures, is effective for various soft-tissue applications.

**Purpose:** The Er:YAG wavelength has a high water-absorption rate. It is ideal for hard-tissue applications such as removing caries (dental decay), cavity preparation, and enamel etching.

**Benefit:** This system represents the first FDA clearance for contact cutting of bone tissue in dentistry. It is based on the precise and safe thermal mechanical ablation of bone utilizing the proprietary contact sapphire tip. Practitioners using the OpusDuo™ can feel the laser hand-piece make contact with the bony tissues being ablated. With previous methods, practitioners had to “point and shoot” in a surgical field.

**Sources:** www.pharmacyonesource.com; www.lumenis.com; www.halas.com

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**Medical Device Alerts**

The FDA is re-issuing a nationwide alert against the use of all lots of pre-loaded syringes containing either heparin or sodium chloride intravenous catheter flushes manufactured by IV Flush, LLC, and distributed by Pinnacle Medical Supply, of Rowlett, Texas. New cases of infections that might be associated with the use of these unapproved, and possibly contaminated, products have been reported.

**Reason for Recall:** On January 31, 2005, the FDA warned consumers and institutions not to use the syringes and to return them to IV Flush or to the original distributor. Since that warning, the FDA has been informed of a cluster of *Pseudomonas fluorescens* infections in patients that may be associated with the heparin flushes.

*P. fluorescens* is an infrequent cause of infection, but it has been reported to cause outbreaks of pseudobacteremia (the presence of a blood culture in the absence of clinical evidence of bloodstream infection). *P. fluorescens* has also been reported as the cause of procedure-related infections and infections resulting from transfusion with contaminated blood components.

**Source:** www.fda.com