**NEW DRUGS**

**Generic Desogestrel/Ethinyl Estradiol Contraceptives**

Watson Pharmaceuticals, Inc., has announced the final approval from the U.S. Food and Drug Administration (FDA) of its Abbreviated New Drug Application (ANDA) for desogestrel and ethinyl estradiol tablets USP, 0.15 mg/0.03 mg, a generic version of Ortho-McNeil’s Ortho-Cept® and Organon’s Desogen®. These products are indicated for the prevention of pregnancy.

(Source: Watson, August 1, 2005.)

**Generic Klonopin Approved**

Barr Laboratories, Inc., has received final approval from the FDA for its application to manufacture and market clonazepam orally disintegrating tablets, 0.125 mg, 0.25 mg, 0.5 mg, 1 mg and 2 mg, the generic equivalent of Hoffman La Roche’s Klonopin® Wafers. Klonopin® can be used alone or as an adjunct in patients with seizures and panic disorder, with or without agoraphobia.

(Source: Barr Pharmaceuticals, Inc., August 11, 2005.)

**Generic Paxil for Depression**

Teva Pharmaceutical Industries Ltd. has announced final approval of its ANDA for paroxetine HCl tablets, 10 mg, 20 mg, 30 mg, and 40 mg. The tablets are the AB-rated generic equivalent of Glaxo-SmithKline’s antidepressant Paxil® Tablets.

(Source: Teva, August 16, 2005.)

**NEW INDICATIONS**

**Extended-Release Adderall® For Adolescents with ADHD**

The FDA has approved Shire’s Adderall XR® (mixed salts, amphetamine) as a once-daily treatment for adolescents 13 to 17 years of age with attention deficit/hyperactivity disorder (ADHD). Since October 2001, the product has been approved in the U.S. for children six to 12 years of age, and since August 2004, it has been indicated for adults 18 years of age and older.

ADHD is a neurobiological disorder that affects approximately 3% to 7% of all school-aged children, or approximately two million U.S. children. It manifests as a persistent pattern of inattention and/or hyperactivity–impulsivity that is more frequent and severe than is typically observed in individuals at a comparable age and maturity. It can profoundly affect a child’s quality of life and can interfere with academics, leading to relationship problems and difficulty in focusing.

(Source: Shire, July 22, 2005.)

**Labeling Expanded for Valsartan**

Novartis Pharmaceuticals has announced that the FDA has approved valsartan (Diovan®), an angiotensin receptor blocker, to reduce cardiovascular deaths in high-risk patients (those with left ventricular failure or dysfunction) after a heart attack.

The FDA also expanded the drug’s labeling for heart failure. Valsartan, indicated for the first-line treatment of hypertension, can now be prescribed for a broader range of patients and is no longer limited to patients with an intolerance of angiotensin-converting enzyme (ACE) inhibitors.

(Sources: FDA, Novartis, August 3, 2005.)

**Celecoxib Approved for Ankylosing Spondylitis . . . But with New Warnings**

Pfizer’s selective cyclooxygenase-2 (COX-2) inhibitor, celecoxib (Celebrex®), has been approved to relieve the signs and symptoms associated with ankylosing spondylitis, a form of arthritis that affects the spine. Celecoxib remains an important treatment for the pain of osteoarthritis, adult rheumatoid arthritis, and menstruation; acute pain; and familial adenomatous polyposis (intestinal polyps).

As expected, the FDA added warnings about potential cardiovascular and gastrointestinal risks. The FDA will require similar warnings for other older arthritis treatments such as ibuprofen and naproxen.

Ankylosing spondylitis, which affects more than 400,000 Americans, is now the sixth approved indication for celecoxib in the U.S.

(Source: Pfizer, Inc., August 1, 2005.)

**Hepatitis A Vaccine Approved for Children**

The FDA has approved inactivated hepatitis A vaccine (Vaqta®, Merck) for children 12 months of age and older. This is the only hepatitis A vaccine that can be used for children as young as 12 months of age. This product was previously approved for use in children two years of age and older.

Hepatitis A is a contagious viral disease that can cause an infection of the liver. The virus is transmitted most commonly by the fecal–oral route through person-to-person contact or by the ingestion of contaminated food or water. No specific treatment is available for hepatitis A, and the source of infection is unknown in nearly 50% of cases.

It has been discovered that young children often transmit hepatitis A in the U.S. Because children do not typically manifest symptoms, they unknowingly pass the infection on to older family members. The expanded age indication may offer improved protection of children against hepatitis A earlier in life.

The primary immunization should be given at least two weeks before an expected exposure to the hepatitis A virus.

(Source: Merck & Co., August 15, 2005.)
Adalimumab for Psoriatic and Early Rheumatoid Arthritis in Europe

The European Commission has approved adalimumab (Humira®, Abbott) to treat psoriatic arthritis and early rheumatoid arthritis (RA) in Europe. A decision regarding the FDA’s approval for these expanded indications in the U.S. is expected by the end of 2005.

The medication will be available immediately to patients with psoriatic arthritis in Germany, the United Kingdom, Spain, Finland, and Denmark and later in other European Union countries as each country adopts pricing and reimbursement policies.

The recommended dose for psoriatic arthritis, as well as the usual dose for RA, is 40 mg every other week by subcutaneous injection.

The drug was previously approved for moderate-to-severe, active RA in adults who did not adequately respond to disease-modifying antirheumatic drugs, including methotrexate.

(Source: Abbott, August 15, 2005.)

Perindopril Erbumine for Reduced Cardiovascular Risk

Solvay Pharmaceuticals, Inc., and CV Therapeutics, Inc., have announced the FDA’s approval of perindopril erbumine (Aceon®) tablets for patients with stable coronary artery disease to reduce the risk of cardiovascular mortality or nonfatal myocardial infarction (MI). Prior to this labeling expansion, Aceon®, an ACE-inhibitor, was indicated for the treatment of essential hypertension.

The only published clinical trial data from the European trial on Reduction of cardiac events with Perindopril in patients with stable coronary artery disease (EUROPA). This was a randomized, double-blind, placebo-controlled trial of 12,218 patients with stable coronary disease and without heart failure. A 20% reduction in the risk of cardiovascular events was observed with 8 mg. The overall discontinuation rate was 22% for those receiving the drug and placebo. The mean follow-up observation period was 4.2 years.

(Sources: Solvay/CV Therapeutics, August 23, 2005.)

NEW FORMULATION

Brimonidine for Glaucoma

Allergan has received approval from the FDA to market brimonidine tartrate ophthalmic solution (Alphagan® P) 0.1%, indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The new product is an optimized formulation of Alphagan® 0.2% and was designed to further minimize drug exposure while maintaining the drug’s favorable efficacy profile.

(Source: Allergan, August 19, 2005.)

DRUG NEWS

Hydroxyurea or Anagrelide For Thrombocythemia?

Patients with essential thrombocythemia have a high risk of thrombosis, particularly in the arteries. Hydroxyurea, often with low-dose aspirin, is widely used to control platelet counts in these patients. However, anagrelide (Agyrlin®, Shire), which inhibits platelet aggregation, is also used in first-line therapy, despite drawbacks such as greater expense and concerns about efficacy.

A trial from the United Kingdom compared hydroxyurea plus aspirin with anagrelide plus aspirin in 809 high-risk patients for 12 to 72 months. The results give hydroxyurea/aspirin a distinct edge.

The anagrelide/aspirin combination was associated with higher rates of arterial thrombosis, hemorrhage, transformation to myelofibrosis, and withdrawal from treatment. Although this therapy also carried a significantly lower rate of venous thromboembolism, the investigators were unsure whether anagrelide reduced the incidence or whether hydroxyurea raised it. They suggest that the optimal treatment of patients with previous venous thrombosis will depend on individual circumstances, but they note that arterial thrombosis is more than three times more common than venous thrombosis in essential thrombocythemia.

Both groups of patients maintained control of platelet counts.


Megestrol Acetate for Hospital-Acquired Malnutrition

How helpful is megestrol acetate (Megace®, Bristol-Myers Squibb Oncology) for elderly patients with malnutrition acquired during their hospital stay? The few studies that have been performed are inconclusive, say researchers from the University of California at Los Angeles.

Megestrol, a synthetic progestin, has been used to treat the wasting syndrome in patients with acquired immunodeficiency syndrome (AIDS).

A nine-week, phase 2 clinical trial was performed to compare 47 patients 60 years of age and older who were randomly assigned to three doses of megestrol with placebo. The patients had recently been discharged from an acute-care hospital with fair or poor appetite. They received either placebo or megestrol at 200, 400, or 800 mg/day. The researchers hoped to find a dose that would have the best effect on nutrition with the least toxicity.

The only published clinical trial data on older people showed modest benefits at 800 mg, a dose considered optimal for patients with AIDS. Because older people have a higher percentage of body fat than younger people and because megestrol...
Short-Acting Insulin Analogues: Little Value in Diabetes?

Short-acting insulin analogues benefit glycosylated hemoglobin (HbA1c) values in adults with type-1 (“juvenile” or insulin-dependent) diabetes only slightly and may have no benefit at all in those with type-2 (non–insulin-dependent) diabetes.

Researchers from Graz, Austria, evaluated data from 42 randomized controlled trials. They compared the analogues with regular insulin in 7,933 patients with type-1, type-2, and gestational diabetes.

They found no trials that compared long-acting insulin analogues, insulin glargine (Lantus®, Aventis), or insulin detemir (Levemir®, Novo Nordisk), with regular insulin. Whether the use of the short-acting analogues, in combination with long-acting analogues, would attain results comparable to continuous subcutaneous insulin infusion remains an open question, the researchers conclude.

On the other hand, short-acting analogues have been touted for improved quality of life. These researchers found that the convenience, flexibility, and continuity of treatment depended largely on the need for patients to inject regular insulin, on average, 30 minutes before meals. However, most patients do not use a fixed interval of 30 minutes; the only study that used a double-blind design found no improvement in quality of life, metabolic control, or overall hypoglycemia.

For safety purposes, the researchers recommended a long-term follow-up trial of large numbers of patients using short-acting analogues along with well-designed studies of pregnant women.

For more on long-acting analogues, see “Pharmaceutical Approval Update” on page 512 of this issue of P&T.

Hypersensitivity with Once-Daily Abacavir

Anything that can help reduce the pill burden faced by patients with human immunodeficiency virus (HIV) infection is welcome. It is therefore good news that abacavir (Ziagen®, GlaxoSmith-Kline) can be taken once a day rather than twice daily. However, researchers from Iowa Drug Information Network and the University of Iowa, who reviewed data on the agent’s safety and efficacy, say that more hypersensitivity reactions and severe diarrhea occurred with the once-daily regimen.

Abacavir is already known to cause rare but life-threatening hypersensitivity reactions (in 8% of patients in clinical trials). The higher risk was noted only in the double-blind, randomized, controlled trial comparing the two regimens, not in open-label comparisons. As a result, more evidence is needed to determine the level of risk.

Typically, the reaction to once-daily abacavir is characterized by two of the following symptoms: fever, rash, nausea, vomiting or diarrhea, malaise or fatigue, and cough or sore throat. If any of these occur, abacavir therapy should be stopped and should not be used again, because the symptoms will recur and will rapidly become life-threatening.

Patients should be informed that the more common adverse drug effects associated with abacavir usually improve over the initial weeks of treatment.

Given that no firm data have shown that patients are more adherent to the once-daily versus twice-daily treatment, the convenience of once-daily abacavir is an advantage that must be weighed carefully against the potential risks.


Alteplase (rt-PA) and Stroke In the Emergency Room

Nearly half of emergency physicians are reluctant—even resistant—to use recombinant tissue–plasminogen activator (rt-PA) (e.g., alteplase [Activase®, Genentech]) to treat acute ischemic stroke, even in patients at risk, according to a survey by researchers from the Uni-
Non-Approvable Letter For Memantine in Mild Alzheimer’s Disease
The FDA has issued a non-approvable letter to Forest Laboratories in response to its supplemental New Drug Application (sNDA) to expand the indication of memantine HCl (Namenda®) to include the treatment of mild Alzheimer’s disease (AD). Memantine was approved for the treatment of moderate-to-severe AD in October 2003.

After the FDA accepted the sNDA for review in November 2004, the agency informed Forest that a single positive study in patients with mild-to-moderate AD would be adequate to extend the drug’s indication. The FDA also acknowledged that the six-month trial for mild-to-moderate AD, which reached statistical significance at the required primary endpoints, was such a study. However, the FDA then decided not to approve the mild AD indication. Forest plans to meet with the FDA to discuss the letter.

Currently, all AD medications approved in the U.S.—other than memantine—belong to a class of agents called acetylcholinesterase inhibitors, which are indicated only for mild-to-moderate symptoms. Memantine can be used alone or in combination with an acetylcholinesterase inhibitor in the moderate and severe stages.

(Source: Forest, July 25, 2005.)

Ranibizumab Helps “Wet” Macular Degeneration
The experimental drug ranibizumab (Lucentis™, Genentech) has improved vision in patients with the “wet” form of age-related macular degeneration (AMD), a serious eye disease of the elderly. In a one-year trial, vision improved on an eye chart in 25% to 34% of patients; only 5% of patients receiving a placebo improved by the same amount.

Lucentis™ appears to be the first drug that can improve vision in patients with AMD; until now, other treatments have been able to only slow or stabilize the condition.

In May, Genentech reported preliminary data but did not state the percentage of improvement. Some researchers also questioned whether the studied patients were representative of AMD patients in general. In one trial, the drug was associated with an elevated risk of uveitis.

Lucentis™ is a modified form of the company’s cancer drug bevacizumab (Avastin®™), which blocks protein factors that promote the growth of blood vessels. Bevacizumab is not readily absorbed into the retina; thus, Lucentis™ was developed as a separate drug. Genentech and some doctors say that risks associated with the drug should be minimal, because Lucentis™ is injected directly into the eye instead of being administered systemically, like bevacizumab.

Genentech plans to ask the FDA to grant “fast-track” status to win an earlier approval based on the one-year data, although Lucentis™ is unlikely to win regulatory approval until at least mid-2006.

(Source: The Wall Street Journal, July 19, 2005.)

Placebos: Pain Relief Might Not Be “All in Our Heads”
For the first time, scientists have found that a placebo with implied pain-relieving properties directly activates the brain’s chemistry involved in regulating and suppressing pain.

The therapeutic benefits were noted after the subjects received an inert substance that was suggested to reduce pain. Implied pain-relieving placebos have also been associated with reductions in the subjects’ ratings of their own pain. The release of endorphins is the body’s natural way of killing pain.

continued on page 495
Considerable evidence indicates that endogenous opioids (endorphins) play a role in pain regulation. The new findings run counter to the common idea that the placebo effect is just psychological or a result of suggestion.

The scientists found that the anticipation of decreased pain could modulate brain chemical transmission between neurons that are associated with pain reduction. This chemical transmission, occurring at the site of the mu-opioid receptors in the endogenous opioid system, correlated with subjects’ reports of decreased pain intensity and unpleasantness.

Positron emission tomography (PET) and molecular imaging were used to quantify the activity of the endorphins. The scientists administered an IV placebo of salt solution, which was presented as a pain-reliever, to seven healthy men while they were experiencing moderate, sustained levels of pain. The other seven volunteers did not receive a placebo while experiencing pain.

PET scans and the imaging techniques revealed that the brains of the volunteers who received placebos released endogenous opioids. The volunteers also confirmed that they felt less pain. The activation of endorphins correlated with decreased elements of the pain experience, depending on the location and magnitude of the endorphins released in the brain.

(Source: J Neurosci, August 24; Society for Neuroscience, August 19, 2005, www.sfn.org.)

**Paroxetine Linked to Suicide Risk in Adults**

A new analysis of a popular antidepressant has revealed that it might increase suicidal tendencies in adults, not only in children and adolescents, as had previously been shown. One of the United Kingdom’s most widely prescribed antidepressant drugs, paroxetine (Seroxat®, GlaxoSmithKline) has been linked to a seven-fold increase in suicide attempts. The drug is sold as Paxil® in the U.S.

An analysis of trials involving more than 1,500 patients documented seven suicide attempts among those taking the drug and only one among those taking a placebo. Suicidal thoughts were also three times more common among those taking paroxetine. The data were available even before Seroxat® was first licensed in 1990, Norwegian researchers found.

Some say that the drug should be withdrawn from sale, but the company and the Medicines and Healthcare products Regulatory Agency (MHRA) have defended it, claiming that its benefits outweighed the risks. However, the MHRA has said that too many drugs in this class, the selective serotonin reuptake inhibitors (SSRIs), have been prescribed, and has warned that they should not be given to patients younger than age 18.

Researchers at the University of Oslo examined 16 studies in which paroxetine had been compared with placebo, including previously unpublished data.

The Norwegian group suggested that the increased suicidal activity seen in children and adolescents taking certain antidepressant drugs might also be present in adults and that the restrictions on the drug’s usage in children and adolescents should also apply to adults.

(Source: BMC Med 2005;3:14; The Times of London Online; August 21, 2005.)

**Merck Found Liable In $250 Million Lawsuit**

On August 19, a Texas jury found Merck liable for the death of Robert C. Ernst. Mr. Ernst died in 2001 after taking the painkiller rofecoxib (Vioxx®) for
eight months. The jury awarded $253.5 million to his widow. The huge award will probably be reduced to $21.1 million because of a Texas law capping punitive damages.

During the six-week trial, jurors were reported to have concluded, from the testimony and documents presented, that Merck had been aware of the drug’s potential heart risks but had hidden those risks from patients. However, according to a Wall Street Journal editorial, the jury might have been duped by a questionable scientific theory introduced by the plaintiff’s attorney.

The theoretical sequence of events that he “concocted” (in an effort to link the drug to the death, namely a blood clot leading to a heart attack and then to a fatal arrhythmia) was contrary to the autopsy findings. The pathologist found no blood clot and no heart muscle damage from a heart attack when Mr. Ernst died: she had attributed the death to arrhythmia. No studies have linked this drug to arrhythmia.

Some experts are calling for experienced medical court judges to help juries understand the technical issues and reach a fair verdict, and they have stated that blaming the death on this drug is “far-fetched.” Juries do not understand medical information up to 80% of the time, according to the Harvard Medical Practice Study of Litigation in New York state.

Time will tell whether the COX-2s can bounce back. Sales of celecoxib (Celebrex®, Pfizer), the only COX-2 remaining in the U.S. market, have already rebounded. Some physicians still consider these agents to be safer anti-inflammatories for the stomach than conventional painkillers such as aspirin.


Bezafibrate May Reduce Heart Attack Risk

Patients with the metabolic syndrome have a high risk of myocardial infarction (MI). Could bezafibrate (e.g., Bezalip®, Roche), a derivative of fibric acid, be helpful?

Researchers from Israel studied 1,470 patients with at least three risk factors for the syndrome: a fasting glucose level of 110 mg/dl; a triglyceride level of 150 mg/dl; a high-density lipoprotein-cholesterol level below 40 mg/dl in men and less than 50 mg/dl in women; a systolic blood pressure of 130 mm Hg or a diastolic pressure of 85 mm Hg; and overweight (a body mass index of 28 kg/m²).

Of these patients, 193 had experienced a new MI. Bezafibrate was associated with a reduced risk of any MI, nonfatal MIs, and cardiac mortality. The decreased risk was “remarkably” strengthened in 575 patients with four to five risk factors, the researchers say.

Fibrates, with their glucose-lowering properties, appeared to target therapeutic goals more selectively in obese patients with insulin resistance and the metabolic syndrome, the researchers said.

In smaller studies, bezafibrate slowed the progression of coronary atherosclerosis and reduced the rate of coronary events. In a trial of 1,568 men with lower-extremity arterial disease, bezafibrate reduced the severity of intermittent claudication and the incidence of nonfatal coronary events, particularly in patients older than 65 years of age.

Research has also shown a lower incidence of type-2 diabetes in patients with impaired fasting glucose levels who were taking bezafibrate.

(Click here to view the full story on page 529.)

Anti-Cholesterol Drugs Might Not Prevent Dementia

Cholesterol-lowering drugs might not reduce the risk of Alzheimer’s disease, vascular dementia, or a combination of the two, as some experts had thought.

Researchers had theorized that statins and other types of drugs, which reduce the risk of heart disease by inhibiting the production of cholesterol or by exerting anti-inflammatory effects, might help prevent dementia as well.

The study, sponsored by the National Heart, Lung, and Blood Institute, evaluated almost 2,800 people 65 years of age and older who were free of dementia at the start of the study. Some took cholesterol-lowering drugs (six kinds of statins and three non-statinos), and some did not.

Over the course of the study, dementia developed in 480 participants. Using drugs to lower cholesterol seemed to make no difference in determining which patients became ill; however, those who used the drugs and then stopped using them were slightly more likely to experience dementia than those who had never used them.

Some studies have suggested that increasing the dosage of cholesterol-lowering drugs might provide added benefits, but no relationship was observed. No one drug was more effective than another against dementia.

The authors acknowledge the study’s limitations. The main reason that the subjects in this study received statins was their risk for heart disease, and some studies have suggested that heart disease itself is a risk factor for dementia. Yet even when only patients without heart disease were considered, no significant reduction in risk was found.

(Click here to view the full story on page 529.)
Herpes Zoster Vaccine Prevents Postherpetic Neuralgia

A zoster vaccine that reduces the incidence of herpes zoster by 51% and decreases pain and discomfort by 61% is certainly big news. But even bigger, perhaps, is the fact that fewer older people would need to fear one of the most devastating types of pain—postherpetic neuralgia (PHN). The zoster vaccine reduced the incidence of PHN by 66%.

The Shingles Prevention Study Group, which conducted the Veterans Affairs Cooperative Study No. 403, studied a live attenuated vaccine in 38,546 adults 60 years of age or older. Although the effect of zoster vaccine on the incidence of herpes zoster was lower among older subjects, the effect on the severity of illness was greater.

Cell-mediated immunity is the key to the protective effect of the vaccine. The minimum potency of the zoster vaccine was at least 14 times greater than that of Varivax, the vaccine currently licensed to prevent the varicella–zoster virus (VZV). A preliminary study indicates that potencies of that magnitude are required to elicit a significant increase in the cell-mediated immunity to VZV among older adults, the study group says.

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Head-to-Head Study of Two Popular Treatments for Chronic Lung Disease

Although the combination treatments of salmeterol/fluticasone propionate (e.g., Advair® Diskus, GlaxoSmithKline) and ipratropium/albuterol (Combivent®, Boehringer Ingelheim) have been widely used to treat chronic obstructive pulmonary disease (COPD), only one published study has compared these agents head to head. Investigators from National Jewish Medical and Research Center in Denver, Baylor College of Medicine in Houston, and St. Francis Hospital and Medical Center in Hartford, Connecticut, conducted an eight-week investigation building on that earlier study.

In the study, 180 patients with moderate-to-severe COPD were given fluticasone propionate 250 mcg/salmeterol 50 mcg (FSC 250/50) mcg twice daily; 181 patients received ipratropium 36 mcg/albuterol 206 mcg (36/206) four times daily.

Although both treatments improved lung function and symptoms, the FSC regimen improved dyspnea and daytime and nighttime symptoms and reduced the number of times that rescue albuterol was needed. The two treatments were similar with respect to COPD exacerbations and other adverse drug events (ADEs).

Purpose: The device is indicated for type-1 and type-2 diabetic patients, 18 years of age and older, who desire better glucose control to improve their health and quality of life.

Benefit: Current standards for assessing blood sugar control include glycosylated hemoglobin (HbA1c) testing and fingerstick measurements, yet both have limitations. The HbA1c test, which measures blood glucose control over a period of two to three months, yields an average value. Fingersticks reveal a value at a single moment in time, and patients must usually perform the test four to five times a day. Both tests might not reveal day-to-day fluctuations that can lead to diabetes-related complications.

Real-time readings enable patients to view glucose trends throughout the day and night and allow them to intervene earlier to reduce the frequency or severity of highs and lows. Patients can also discover how diet, exercise, medication, and lifestyle affect glucose levels.


Name: Portable Cardiac Monitor
Manufacturer: Criticare Systems Inc., Waukesha, WI
Approval Date: August 16, 2005

Use Classification: This advanced system is used to monitor physiological parameters of patients in many types of health care environments.

Description: The system can incorporate certain popular oxygen saturation and temperature measurement technologies as options to satisfy specific clinical and economic requirements.

Purpose: The monitor captures important physiological data in a rapid,
flexible manner.

**Benefit:** The unique design allows a wide variety of optional configurations that can be tailored for specific market requirements. The product line was designed for worldwide marketing and offers different systems to meet the needs of particular clinical environments.

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

**Name:** Invader® UGT1A1 Molecular Assay  
**Manufacturer:** Third Wave Technologies, Inc., Madison, WI  
**Approval Date:** August 22, 2005  
**Use Classification:** The assay is used to identify patients who might be at increased risk for adverse reactions to the chemotherapy drug irinotecan (Camptosar®, Pfizer Oncology) by detecting and identifying specific mutations in the UGT1A1 gene that have been associated with that risk.

**Description:** The test detects differences in the UGT1A1 gene, which makes an enzyme (UDP-glucuronosyl transferase 1A1) that helps to metabolize drugs. These differences affect the amount of irinotecan entering the bloodstream. Higher blood concentrations of the drug may lead to more adverse effects.

**Purpose:** Irinotecan, which is used to treat colorectal cancer, was recently relabeled to include dosing recommendations based on a patient’s genetic profile. Selecting the correct dose is a challenge in the treatment of cancer patients.

**Benefit:** This is the first FDA-approved pharmacogenetic test for use as a companion diagnostic to a specific drug therapy. Future data might be able to link the test to other drugs. The test is built on the accuracy, scalability, and ease of use of the unique patented Invader® chemistry. In a study submitted to the FDA as part of the company’s clearance application, the assay was 100% accurate.

**Sources:** www.pharmacyonesource.com; www.prnewswire.com/cgi-bin/stories.

**Warning Letter: Boston Scientific Devices**

The FDA has sent the Boston Scientific Corporation a warning letter identifying “serious regulatory problems” in some of its medical devices that were shipped from a distribution plant in Quincy, Massachusetts. Despite the existence of a quality control problem, the devices were shipped to hospitals. The letter mentioned Taxus drug-coated stents, Vaxcel low-profile infusion ports, and Symmetry balloon catheters.

Inspectors found that these devices were adulterated and that the company’s methods or facilities had not conformed to Current Good Manufacturing Practice requirements.