NEW DRUGS

Stendra For Erectile Dysfunction

Oral avanafil (Stendra, Vivus) is now approved for men with erectile dysfunction. The drug is taken 30 minutes before sexual activity.

Avanafil, a phosphodiesterase type-5 (PDE_5) inhibitor, helps to increase blood flow to the penis. Men who take nitrates should not use avanafil because the combination can result in a sudden drop in blood pressure. PDE_5 inhibitors may also cause color vision changes, a sudden loss of vision in one or both eyes, and a sudden loss or decrease in hearing.

Avanafil is discussed in detail in the Pharmaceutical Approval Update column on page 332.

Source: FDA, April 27, 2012

Generic Versions of Plavix

The FDA has approved several generic versions of Plavix (clopidogrel bisulfate, Bristol-Myers Squibb/Sanofi). Clopidogrel helps to reduce the risk of heart attack and stroke by inhibiting platelets from forming clots in the arteries.

A boxed warning mentions that clopidogrel might not be effective in patients with certain genetic factors that affect drug metabolism. In addition, the proton pump inhibitors omeprazole (Prilosec) and esomeprazole (Nexium), both made by AstraZeneca, reduce the effect of clopidogrel, leaving patients at a higher risk for heart attack and stroke.

Dr. Reddy's Laboratories, Gate, Mylan, and Teva received approval to sell the 300-mg strength of clopidogrel. Apotex Corp., Aurobindo Pharma, Mylan, Roxane Laboratories, Sun Pharma, Teva, and Torrent may sell the 75-mg strength.

Source: FDA, May 17, 2012

Elelyso, an Orphan Drug, For Type-1 Gaucher's Disease

Taliglucerase alfa injection (Elelyso, Pfizer/Protalix Bio Therapeutics) has been approved as an enzyme replacement therapy for patients with type-1 (non-neuropathic) Gaucher's disease, a rare genetic disorder. Patients with a deficiency of the enzyme glucocerebrosidase may experience liver or spleen damage, anemia, low platelet counts, and bone problems. Injections are given every other week to replace the missing enzyme.

The drug is expressed from carrot cells rather than from mammalian cells. By contrast, competitor drugs in this class—imiglucerase (Cerezyme, Genzyme/Sanofi) and velaglucerase alfa (Vpriv, Shire)—are expressed from Chinese hamster ovary cells and a human fibroblast cell line, respectively.

Source: FDA, May 1, 2012

NEW INDICATIONS

Votrient For Soft-Tissue Sarcoma

Pazopanib (Votrient, GlaxoSmithKline), a once-daily tablet, has been approved for the treatment of soft-tissue sarcoma in previously treated patients. Pazopanib is a selective tyrosine kinase inhibitor that targets growth factor receptors associated with angiogenesis and tumor cell proliferation. The drug was approved for the treatment of advanced renal cell carcinoma in 2009.

Pazopanib confers a risk of severe and potentially fatal liver damage. A boxed warning advises clinicians to monitor liver enzymes for at least the first 4 months of treatment. The drug is not approved for patients with adipocytic soft-tissue sarcoma or gastrointestinal stromal tumors.

Sources: FDA; GlaxoSmithKline, April 26, 2012

Afinitor and Noncancerous Kidney Tumors

Everolimus tablets (Afinitor, Novartis) have been approved for adults with renal angiomyolipomas and tuberous sclerosis complex (TSC) who do not need surgery immediately. A rare genetic disease, TSC causes the growth of various noncancerous tumors in the brain, kidney, and other vital organs and can lead to kidney failure and bleeding.

Taken once daily, everolimus blocks the uncontrolled activity of a protein, mTOR kinase, which promotes the development of the tumors in TSC.

Everolimus is already approved for the treatment of advanced renal cell carcinoma that has progressed after treatment with sunitinib (Sutent, Pfizer) or sorafenib (Nexavar, Bayer/Onyx). It is also approved for patients with subependymal giant-cell astrocytoma associated with TSC who need treatment but who cannot undergo tumor excision and for patients with progressive metastatic or inoperable neuroendocrine pancreatic tumors.

Everolimus is available in 5-mg and 10-mg dosage forms.

Sources: FDA; www.afinitor.com; Monthly Prescribing Service, www.empr.com

Levaquin to Prevent Plague

The antibacterial agent levofloxacin (Levaquin, Ortho-McNeil/Janssen) is now approved for the prevention and treatment of plague. The most famous form of the disease, bubonic plague ("The Black Death"), devastated Europe in the mid-1300s.

The new indication was approved under the FDA's Animal Efficacy Rule, which allows evidence from animal studies to guide regulatory approval if it is not feasible or ethical to conduct studies in humans. Human trials of the drug would be difficult because plague—caused by the bacterium *Yersinia pestis*—is rare, with only about 1,000 to 2,000 cases reported worldwide each year.

In April, an FDA advisory committee recommended the approval of both levofloxacin and ciprofloxacin (Cipro, Bayer) on the basis of a study of African green monkeys. *Y. pestis,* which is primarily an animal pathogen, can also infect the lungs (pneumonic plague) and the blood (septicemic plague) in humans.

Source: FDA, April 27, 2012

NEW FORMULATION

Irinotecan HCl Injection

Sagent Pharmaceuticals has announced the launch of irinotecan injection, the generic form of Camptosar, a chemotherapy drug. The product will be available in two latex-free, preservative-free, single-dose vials.

Irinotecan HCl is an antineoplastic agent of the topoisomerase I inhibitor class. It is indicated in combination with 5-fluorouracil and leucovorin for metastatic carcinoma of the colon or rectum after initial fluorouracil-based therapy.

Source: Sagent, www.sagentpharma.com, May 17, 2012

DRUG NEWS

Warning and Label Change for Gilenya

Fingolimod (Gilenya, Novartis), which is used to prevent flare-ups in multiple sclerosis, should not be given to patients with pre-existing or recent heart conditions or stroke. The warning follows the FDA's evaluation of a report of a patient who died within 24 hours after receiving the first dose of fingolimod.

Although it was not concluded that the death was related to fingolimod, the FDA has concerns about the drug's cardiovascular effects after the first dose. The maximum heart rate–lowering effect of the drug usually occurs within 6 hours of taking the first dose, but this effect can occur as late as 20 hours after the first dose.

The FDA advised that patients be monitored for signs of bradycardia for at least 6 hours after the first dose, undergo hourly pulse and blood pressure monitoring, and have an electrocardiogram starting therapy and at the end of the observation period. Monitoring should also continue overnight in patients who experience severe bradycardia after the first dose of fingolimod, who have pre-existing conditions in whom bradycardia may be poorly tolerated, who take other drugs that cause bradycardia, or who have a prolonged QT interval before fingolimod therapy. Patients should seek immediate care if they experience dizziness, fatigue, or arrhythmias with treatment.

Sources: Health Day, http://health.news.com; Med Page Today, May 14, 2012

Few Benefits of Urinary Incontinence Drugs in Women

Drugs for urgency urinary incontinence (UUI) are not as effective as investigators had hoped they would be, and adverse effects cause many women to stop taking them after a year of treatment. A study conducted at the University of Minnesota suggests that these agents should be reserved for specific patients.

Researchers analyzed data from 94 randomized trials. Overall, the rates of continence and clinical improvement were better with drugs than with placebo. However, fewer than 200 cases of continence per 1,000 treated patients with UUI were attributable to drug treatment. Patients with frequent UUI were helped slightly more with some drugs, such as tolterodine (Detrol, Pfizer) and fesoterodine (Toviaz, Pfizer), than with placebo. Trospium (Sanctura, Allergan) was better than placebo in resolving UUI in patients experiencing fewer than five episodes per day.

Any benefits derived from drug therapy usually were not long-lasting because adverse effects often forced women to stop treatment. More than 50% of the patients taking UUI drugs stopped taking them after 1 year. The 5-mg dose of solifenacin (VESIcare, Astellas) was associated with the lowest discontinuation rate.

Adverse drug effects ranged from bothersome, such as dry mouth and constipation, to dangerous. Tolterodine was associated with a risk of hallucinations during long-term treatment. Older women using UUI drugs with antihistamines or cytochrome P450 inhibitors had an increased risk of ventricular arrhythmia or sudden death. Not surprisingly, adverse effects were more common in women taking seven or more concomitant medications.

Because all of the drugs studied were similar in effectiveness, the researchers suggested that therapeutic choices should be based on a drug's safety profile and the patient's age. Trospium, oral oxybutynin (Ditropan, Ortho-McNeil), and darifenacin (Enablex, Warner Chilcott) improved UUI in older women. Women with UUI who had not responded to previous treatments might benefit from solifenacin; the 5-mg dose was associated with improved quality of life.

Interestingly, oxybutynin transdermal patches (Oxytrol, Watson Pharma) did not improve quality of life when compared with placebo, and patients tended to be dissatisfied with this delivery system. Oxybutynin was often associated with dry mouth; however, in one study, severe dry mouth was less common with the transdermal formulation than with the immediate-release oral formulation.

Few randomized controlled trials have examined how patient characteristics might modify drug effects, and none of the trials provided strong evidence for individualized treatment decisions.

UUI is discussed in the article on urinary incontinence on page 348.

Source: *Ann Intern Med*, April 9, 2012

Azithromycin and Sudden Death

Patients who took azithromycin (Zithromax, Pfizer), for 5 days had a slightly increased risk of sudden cardiac death compared with those receiving amoxicillin (e.g., Amoxil, GlaxoSmithKline) or no antibiotics. The small risk was greater among patients with the most risk factors for cardiovascular disease at baseline. Some deaths might have occurred as a result of differences in illness severity.

Researchers examined data from patients enrolled in the Tennessee Medicaid program between 1992 and 2006. In the study, the risks from cardiovascular death were similar for ciprofloxacin (Cipro, Bayer) and amoxicillin and for levofloxacin (Levaquin, Janssen) and azithromycin. A 10-day course of ciprofloxacin was not associated with an increase in mortality risk when compared with amoxicillin, but when a 5-day course of azithromycin was compared with the first 5 days of a course of ciprofloxacin, the hazard ratio for cardiovascular death was 3.49. There also was a trend toward an increase in cardiovascular death for levofloxacin.

In rare cases, levofloxacin has caused serious arrhythmias and sudden death; the new study suggests that azithromycin has a similar level of adverse cardiac effects. However, the findings should be interpreted with caution. Azithromycin might have been prescribed for sicker patients who were affected by the drug's proarrhythmic properties. It was not known how many deaths were drug-related and how many were illness-related. Patients who took azithromycin were more likely to have respiratory problems and to be taking heart and blood pressure medications.

Possible confounding factors included cardiovascular disease risk factors, including smoking and diet. Some causes of death might also have been misclassified. Nonetheless, the researchers concluded that azithromycin was associated with a small absolute increase in cardiovascular deaths.

Patients should not stop taking azithromycin without obtaining medical advice. The FDA emphasized that health care professionals should be aware of the potential for prolongation of the QT interval and heart arrhythmias in patients taking antibacterial drugs.

Sources: *N Engl J Med* 2012;366:1881–1890 (May 17); www.medscape.com, May 16, 2012

HDL-Cholesterol Not So 'Good'

Boosting high-density lipoprotein-cholesterol (HDL-C) levels might not be as beneficial for reducing the risk of myocardial infarction (MI) as previously thought. A genetic variant that substantially raises HDL-C levels did not alter the risk of MI, whereas genetic polymorphisms related to plasma low-density lipoprotein-cholesterol (LDL-C) were consistently associated with an increased risk of MI.

The data question the concept that raising plasma HDL-C translates into a lower risk of MI. In May, Roche stopped the phase 3 dal-OUTCOMES trial of dalcetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, after it was shown that this HDL-C–boosting drug did not reduce cardiovascular adverse events. The AIM–HIGH study, in which niacin was given with statin therapy, showed that the vitamin increased HDL-C levels but did not reduce death rates from heart disease, nonfatal MI, ischemic stroke, acute coronary syndrome, or coronary or cerebral revascularization. A trial of torcetrapib, another CETP inhibitor, was stopped in late 2006 because the drug increased the risk of death and cardiovascular events.

In the present study, it was concluded that lifestyle or medication interventions that raise HDL-C levels cannot be assumed to lower the risk of MI.

Sources: *Lancet, The New York Times*, May 16, 2012; heart*wire*, May 17, 2012

Victrelis for Hepatitis C: Do Not Use With HIV Drugs

The FDA has issued a warning against using the hepatitis C drug boceprevir (Victrelis, Merck) with anti-HIV agents that contain the protease inhibitor ritonavir (Norvir, Abbott) because of potentially dangerous interactions. However, patients who are taking boceprevir and an HIV regimen containing ritonavir should not stop therapy without consulting their physicians.

In February, the FDA warned of drug interactions between boceprevir and three HIV medications boosted with ritonavir: atazanavir (Reyataz, Bristol Meyers-Squibb), lopinavir (Kaletra, Abbott), and darunavir (Prezista, Janssen).

Approved in 2011, boceprevir targets the NS3/4A protease of hepatitis C. Ritonavir is a weak HIV protease inhibitor that boosts the action of other anti-HIV drugs.

The prescribing information for another hepatitis C agent, telaprevir (Incivek, Vertex), already includes cautions about drug–drug interactions with HIV medications.

In a study of healthy volunteers, boceprevir with ritonavir-boosted HIV protease inhibitors reduced exposure to the HIV drugs and vice versa; boceprevir reduced average trough levels of ritonavir-boosted atazanavir by 49%, lopinavir by 43%, and darunavir by 59%. Administering ritonavir-boosted atazanavir did not alter the exposure of boceprevir, but combining it with lopinavir/ritonavir or darunavir/ritonavir decreased the exposure of boceprevir by 45% and 32%, respectively.

Source: Med Page Today, April 26, 2012

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Statins May Lower Death Rates From Stroke

Patients who were using statins at the time that they had a stroke were less likely to die in the hospital than patients who were not taking the cholesterol-lowering drugs, according to a study from the 2012 annual meeting of the American Academy of Neurology, held in April.

Among stroke patients taking statins, the early mortality rate in the hospital was 2.1%, compared with 12.5% in similar patients who were not taking statins before being admitted for stroke. This difference also applied to patients who did not have high cholesterol levels but who were taking statins for heart disease or diabetes. Among these patients, the early in-hospital mortality rate was 2.5%, whereas that rate for non-statin users was 7.0%.

The researchers were surprised to find that statin therapy among those who did not have cholesterolemia appeared to improve outcomes. The statin patients also tended to do better at hospital discharge.

Source: Med Page Today, April 26, 2012

Treating Diabetic Children Is a Challenge

According to a long-term study, the only medication approved in the U.S. for the treatment of children with type-2 diabetes—generic metformin—appears to be largely ineffective. Fewer than half of the participants taking metformin alone achieved glucose control despite good compliance. The findings suggested that more than one drug is needed to control diabetes without resorting to insulin.

Type-2 diabetes had been viewed as a disease that affected adults until it became more common among adolescents in the previous 15 to 20 years, along with rising rates of obesity.

The risks of heart attack, stroke, kidney disease, blindness, amputation, and infertility in adult life are increased in children with diabetes because the risk of complications grows with the duration of the disease. Minority children are at a higher risk than Caucasian children, and girls are at higher risk than boys.

In the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study, after a follow-up period of about 4 years, 52% of patients receiving metformin alone failed to achieve blood glucose control, compared with 47% who received metformin plus a lifestyle change and with 39% who received metformin plus rosiglitazone (Avandia, GlaxoSmithKline). Only the metformin/rosiglitazone combination was considered superior to metformin. However, the use of rosiglitazone was sharply curtailed in the U.S. in 2010 after the drug was linked to an increase in heart attacks.

Sources: *N Engl J Med* (online); Med-Page Today, April 29, 2012; *The Wall Street Journal,* April 30, 2012

Does Switching From Xarelto To Warfarin Increase Stroke Risk?

Patients with atrial fibrillation (AF) who are switched from rivaroxaban (Xarelto, Janssen) to warfarin may experience an increased risk of stroke, according to a recent subanalysis of the ROCKET-AF trial.

At the completion of this study, the risk of stroke for those who switched from rivaroxaban to warfarin was 6.42 per 100 patient-years compared with 1.73 per 100 patient-years for those who continued with warfarin. However, patients who temporarily or permanently stopped rivaroxaban or warfarin during the trial had similar rates of stroke or non–central nervous system embolism.

Patients who take oral anticoagulants are sometimes advised to stop taking these drugs before surgery because of side effects. However, it is unclear how to provide optimal anticoagulation coverage during periods of transition.

In the original ROCKET–AF trial, rivaroxaban was found to be non-inferior to warfarin in preventing stroke and blood clots in patients with moderate-risk to high-risk nonvalvular AF. The risk of bleeding was also similar with the two treatments. As a result, the FDA approved rivaroxaban for this patient population. However, a warning was issued about increased rates of stroke and blood clots after discontinuation of rivaroxaban.

Researchers enrolled 8,245 patients who temporarily stopped treatment for 3 days or more while they were taking either rivaroxaban or warfarin; 4,895 patients who permanently stopped taking either drug; and 9,239 patients who were switched to open-label therapy (more than 90% of them to vitamin K antagonists). The most common reasons for temporarily interrupting treatment included surgery or invasive procedures, non-bleeding adverse events, and subject error. The most common reasons for early permanent cessation of treatment included non-bleeding adverse events, withdrawal of consent, and the investigator's belief that the clinical efficacy endpoint had been reached.

The researchers found no differences in the rates of stroke or blood clots related to temporary or permanent discontinuations or a combination of both. However, there was a greater risk of a primary event, particularly stroke, in patients who switched from rivaroxaban to warfarin at the end of the study as well as a greater risk of the combined secondary endpoint of stroke, heart attack, and death from vascular disease.

At 3 months after being switched to open-label therapy, 81% of the warfarin group had a therapeutic International Normalized Ratio (INR), compared with 49% of the rivaroxaban group. This dif-

ference might explain the higher rate of adverse events in the study drug arm, according to one investigator.

Sources: American Heart Association Emerging Science Series, Abstract 141, 2012; Med Page Today, April 26, 2012

Risks of Opioid Treatment In War Veterans

Many veterans return home from combat not only with physical health problems but also with comorbid mental health problems, notably post-traumatic stress disorder (PTSD). Veterans with PTSD are at high risk for substance abuse and misuse of prescription pain medications, such as opioids, say researchers from California and Indiana. In their study, veterans returning from Iraq and Afghanistan with mental health diagnoses, especially PTSD, were likely to receive opioids for pain and were just as likely to have adverse clinical outcomes, including injury to themselves or others.

The study population consisted of 141,029 Iraq and Afghanistan veterans who received a diagnosis of new noncancer pain within 1 year after entry into the Veterans Affairs health system. Most of the veterans had two or more pain diagnoses, and half had received at least one mental health diagnosis, including PTSD.

All veterans were observed for 1 year after the initial pain diagnosis to determine whether they received an opioid prescription and whether they experienced accidents resulting in injuries, opioid-related accidents and overdose, and self-inflicted injuries during that year.

Of the veterans with pain diagnoses, 15,676 (11%) received prescription opioids for 20 or more consecutive days. Veterans with PTSD were more likely to receive opioids for pain diagnoses than those without mental health disorders (17.8% vs. 6.5%, respectively). Veterans with mental health disorders but not PTSD (e.g., depression, anxiety, or traumatic brain injury) were also more likely to receive opioids compared with veterans without mental health disorders (11.7% vs. 6.5%, respectively).

Moreover, of the veterans who were prescribed pain medications, those with PTSD were more likely than those without mental health disorders to receive higher-dose opioids (22.7% vs. 15.9%, respectively); to receive two or more opioids concurrently (19.8% vs. 10.7%%, respectively); and to receive sedative hypnotics concurrently (40.7% vs. 7.6%, respectively).

Veterans with mental health disorders who were prescribed opioids had about double the risk of an emergency department or inpatient admission for alcohol-related, drug-related, or opioid-related accidents and overdose, and double the risk of self-inflicted or violence-related injuries, compared with veterans without mental health disorders. Rates of adverse clinical outcomes were highest among veterans with PTSD, with or without another mental health diagnosis.

Veterans with mental health problems tend to use the VA's primary care system rather than specialized mental health facilities. In this study, 77% of opioids were prescribed by VA primary care physicians. However, most of these physicians lacked specialized training in managing comorbid pain and PTSD.

When treating patients with both mental and physical pain, in addition to high-risk medical and psychiatric comorbidities, the physicians might have prescribed high-dose, high-risk opioids for patients who could not handle them. Instead, the authors suggest, these patients may have benefited from nonpharmacological therapies and non-opioid analgesics, as well as from integrated treatments that simultaneously target both mental and physical pain.

Source: *JAMA* 2012(9);307:940–947 (March)

Sublingual Therapy for Allergies

Subcutaneous (SQ) immunotherapy for allergies has one major drawback; because it's an injection, adherence is poor, especially among children. Even among adults, adherence to SQ therapy is low. By contrast, sublingual (SL) immunotherapy is economical and easy to use.

Why aren't SL drugs available in greater quantities in the U.S.? One reason is that the efficacy of these formulations is still being debated.

Researchers from Wisconsin evaluated quality-of-life outcomes in 51 adults with allergic rhinoconjunctivitis. The patients were recruited from Allergy Associates of La Crosse, which had been offering SL immunotherapy for 41 years. Most patients had positive reactions to more than one allergen, including dust, grass, trees, and weeds. Doses for each patient were tied to skin test results and were adjusted over the course of treatment.

After 4 months of treatment, new patients had fewer activity limitations; non-nose/non-eye, nasal, and eye symptoms, and emotional problems. Patients reported improved sleep, although this did not reach statistical significance. Sneezing and irritability decreased over the first 4 months of therapy. Improvements were sustained after 10 to 12 months.

Source: *J Allergy*, February 2012 (online)

RESEARCH NEWS

Brain Changes and Sleep Problems in the Elderly

A new study might help explain why elderly people often experience trouble sleeping at night and are drowsy during the day. Older animals have shown cellular changes in the brain "clock" that sets sleep and wakeful periods.

Like humans, mice experience shifts in daily activities and sleep patterns as they age. Researchers in the Netherlands

studied the electrical activity of cells in the suprachiasmatic nucleus (SCN), an area of the brain that helps to establish sleep–wake cycles. Aged mice showed disrupted sleep behavior and weakened brain network activity in the SCN; however, changes in individual SCN cells, not just in their networks, were also observed. In fact, the changes at the single-cell level were more severe than the changes at the network level. This represents a shift in understanding of the effects of aging on the brain.

The researchers made electrophysiological recordings from isolated SCN neurons—a difficult step, given the advanced age of the animals and the small size of the neuron. They found that aged SCN neurons lacked day–night rhythms in some membrane properties. The investigators also identified age-related reductions of specific potassium currents, which affect the rhythmic firing of neurons.

Because potassium and other ion channels can be manipulated with drugs, this study provides a possible target for therapy that might reduce the age-related decline in the sleep–wake cycle.

Source: *J Neurosci*, April 25, 2012

Nitroglycerin and Prostate Cancer

Researchers at Queen's University in Ontario, Canada, are planning to study the effects of nitroglycerin, a century-old heart drug for relieving angina, on prostate cancer. If the trial is successful, it could provide a radically new way to treat cancers. Previous work had shown that nitric oxide–mimicking agents, such as nitroglycerin, were effective in overcoming the resistance of cancer cells to immune attack.

In 2009, the investigators found that nitroglycerin slowed disease progression in a small study of recurrent prostate cancer. They spent more than a decade looking at the interactions between cancer and its host environment and recently identified an enzyme responsible for making cancer cells resistant to immune attack. The new study will evaluate the potential benefits of low-dose nitroglycerin, given via a skin patch, in men with early, recurrent prostate cancer. Researchers are planning a 1-year trial to learn whether nitroglycerin can boost the body's natural immune response to cancer.

Source: PARTEQ Innovations, April 26, 2012

NIH News

Turning Theories Into Treatments

The National Institutes of Health (NIH) is planning a collaborative program that will match researchers with pharmaceutical industry compounds to help scientists explore new treatments for patients. The agency's new National Center for Advancing Translational Sciences (NCATS) will work with Pfizer, AstraZeneca, and Eli Lilly. These companies have agreed to make dozens of their compounds available for the initiative's pilot phase.

Researchers have identified the causes of more than 4,500 diseases, but it has proved difficult to translate this knowledge into new therapies; effective treatments exist for only about 250 of these conditions. NCATS was established last year to help address this gap.

Initially, some compounds were not effective for the specific use for which they were developed. Azidothymidine (AZT, zidovudine), for example, failed to show efficacy against cancer but was later found to be effective against HIV infection.

President Obama's budget for fiscal year 2013 proposed $575 million for NCATS; about $20 million will be used for research grants to promote preclinical and clinical feasibility studies. These investigations will test more than 20 compounds provided by industry partners. The participating companies will retain ownership of their compounds, and academic research partners will own any intellectual property they discover through the project, with the right to publish the results of their work.

Source: NIH, May 3, 2012

Viread Does Not Affect Infant Birth Weight or Size

A study from the National Institutes of Health has found that infants born to women who used tenofovir (Viread, Gilead) as part of an anti-HIV drug regimen during pregnancy did not weigh less at birth. In addition, they were not shorter than infants born to women who used anti-HIV drug regimens that did not include tenofovir during pregnancy. At 1 year of age, however, children born to the tenofovir-treated mothers were slightly shorter and had a slightly smaller head circumference (about 1 cm each, on average), compared with infants whose mothers did not take tenofovir.

Earlier investigations had found that laboratory animals exposed to tenofovir in the womb were smaller at birth than their unexposed peers, but the newer study did not identify any serious concerns with tenofovir during pregnancy. The researchers called for additional studies to follow the children as they grow in order to identify potential long-term effects of treatment.

Source: NIH, May 1, 2012

DEVICE NEWS

New Use for Respiratory Panel

The FDA has expanded the indication for the FilmArray Respiratory Panel (Idaho Technology). The test can simultaneously detect both viral and bacterial causes of respiratory infection from a single sample. Three bacteria have been added—*Bordetella pertussis*, the cause of

whooping cough; *Mycoplasma pneumoniae,* a common cause of respiratory infection; and *Chlamydophila pneumoniae*, which causes community-acquired pneumonia. The test was originally approved in December 2011.

Source: FDA, May 15, 2012

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: Percutaneous Surgical Set

Manufacturer: Ethicon Endo-Surgery, Inc./Johnson & Johnson, Cincinnati, Ohio

Approval Date: April 30, 2012

Purpose: The set is intended to be used during minimally invasive laparoscopic abdominal surgery.

Description: A camera and surgical instruments are inserted through one or more small incisions in the abdomen.

Benefit: This is the first surgical set that can be assembled and disassembled inside the body. With a laparoscopic procedure, fewer and smaller incisions are needed and patients usually have shorter hospital stays, reduced recovery time, and less pain.

The FDA reviewed data for the device using the *de novo* classification process. The Percutaneous Surgical Set represents the fourth device that was granted a *de novo* petition this year.

Caution: The set is indicated for use in the abdomen only. Associated risks include device failure, clinician error, damage to the abdominal cavity, infection, and tissue inflammation.

Source: www.fda.gov; *The Wall Street Journal*, May 1, 2012

Name: Rotor-Gene Q MDx

Manufacturer: Qiagen, The Netherlands

Approval Date: April 17, 2012

Purpose: This automated molecular detection platform is based on real-time polymerase chain reaction (PCR) technology. The system is intended for *in vitro* diagnostic use with FDA-approved nucleic acid tests, such as those used for hepatitis B and C and HIV infections, in clinical laboratories.

Description: A centrifugal rotary design amplifies and quantifies DNA molecules, enabling thermal and optical uniformity and a rapid data-acquisition rate. A heating and cooling design allows optimal reaction conditions to be achieved. With a choice of up to six excitation sources and six detection filters, combined with a short, fixed optical path, the device can be used for multiplex reactions. Minimum fluorescence variability between samples is ensured, and the need for calibration or compensation is eliminated.

The tube spins in a chamber of moving air, keeping all samples at the same temperature during rapid thermal cycling. Detection is also uniform. When each tube aligns with the detection optics, the sample is illuminated and the fluorescent signal is rapidly collected from a single, short optical pathway.

Benefit: The rotary format ensures thermal and optical uniformity between samples, which is crucial for precise, reliable analysis.

Source: www.qiagen.com

Name: *artus* Influenza A/B Rotor Gene RT-PCR Kit

Manufacturer: Qiagen, The Netherlands

Approval Date: April 17, 2012

Purpose: The kit is the first in a series of *in vitro* molecular diagnostics that the company plans to launch on the Rotor-Gene Q MDx platform in the U.S.

Description: The real-time PCR *in vitro* test is used to detect and identify influenza A and B viral infections in nasopharyngeal swab samples using the Rotor-Gene Q MDx instrument.

Benefit: Because many flu-like symptoms may be caused by various pathogens, testing for influenza viruses helps to reduce the inappropriate use of antibiotics and to determine whether antiviral therapy would be appropriate. In the U.S., approximately 250,000 influenza tests are performed in laboratories during the annual flu season. Former versions of the kit were among the most widely used assays in the influenza epidemics of 2005–2006 and 2009–2010 worldwide.

Sources: www.genengnews.com; www.news-medical.net; http://seekingalpha.com

Product Recall: Epinephrine Injection, USP

On April 24, 2012, American Regent voluntarily recalled Epinephrine Injection, USP, 1:1000, 1-mL ampules, lot No. 1395, NDC No. 0517-1071-25 (expiration date, July 2012). Discoloration and small visible particles were present in some ampules.

Potential adverse events after intravenous administration of solutions that contain particulates may include disruption of blood flow within small pulmonary blood vessels, localized inflammation, and granuloma formation. Muscle and adipose tissue damage may occur if intramuscular or subcutaneous solutions containing particulates are injected.

It is possible that intraspinal injections that contain particulates might cause inflammation. It is unknown whether topical ocular administration with epinephrine solutions containing particles would cause adverse events, but ocular pain or irritation may result.

The lot was distributed to wholesalers and distributors nationwide. Hospitals, retail pharmacies, clinics, physician offices, and other health care facilities and providers should not use this product.

Source: www.fda.gov/safety/recalls/ucm301783.htm ■