**NEW DRUGS**

**Eliquis for Nonvalvular Atrial Fibrillation**

Apixaban (Eliquis, Bristol-Myers Squibb/Pfizer), an oral anticoagulant, has been approved to reduce the risk of stroke and systemic embolism in patients with atrial fibrillation not caused by a heart-valve problem.

In a clinical trial of more than 18,000 patients, apixaban therapy resulted in fewer strokes compared with warfarin (Coumadin, Bristol-Myers Squibb).

Patients with prosthetic heart valves or with valvular atrial fibrillation should not take apixaban. Bleeding is the most serious risk with this medication, and no agent is available to reverse the drug’s anticoagulant effect.

Apixaban is being dispensed with a patient medication guide.

Recently approved competitors to apixaban include dabigatran (Pradaxa, Boehringer Ingelheim) and rivaroxaban (Xarelto, Janssen/Bayer).


**Sirturo for Pulmonary TB**

The FDA has approved bedaquiline (Sirturo, Janssen) as part of combination therapy to treat adults with multidrug-resistant pulmonary tuberculosis (TB) when an alternative is not available. Multidrug-resistant TB occurs when *Mycobacterium tuberculosis* becomes resistant to isoniazid and rifampin, two powerful drugs most commonly used to treat TB. Bedaquiline inhibits an enzyme needed by the organism to replicate and spread throughout the body.

A boxed warning states that the drug can prolong the QT interval, which can lead to potentially fatal arrhythmias. Janssen is providing educational materials to help ensure appropriate use of the drug.

Bedaquiline was granted an orphan product designation.

Source: FDA, December 28, 2012

**Varizig Relieves Chickenpox Symptoms**

Varizig (Cangene Corp., Canada) has been approved to reduce the severity of varicella zoster virus (VZV) infections in high-risk individuals when given within 4 days after exposure. Varizig, a varicella zoster immune globulin (VZIG) preparation, is the only immunoglobulin approved in the U.S. for VZV after exposure.

VZV causes chickenpox in children and shingles in adults. Varizig was designated as an orphan drug by the FDA. The antibody preparation is obtained from the plasma of healthy donors with high anti-VZV antibody levels. The donated plasma comes from FDA-licensed collection facilities in the U.S. and Canada.

Most people in the U.S. have immunity to VZV from vaccinations or from having had chickenpox during childhood. However, people with no immunity to VZV who are exposed to the virus may experience severe infections that can be fatal. Those at high risk include immunocompromised children and adults, newborns, pregnant women, premature infants, children younger than 1 year of age, and adults with no immunity to VZV. Occasionally, healthy people without immunity to VZV may contract severe infections.

Two or more injections are given, according to body weight, within 96 hours after exposure.

Source: FDA, December 21, 2012

**Juxtapid Reduces Low-Density Cholesterol in Rare Disorder**

Aegerion’s lomitapide capsules (Juxtapid) have been approved to reduce low-density lipoprotein-cholesterol (LDL-C), total cholesterol, apolipoprotein B, and non–high-density lipoprotein-cholesterol (non–HDL-C) levels in patients with homozygous familial hypercholesterolemia (HoFH). This drug is intended for use in combination with a low-fat diet and other lipid-lowering treatments.

In patients with HoFH, a rare inherited condition, LDL-C is unable to be eliminated from the blood. In the U.S., HoFH occurs in approximately one in one million individuals. Patients typically have heart attacks or die before age 30. Lomitapide interferes with lipid formation.

The capsules are taken once daily without food at least 2 hours after the evening meal. Patients should take supplements that contain fat-soluble vitamins and essential fatty acids daily during lomitapide therapy.

A boxed warning mentions a risk of liver toxicity. The FDA approved Lomitapide with a REMS and is requiring three
NEW DRUGS

DRUG NEWS

postmarketing studies.
Source: FDA, December 26, 2012

Botanical Fulyzaq for Diarrhea
In HIV/AIDS
Crofelemer (Fulyzaq, Salix/Napo) has been approved to relieve symptoms of noninfectious diarrhea in patients with HIV/AIDS who are taking antiretroviral therapy. The drug is taken twice daily.
Derived from the red sap of the Croton lechleri plant, crofelemer is the second botanical prescription drug approved by the FDA. In 2006, sinecatechins (Veregen, PharmaDerm) was approved to treat external genital and perianal warts. Physicians should rule out microbial causes of diarrhea before prescribing crofelemer.
Sources: FDA, December 31, 2012; DrugsUpdate.com, January 4, 2013

Uceris for Remission
Of Ulcerative Colitis
The FDA has approved budesonide (Uceris, Santarus/Cosmo) extended-release tablets for the induction of remission in patients with active, mild-to-moderate ulcerative colitis. This oral tablet utilizes a multimatrix system colonic delivery technology. The approved dose for adults is one 9-mg tablet taken orally once daily in the morning for up to 8 weeks.
Sources: Fierce Biotech, January 15, 2013; Santarus, http://ir.santarus.com

Generic Lamotrigine
Wockhardt has received the FDA’s approval to sell extended-release tablets of lamotrigine, a drug that is used in the treatment of epilepsy. Lamotrigine is the generic name for GlaxoSmithKline’s Lamictal XR. The tablets are available in 25-mg, 50-mg, 100-mg, 200-mg and 300-mg strengths.
Manufacturing will take place at the company’s facility in Aurangabad, India. The technology was developed in-house.

NEW INDICATION
Tamiflu for Infants
Oseltamivir (Tamiflu, Roche) is now approved for children as young as 2 weeks of age who have had influenza symptoms for no more than 2 days. Oseltamivir is the only agent approved to treat flu in patients younger than 1 year of age. The new age range does not apply to its use in prevention; that indication applies only to those 1 year of age and older.
The dosage for the younger age group must be calculated according to each child’s exact body weight (3 mg/kg twice daily for 5 days). Pharmacists will use a special dispenser for the smaller doses.
The FDA emphasized that treatment with oseltamivir is not an alternative to an annual influenza vaccination.

NEW FORMULATION
Fluarix Quadrivalent
GlaxoSmithKline may now sell the quadrivalent formulation of its influenza virus vaccine, Fluarix. The new approval marks the second wave of vaccines that offer protection against two types of both influenza A and B strains, which began with the early 2012 approval of FluMist Quadrivalent (influenza intranasal live-attenuated vaccine (AstraZeneca/ MedImmune). Fluarix Quadrivalent was approved for individuals 3 years of age and older and is the first widely indicated intramuscular vaccine in the seasonal influenza market. It is approved only for those between ages 2 and 49. Originally sold in a trivalent formulation, Fluarix was launched in Europe.
Source: GlobalData, December 19, 2012

No Pradaxa for Patients
With Mechanical Heart Valves
The oral anticoagulant dabigatran (Pradaxa, Boehringer Ingelheim) should not be prescribed for patients with mechanical heart valves. The RE-ALIGN trial was halted because patients taking dabigatran experienced more strokes and heart attacks, thrombi on their mechanical heart valves, and more bleeding after heart-valve surgery, compared with those taking warfarin.
Dabigatran was approved in 2010 for the prevention of stroke in patients with nonvalvular atrial fibrillation. Although there had been concern about bleeding risk and reports of deaths attributed to the drug, the FDA later determined that there was no excess risk of bleeding associated with dabigatran.
Adverse events have been associated with the drug’s use in patients with mechanical heart valves, but the drug has not been studied in patients with valves made from natural body tissues. Patients

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Lower Doses for Sleep Drugs

The FDA is requiring the manufacturers of Ambien, Ambien Controlled Release (CR), Edluar, and Zolpimist, all of which contain zolpidem for insomnia, to decrease the current recommended doses. New data show that zolpidem blood levels in some patients may be high enough the morning after use to impair activities that require alertness, such as driving.

Because zolpidem is eliminated more slowly in women than men, the recommended dosage for women is being lowered by half, from 10 mg to 5 mg for the immediate-release (IR) forms (Ambien, Edluar, and Zolpimist) and from 12.5 mg to 6.25 mg for the extended-release (ER) product (Ambien CR). For men, lower doses (5 mg for IR products and 6.25 mg for ER formulations) can be considered.

The risk of next-morning impairment is highest with ER forms. People who are currently taking 10 mg or 12.5 mg should continue taking these doses until they are advised how to make adjustments safely. Alertness can be impaired even in people who do not feel tired. The FDA is also evaluating other insomnia drugs, including nonprescription medications.

Source: FDA, January 10, 2013

Aspirin: Benefits and Risks

Few GI Problems With Prednisolone

Because aspirin and prednisolone are individually associated with adverse gastrointestinal (GI) events, giving them together might be expected to intensify that potential. However, in a retrospective analysis from Singapore, data from 142 cancer patients suggested that the clinical impact of any aspirin/prednisolone drug–drug interaction was minimal.

In earlier studies, the researchers had identified prednisolone and aspirin as one of the most prescribed interacting drug combinations among patients with cancer in Singapore. In the current study, the prevalence of adverse GI events was actually low, at 4%.

Aspirin/prednisolone was prescribed for a mean of 56 days. All patients received aspirin 100 mg daily, although one patient took 900 mg daily in three doses. The total daily dose of prednisolone varied from 1 to 100 mg, in one to three doses.

Nearly all patients received at least one gastrotoxic drug during the study period (usually antibiotics, thrombocyte-aggregation inhibitors, or nonsteroidal anti-inflammatory drugs) and 112 received at least one gastroprotectant agent (usually a proton pump inhibitor).

Of the six cases of GI adverse effects, four occurred within the 2 weeks after the drug–drug interaction period. Four patients had abdominal pain, diarrhea, dysphagia, and vomiting; three had signs of GI injury (duodenal ulcers, iron-deficiency anemia, and Mallory–Weiss tears).

Most patients had other risk factors that might have predisposed them to a GI event. Thus, although there was a weak association between GI events and aspirin/prednisolone therapy, the researchers concluded that the probability that an adverse event—even among patients experiencing GI events—was relatively low with the combination.

Source: Clin Ther 2012;34:2259–2267

Eye Damage

Aspirin may be associated with an increased risk of late-stage, age-related macular degeneration (AMD). In a longitudinal cohort study conducted at the University of Wisconsin in Madison, regular aspirin use over a 10-year period was associated with a 63% increased risk of late AMD but not early AMD. Five-year use of aspirin had no effect on either early or late AMD.

In the Beaver Dam Eye Study, adults (43 to 86 years of age) underwent eye examinations every 5 years for 20 years. Patients were asked if they had regularly used aspirin at least twice weekly for more than 3 months. During a mean follow-up of about 15 years, there were 512 cases of early AMD and 117 cases of late AMD.

Aspirin use for 10 years before the retinal examination was associated with a greater risk of late AMD. The estimated incidence of late AMD was 1.76% for regular aspirin users and 1.03% for non-aspirin users. The incidence of late AMD was also higher with 5 years of aspirin use, but the finding was not significant.

Regular aspirin use for more than 10 years was associated with neovascular AMD, but this was not tied to pure geographic atrophy (which causes retinal cells to die) or to early AMD with 5 years or 10 years of aspirin use.

No relationship was noted between long-term, 10-year use of nonsteroidal anti-inflammatory drugs (NSAIDs) or warfarin and the risk of AMD. The findings suggest that the mechanisms underlying aspirin’s relationship with late AMD might be different from its immediate effects on clotting, with aspirin possibly enhancing choroidal neovascularization. The researchers concluded that in the presence of injury, aspirin might encourage the growth of aberrant new vessels.

Sources: JAMA, December 19, 2012; MedPage Today, December 20, 2012

Biaxin and Miscarriage Risk

In a large cohort study from Denmark, use of the antibiotic clarithromycin (Biaxin, Abbott) in the first trimester of pregnancy was linked to an increased risk of miscarriage (by 56%) compared with women not taking the drug. However, there was no increase in the risk of birth defects.

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Cognitive Impairment, Adherence, and Heart Failure

Mild cognitive impairment can be easy to miss, but it may have a disproportionately significant impact on adherence to treatment in patients with heart failure. A study from Loma Linda, California, found a high prevalence of unrecognized cognitive impairment among 251 veterans and a robust association between the presence of cognitive impairment and poor adherence. In fact, of all the study variables, such as alcohol use and older age, only cognitive impairment was significantly associated with medication adherence.

Veteran outpatients with heart failure were screened for cognitive impairment, depression, and a tendency to adhere to the prescribed regimen. The results showed that 58% of the veterans had unrecognized cognitive impairment. Verbal learning, immediate recall, and delayed verbal memory were the variables that were most often impaired.

Patients without cognitive impairment had regimen-adherence rates of 78%, compared with 70% for those with mild cognitive impairment and 73% for those with severe cognitive impairment.

Age, African-American ancestry, use of alcohol, and depression were also risk factors for cognitive impairment.

Adherence worsened with mild cognitive impairment but did not continue to worsen with severe cognitive impairment. The researchers say this is important in clinical practice because mild cognitive impairment is easily missed. The patient may deny needing any help with taking their medications and may hide memory loss. It is also possible that patients with worse cognitive impairment were being helped by family members or others.

Both overusing and underusing prescribed medications were common, although there was no statistically significant pattern. Taking excess medications is a potentially serious safety problem, compounded when multiple drugs are prescribed by multiple health care providers. In this study, it was common to find patients with several bottles of the same drug who took tablets from all the bottles. Patients also usually knew their medications by color and shape rather than by name or indication. This is important in the VA system, because generic drugs are mailed to patients’ homes from a centralized pharmacy. A change in vendor used by the pharmacy often meant a change in the drug’s appearance, with patients not recognizing that the new tablet was the same drug as before.

Although cognitive impairment is not recognized in current clinical practice guidelines as a risk factor for poor adherence, many cognitively impaired patients do not remember what their health care provider has just instructed them to do after they leave the clinic. The researchers recommend screening all patients with heart failure using a tool such as the St. Louis University Mental Status (SLUMS) test, which takes only 10 minutes or less.

In this study, the average patient was mildly depressed. Depression can affect the ability to process information and is associated with worse outcomes in non-veterans with heart failure. Here, too, the investigators advocate screening to identify patients at risk.

Source: Heart Lung 2012;41:573–582

Resistant Organisms In Older Patients

Older patients could be bringing multidrug-resistant organisms into the hospital with them, according to a 12-year surveillance study. As reported from Beth Israel Deaconess Medical Center in Boston, the prevalence of resistant organisms among elderly patients was two to three times higher than that in younger patients.

The researchers compared rates of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and multidrug-resistant gram-negative bacteria from
clinical cultures taken within the first 48 hours of admission. An average of 7,534 positive bacterial cultures was collected each year. Older patients had approximately twice the prevalence of MRSA and VRE and triple the prevalence of the gram-negative bacteria.

Several reasons might have accounted for this high incidence. Higher rates of colonization and cross-transmission of multidrug-resistant organisms have been documented in long-term care facilities; moreover, residents in these facilities are often prescribed antimicrobials, have comorbidities, and are hospitalized.

In 1998, only 2.2% of isolates were multidrug-resistant, compared with 14% in 2009. The increase was significantly higher in older age groups, yet there have also been declines in MRSA infections in the past 6 or 7 years, even among elderly patients. Programs targeting MRSA and better compliance with infection control efforts may be responsible.

Choosing the right antimicrobial therapy for elderly groups can be problematic. In the last year of the study, 57% of all *S. aureus* isolates recovered from older patients were resistant to methicillin, 25% of enterococcal isolates were resistant to vancomycin, and 14% of gram-negative isolates were multidrug-resistant. Given those findings, the researchers suggest that older patients might benefit from the empirical use of broad-spectrum antimicrobials; however, this approach also needs to address the potential further emergence of antimicrobial resistance.

Source: *Arch Gerontol Geriatr* 2013; 56:227–230

**RESEARCH NEWS**

**Beta Blockers May Decrease Risk of Dementia**

In a study of older Japanese-American men, beta blockers appeared to reduce the risk of dementia and Alzheimer’s disease (AD). Autopsies showed that men who had taken beta blockers for hypertension had fewer microinfarctions, less brain atrophy, and fewer AD brain lesions than those who had used other drugs.

Although beta blockers alone were superior to other treatments, any drug treatment was better for dementia-related and AD-related damage than no drug treatment. A systolic blood pressure (BP) higher than 120 mm Hg in midlife predicted the population-attributable risk of dementia in 17% to 27% of cases.

The participants, 71 to 93 years of age, were enrolled in the Honolulu–Asia Aging Study from 1991 to 2012. Of the 774 subjects, 610 had high BP or were using antihypertensive drugs. Among those receiving treatment, 15% received only a beta blocker, 18% received a beta blocker and another drug, and the remaining 67% received other BP medications.

Men who received only beta blockers had fewer microinfarctions and AD-associated brain lesions than those who received no treatment or a drug other than a beta blocker. Those receiving a beta blocker in combination with other BP drugs had an intermediate reduction in the number of brain abnormalities.

Patients needing only one drug (a beta blocker) might have had less disease to begin with. Findings are scheduled to be presented in March at the American Academy of Neurology’s meeting.


**DEVICE NEWS Approvals**

**Rebif Auto-Injector for MS**

A single-use auto-injector for the self-administration of interferon beta-1a (Rebif, EMD Serono/Pfizer) is available for treating relapsing multiple sclerosis (MS). In a 12-week, phase 3b study, most patients found the Rebif Rebidose device easy to use. Interferon beta-1a is not indicated for chronic progressive MS.

Source: EMD Serono/Pfizer, January 3, 2013

**Sealing Lung Punctures After Biopsy**

The FDA has approved a new indication for the Bio-Seal Lung Biopsy Tract Plug System (Angiotech). The device seals punctures left by biopsies and reduces the risk of a collapsed lung during the procedure. The system was first approved as the Lung Biopsy Site Marker.

Source: FDA, December 19, 2012

**Test Identifies Origins Of Infectious Gastroenteritis**

The xTAG Gastrointestinal Pathogen Panel can simultaneously detect 11 common viral, bacterial, and parasitic causes of infectious gastroenteritis from a single patient sample.

Infectious gastroenteritis is an inflammation of the stomach and intestines caused by viruses, bacteria, or parasites. Symptoms (e.g., vomiting and diarrhea) can be more severe in infants, the elderly, and immunocompromised people. Gastroenteritis can be spread easily through person-to-person contact and through contaminated food, water, and surfaces.

Source: FDA, January 15, 2013

**Recalls Oxygen Cylinder**

Praxair has issued a Class I recall of all Grab’n Go Portable Oxygen Cylinders after it was discovered that fires could occur within the devices if the cylinder unit was dropped or knocked over. Although the fires are self-extinguishing, they may expose patients to burns or deprive them of oxygen.

A few isolated incidents of ignition appeared to involve units with a certain type of O-ring. The recall is being handled as a field correction, and the device is being adjusted during regular servicing. If necessary, the O-ring is being replaced. As of January 2013, more than 50% of the units in the U.S. had already been modified and have a decal with a “T” affixed to their green shroud.
The cylinders were manufactured from June 17, 2009, through November 16, 2012.
Source: FDA, January 3, 2013

**Pinholes in Oxygen Device**
The Fisher & Paykel Healthcare Reusable Breathing Circuit has been recalled because of leaky tubes that may contain pinholes. The device is used for oxygen therapy in adults. If the pinholes are not detected during a standard leak test, gas pressure could be reduced to a useless level and death could result.
Lot numbers 110810 and 111020 are affected by the Class 1 recall. The devices were manufactured from August to October 2011 and were distributed through September 27, 2012. Customers were instructed to discard any affected circuits.
Source: FDA, January 3, 2013

**NEW MEDICAL DEVICES**

**Marvin M. Goldenberg PhD, RPh, MS**

**Name:** TxCell Scanning Laser Delivery System
**Manufacturer:** Iridex Corp., Mountain View, Calif.
**Approval Date:** December 3, 2012
**Purpose:** TxCell offers fast, noninvasive treatment of retinal diseases.
**Description:** MicroPulse is a tissue-sparing laser technique that electronically “chops” the laser emission into “trains” of microsecond pulses. This enhances the physician’s ability to control the laser effects on target tissues.
**Benefit:** The device saves time during various laser photocoagulation procedures and enables physicians to deliver the laser in a multipot scanning mode. This is a more efficient method than the traditional single-spot mode. The system is easy to use and promotes workflow efficiency. There are fewer collateral adverse effects with this technology compared with conventional laser treatments. The physician is able to visualize the treated tissue by identifying the perimeter of the target area.
**Sources:** www.rtnews.com; www.iridex.com; www.deviceoptical.com

**Name:** Marijuana Metabolite Test
**Manufacturer:** Omega Laboratories, Inc., Mogadore, Ohio
**Approval Date:** December 20, 2012
**Purpose:** The test is used to detect the presence of marijuana in individuals via human hair analysis. The marijuana metabolite can be detected in even a very small hair sample (0.002 pg/mg). Only the metabolite (THC-COOH), which is produced in the body, is detected.
**Description:** In the assay, developed by Omega and Agilent, hair samples are screened using enzyme immunoassay technology. Positive samples are subjected to confirmation testing. Because hair growth is fed by the bloodstream, the ingestion of drugs of abuse can be revealed by analyzing a small sample of hair. About 90 to 120 strands are required to account for differences such as thick and coarse versus thinning and fine hair. The hair can be collected from several sites on the head, and body hair may be used as a substitute for head hair. If no hair can be collected, oral fluid or urine testing may be used. Colored hair does not affect the results significantly.
**Benefit:** Hair testing eliminates the possibility of an external source of contamination. The results cannot be significantly altered with shampoos or other external chemicals. Hair analysis is more efficient and less intrusive than urinary analysis, and there is a wider window of detection. Drug testing of the hair has uncovered significantly more complicated blockages.
**Sources:** http://avenger.com/pad; http://bmctoday.net

**Class I Recall**
Natus Medical, Inc., has recalled all serial numbers of the Olympic Cool-Cap System, designed to prevent neurological injury in full-term infants at 36 weeks’ gestational age. A cooling water cap is placed on the infant’s head, and the body is warmed with radiant warmers. The cap is used for infants with hypoxic–ischemic encephalopathy. The cap supplies the correct oxygen level and is intended to prevent brain damage. Cooling is monitored for 72 hours.
A defect makes it appear that the technology is working when it is not, thereby increasing the risk of adverse events, including death. The control module’s screen may freeze; the on-screen data remain on display, but the system is not providing cooling. The clock display in the upper right corner of the screen stops working, and the power supply may fail.
**Sources:** http://globalregulatory-science.com, January 2, 2013; FDA, May 9 and 14, 2012; www.natus.com

**Name:** Ocelot/Pixl Imaging Device
**Manufacturer:** Avinger, Inc., Redwood City, Calif.
**Approval Date:** December 18, 2012
**Purpose:** Ocelot/Pixl is used to treat patients with peripheral artery disease.
**Description:** With its smaller profile and longer length than the original Ocelot (approved in 2012), Ocelot/Pixl is designed to visualize smaller arteries.
**Benefit:** Physicians can choose a working length of 135 cm or 150 cm to navigate lesions. With its 5 French sheath compatibility and reinforced distal coil for steerable, intravascular imaging is provided at all times. The lightbox console allows physicians to see from inside an artery during the procedure. In the past, operators relied on x-rays, as well as touch or feel, to guide catheters through complicated blockages.
**Sources:** http://avenger.com/pad; http://bmctoday.net