**NEW DRUGS**

**Stivarga for Advanced Colon Cancer**

Regorafenib (Stivarga, Bayer) has been approved for patients with treatment-refractory metastatic colorectal cancer. The drug is a multikinase inhibitor.

The FDA's approval was based primarily on the 760-patient CORRECT trial. Progression-free survival was only slightly improved (a median of 2 months with the study drug versus 1.7 months with placebo).

A boxed warning mentions the risk of severe and fatal liver toxicity.

Regorafenib was approved 1 month ahead of schedule and was reviewed under the FDA's fast-track system. This medication has also shown promise for treating gastrointestinal stromal tumors.

Regorafenib is discussed in this month’s Pharmaceutical Approval Update column on page 622.

Source: FDA, September 27, 2012; Fierce Biotech, MedPage Today, September 27, 2012

**Jetrea for Adhesion in the Eye**

Ocriplasmin (Jetrea, ThromboGenics) is the first drug that has been approved to treat symptomatic vitreomacular adhesion (VMA). Ocriplasmin is an enzyme that breaks down proteins in the eye that cause VMA. The breakdown of these proteins can reduce the risk that tugging of the macula will occur. The alternative treatment for this condition is vitrectomy.

In two clinical studies, 652 patients received a single injection of ocriplasmin or a placebo substance. VMA resolved in 26% of patients treated with ocriplasmin compared with 10% of those receiving the inactive product.

Treatment-related adverse effects included “floaters,” bleeding of the conjunctiva, ocular pain, flashes of light, blurred vision, vision loss, retinal edema, and macular edema.

Source: FDA, October 18, 2012

**Jetrea**

**New Drug Approval**

Jetrea is a human recombinant DPPIV enzyme that breaks down proteins in the eye that cause VMA. Ocriplasmin is an enzyme that breaks down proteins in the eye that cause VMA. The FDA’s approval was based on data from a phase 3 trial that showed improvement in progression-free survival in patients taking perampanel compared with those taking placebo.

A boxed warning mentions the risk of serious and possibly life-threatening neuropsychiatric events (e.g., irritability, aggression, anger, anxiety, paranoia, euphoric mood, agitation, and mental status changes). Violent thoughts or threatening behavior was also observed in a few patients. Patients should be closely monitored during the titration period when higher doses are used. A medication guide will be dispensed.

Source: FDA, October 22, 2012

**Generic Irbesartan Approved For Hypertension**

Mylan Pharmaceuticals, Inc., has received final approval from the FDA for its Abbreviated New Drug Application (ANDA) for irbesartan tablets USP, 75 mg, 150 mg, and 300 mg (the generic version of Avapro, Sanofi). Mylan also received approval for its ANDA for irbesartan and hydrochlorothiazide (HCTZ) tablets USP, 150/12.5 mg and 300/12.5 mg (the generic version of Sanofi’s Avalide). Both brand-name drugs are made by Sanofi.

Irbesartan is indicated for the treatment of hypertension and type-2 diabetic nephropathy. Irbesartan/HCTZ is indicated when blood pressure is not adequately controlled with a single drug and as initial therapy when multiple drugs might be needed to achieve blood pressure control.


**Humira for Ulcerative Colitis**

Adalimumab (Humira, Abbott) is now approved to treat moderate-to-severe ulcerative colitis in adults who do not respond to corticosteroids or immunosuppressive drugs. In two clinical trials, 16.5% to 18.5% of patients receiving adalimumab achieved clinical remission compared with 9.2% to 9.3% of patients receiving placebo. In the second study, 8.5% of adalimumab-treated patients sustained remission compared with 4.1% of patients treated with placebo.

Ulcerative colitis is the seventh indication approved for adalimumab, which is also approved for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn’s disease, plaque psoriasis, and juvenile idiopathic arthritis.

Source: FDA, September 28, 2012

**Alimta Maintenance Therapy in Non–Small-Cell Lung Cancer**

Pemetrexed injection (Alimta, Eli Lilly) has been approved to include maintenance therapy in combination with cisplatin (Platinol, Bristol-Myers Squibb) for patients with nonsquamous non–small-cell lung cancer (NSCLC). The FDA’s decision was based on data from a phase 3 trial that showed progression-free and overall survival advantages with continued maintenance therapy.

Pemetrexed was initially approved in 2004 as a combination therapy with cisplatin for unresectable malignant pleural mesothelioma and as a second-line treatment for locally advanced metastatic NSCLC after prior chemotherapy treatment. In 2008, pemetrexed was approved as a
first-line treatment for locally advanced or metastatic NSCLC in patients with nonsquamous histology. In 2009, the drug was given approval as maintenance therapy for locally advanced or metastatic NSCLC in patients with nonsquamous histology following four cycles of platinum-based first-line chemotherapy without disease progression.

Pemetrexed is not indicated for the treatment of squamous cell NSCLC.

Sources: Street Insider.com, October 17, 2012; MedPage Today, October 19, 2012

**Solvent-Free Abraxane For Non–Small-Cell Lung Cancer**

Albumin-bound paclitaxel (Abraxane, Celgene) has been approved as a first-line therapy in combination with carboplatin (Paraplatin, Bristol-Myers Squibb) for patients with non–small-cell lung cancer (NSCLC) that is not amenable to surgery or radiation therapy. Albumin, a human protein, is free of solvents.

The approval was based on results of a clinical trial (1,038 patients) showing a significantly higher response with protein-bound paclitaxel plus carboplatin (33%) compared with conventional paclitaxel and carboplatin (25%). The protein-bound paclitaxel/carboplatin regimen also demonstrated superior response rates in patients who had squamous cell tumors (41% vs. 24%, respectively) and those with large-cell carcinoma (33% vs. 15%, respectively).

Abraxane is also approved for patients with metastatic breast cancer and has recently demonstrated favorable results in metastatic melanoma.

Sources: www.marketwatch.com; MedPage Today, October 12, 2012

**NEW FORMULATIONS**

**Suboxone Tablets To Be Replaced by Film**

Up to now, Reckitt Benckiser’s buprenorphine–naloxone combination product (Suboxone), an opioid-dependence therapy, has been available in a sublingual tablet form. The tablets are being pulled from the U.S. market because the child-resistant packaging isn’t considered effective enough. A sublingual film formulation with the same dosage of buprenorphine and naloxone will replace the tablets.

Although the 30-tablet bottles have child-resistant caps, recovering adults sometimes leave the tops off the bottles, creating a risk that a child might have access to the tablets. The film is sold in individual packets that may be less available or tempting to an unsupervised child. Patients currently taking the tablets should talk to their physicians about switching to the film version.

The company has been encouraging the use of the film version, as it anticipates the entry of generic competition to its tablets.

Sources: Reuters and MedPage Today, September 25, 2012

**Liquid Tamoxifen (Soltamox) For Breast Cancer**

A liquid version of tamoxifen citrate became available in October under the brand name Soltamox (Dara Bio-sciences). In a 2011 study, a 5-year course of tamoxifen treatment in women with estrogen receptor–positive breast cancer cut their risk of death by about one-third over a 15-year period.

For some patients, the tablet form of tamoxifen can be difficult to swallow for a variety of reasons, including the effects of radiation, surgery, and chemotherapy. Some patients prefer liquid medications or hope to reduce the number of tablets they need to take daily. Patients who have trouble swallowing pills often skip doses or discontinue their regimen entirely but may find that a liquid formulation helps to promote compliance.

Sources: Lancet, August 2011; News-Medical, October 22, 2012

**Oxcellar XR as Adjunctive Therapy for Partial Seizures**

Oxcarbazepine extended-release tablets (Oxcellar XR, Supernus Pharmaceuticals) have been approved as adjunctive therapy in the treatment of partial seizures in adults and in children 6–17 years of age. This once-daily extended-release formulation of oxcarbazepine was previously known as SPN-804.

The recommended dose for adults is 1,200 to 2,400 mg once daily; for pediatric patients, the dose is 900 to 1,800 mg according to weight. The tablets will be available in strengths of 150 mg, 300 mg, and 600 mg in 100-count bottles. The product’s launch is expected in the first quarter of 2013.


**DRUG NEWS**

**Fewer Drug Shortages in 2012**

So far this year, the FDA has tracked about 100 drug shortages, down by more than half from this time last year (251 shortages in 2011 and 181 in 2010). The agency credited the drop in shortages to improved product quality, thereby reducing the need for recalls, although some firms are still experiencing problems.

In the previous year, the FDA sometimes imported non-approved medications to ease shortages. The FDA’s efforts could be bolstered by its user-fee reauthorization, which Congress passed this summer. Under the new law, drug-makers must notify the FDA within 6 months if they foresee a possible disruption in the supply or manufacture of products that could cause a shortage. The FDA also plans to create a way for providers to sort through data by specialty so that specialists can concentrate on drugs used in their own fields.

Sources: MedPage Today, September 24, 2012
Infection Rates High in Women With Urinary Blockages

More men than women tend to develop kidney stones and other obstructions in the urinary tract, but women are more than twice as likely to experience infections related to the condition. In a study reported from the Henry Ford Hospital in Detroit, women were observed to be more susceptible to infection if they had kidney stones. The researchers also noted increased rates of infection, including sepsis.

Nearly 400,000 adults hospitalized with infected urolithiasis from 1999 to 2009 were identified from an inpatient-care database in the U.S. The researchers then determined how often the hospitalized patients were treated with either retrograde ureteral catheterization (RUC) or percutaneous nephrostomy (PCN). During the 10-year period analyzed, the incidence of infective urolithiasis in women increased from 15.5 to 27.6 per 100,000. In men, the incidence increased from 7.8 to 12.1 per 100,000. In addition, the rate of urolithiasis-related sepsis rose from 6.9% to 8.5%, and the rate of severe sepsis rose from 1.7% to 3.2%.

Although PCN was found to be associated with higher rates of sepsis, severe sepsis, and prolonged hospital stays, the researchers cautioned that several important variables required for comparison were not included in the available data.


Some Blood Pressure Drugs Lower Dementia Risk More Than Others

Diabetes is an important risk factor for dementia; so is hypertension. With 60% to 80% of patients with diabetes possibly also having hypertension, managing blood pressure (BP) in these patients should help—with the right medication.

Researchers from Texas tested for an association between hypertension, antihypertensive drugs, and the risk of dementia in almost 378,000 elderly diabetic patients. During 2 years of follow-up, 14,580 patients (4%) developed dementia. The incidence of dementia increased from 2.4% in the 65- to 75-year age group to 8.3% in the over-85 age group. Patients between 75 and 85 years of age had more than double the risk of dementia compared with patients 65 to 75 years of age, and patients older than 85 had more than triple the risk. Approximately 82% of the patients also had hypertension, which was significantly associated with dementia. An increased length of time having diabetes and higher comorbidity rates were both associated with a higher incidence of dementia.

Angiotensin-receptor blockers (ARBs) offered the most protection against dementia (a 24% reduced risk), compared with a reduced risk of 14% with diuretics, 11% with angiotensin-converting enzyme (ACE) inhibitors, 7% with calcium-channel blockers, and 4% with beta blockers. Patients taking statins, oral hypoglycemic agents, and digitalis had a lower incidence of dementia than patients not taking those drugs, whereas patients taking insulin and non-opioid analgesics had a higher incidence of dementia than those not taking these drugs.

In the subgroup without hypertension, only ACE inhibitors and ARBs were protective against dementia, perhaps because both drug types act on the renin-angiotensin system. In other research, patients with albuminuria who took ACE inhibitors or ARBs had a lower chance of cognitive decline, although the results were not always statistically significant. The researchers suggest that those drugs may be protective against dementia apart from their antihypertensive effects.

Source: *Alz Dementia* 2012;8:437–444

When Does Niacin Work Best?

Extended-release (ER) niacin might not be doing the job it is expected to do. Researchers from University of Pennsylvania, Einstein Medical Center, and York Hospital suggest that when taken before bedtime, ER niacin becomes ineffective before it is needed and fails to suppress triglyceride levels after the next meal, which is usually breakfast. They therefore sought to determine whether changing the dosing time would make a difference.

In the study, 22 healthy volunteers took 2 g of ER niacin or matching placebo after a 12-hour overnight fast. After 1 hour, they drank heavy cream. Blood was sampled hourly for 12 hours. Subjects were able to cross over to alternative treatment after at least 1 week.

ER niacin reduced postprandial triglycerides by 33% compared with placebo. In earlier research, by contrast, niacin did not suppress postprandial triglycerides when taken the night before a fatty meal.

The researchers claim that niacin has an acute pharmacodynamic effect and that taking the drug at bedtime might not be the opportune time, because the rapid decrease in free fatty acids is long gone by the next meal. Nighttime dosing might also risk the patient’s having breakfast during the free fatty acid rebound, which interferes with any benefits. A dose at bedtime boosts fasting free fatty acid levels well into the next morning, which may promote the production of very-low-density lipoprotein-cholesterol (VLDL-C) and undermine triglyceride suppression.

African-Americans did not respond to niacin in this study, which was the first to show significant inefficacy of ER niacin in this group. The authors noted that this population has lower fasting triglycerides and postprandial triglycerides; moreover, their study subjects were healthy and fit.

Although health care professionals have historically prescribed ER niacin at night in order to time the disagreeable dermal response with sleep, the authors propose that after patients develop tolerance to this response, bedtime dosing is
neither required nor advantageous.

*Source: Am J Med 2012;125:1026–1035*

**Stelara Relieves Symptoms In Crohn’s Disease**

Ustekinumab (Stelara, Janssen), a human monoclonal antibody proven to treat plaque psoriasis, has shown positive results in decreasing the debilitating effects of Crohn’s disease.

Researchers at the University of California–San Diego evaluated ustekinumab in adults with moderate-to-severe Crohn’s disease that was resistant to anti–tumor necrosis factor (TNF) therapy for at least 3 months. The patients received ustekinumab for 36 weeks.

One-third of patients with moderate-to-severe Crohn’s disease do not respond to current treatment with TNF inhibitors, which regulate the body’s immune system and inflammation. Another one-third of patients experience only a temporary response.

Ustekinumab blocks two proteins that cause inflammation, interleukins 12 and 23. In the new study, the primary endpoint (clinical response at 6 weeks) was reached by 36.6%, 34.1%, and 39.7% of patients treated with 1, 3, and 6 mg/kg of ustekinumab, respectively, compared with 23.5% of those given placebo.

At 22 weeks, rates of clinical remission were significantly increased with ustekinumab maintenance therapy compared with placebo (41.7% vs. 27.4%, respectively; *P* = 0.03). Response rates were also significantly greater with ustekinumab (69.4% vs. 42.5%; *P* < 0.001).

Serious infections occurred during induction and during maintenance therapy. Basal cell carcinoma developed in one patient receiving ustekinumab.

*Sources: N Engl J Med, October 18, 2012; MedPage Today, October 17, 2012*

**Lead Poisoning Detected After Ayurvedic Treatment**

High lead levels in a 56-year-old male patient puzzled his doctors until they discovered that he had been taking a daily Ayurvedic therapy for diabetes. The patient was admitted to the emergency department at a university hospital in suburban New York with diffuse abdominal pain (which had begun 3 months earlier), reduced oral intake, and constipation. His hemoglobin count had dropped to 9.7 g/dL from a baseline of 14 g/dL a year earlier. Serum iron, transferrin, haptoglobin, vitamin B₁₂, and folic acid were within normal limits. However, a peripheral blood smear showed prominent basophilic stippling within the erythrocytes, and serum lead and urine porphyrin levels were markedly high. After emergency chelating with dimercaprol (British anti-Lewisite) and calcium EDTA, the patient was discharged with oral succimer (Chemet, Lundbeck) for 2 weeks.

Ayurvedic formulations often contain large amounts of lead, mercury, and arsenic, according to case reports. It’s possible, the authors note, that the minerals are added intentionally after the formulations have been “detoxified.” The patient’s Ayurvedic powder was found to have a lead content of 62% by weight. In Ayurvedic medicine, a traditional medical system in India, lead is considered an impotence associated with diabetes.

Lead toxicity from Ayurvedic medicine used for diabetes has rarely been reported, but this case underlines the need to ask patients whether they are taking complementary or unconventional treatments; patients do not always reveal this information on their own.

*Source: Am J Med 2012;125:e4*

**Antianxiety Drugs and Dementia**

In a French study, elderly patients who used benzodiazepines for anxiety or insomnia (e.g., Xanax, Ativan) had a higher risk of developing dementia than non-users. Among 1,063 individuals who were 65 years of age and older, the risk of new-onset dementia during the follow-up period was 60% greater for those who had used benzodiazepines compared with never-users.

The possibility that benzodiazepines might impair cognition over the long term is not new, and the short-term effects have been recognized. However, some earlier studies found an increased risk of cognitive impairment or dementia, whereas others detected no relationship or even a protective effect.

Data were analyzed from the Paquid (Personnes Agées Quid) cohort study. A total of 3,777 people were observed for up to 20 years starting in the late 1980s, with clinic visits every 2 to 3 years. The following groups were excluded: individuals who did not stay in the study for at least 5 years, those with prevalent dementia at the 5-year follow-up, and those with a history or current use of benzodiazepines at year 3 or with missing data on the use of these drugs. That left 1,063 participants for analysis, with a mean age of 78 at enrollment.

Participants who had ever used benzodiazepines were more likely to have dementia after 8 years. This finding was almost identical for those with recent benzodiazepine use and for those whose use was earlier in the past. However, there were few recent benzodiazepine users, and the increase in dementia risk was not statistically significant.

The researchers suggested that future studies examine possible correlations between benzodiazepine dosage or cumulative length of exposure and dementia.

*Source: BMJ, September 28, 2012; Medical News Today September 28, 2012*

**Approval Rating Lowered For Budeprion XL 300-mg Tablets**

Teva’s budeprion XL 300-mg (bupropion HCl extended-release tablets, Impax/Teva) is not considered to be therapeu-
Group Wants Boxed Warning For Blood Pressure Drugs

The consumer watchdog group Public Citizen has petitioned the FDA to add a boxed warning to three classes of hypertension drugs when they are used in combination. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and aliskiren (Tekturna, Novartis) are often used together, but Public Citizen claims that their combined use can cause kidney failure, hypotension, and hyperkalemia.

In addition to the warning, the group wants a medication guide to be given to patients and a letter sent to physicians.

In April, the FDA warned of aliskiren use with ACE inhibitors and ARBs, but Public Citizen called that warning on the labels of aliskiren and five ACE inhibitors insufficient. The group claims that the drugs in combination provide no clinical benefit; however, studies have shown that they do lower the risk of atrial fibrillation and reduce the size of enlarged heart chambers. The group calls those studies flawed. The FDA has until early April 2013 to respond to the petition.


Blood Pressure Drugs And Fracture Risk

A risk of hip fractures was increased among older patients in Canada who began taking antihypertensive therapy, particularly beta blockers and angiotensin-converting enzyme (ACE) inhibitors. Among a large cohort of elderly residents of Ontario, the risk of a hip fracture during the first 45 days after they began treatment rose by 43%. For those starting ACE inhibitors, the risk increased by 53%. The findings were reported at a meeting of the American Society for Bone and Mineral Research (ASBMR).

For patients using beta blockers, the increase in the risk of a hip fracture reached 58% during the first 45 days of treatment. Although older patients who begin antihypertensive therapy have an increased risk of falling, the evidence for fracture risk has been conflicting. To explore the potential risk, researchers evaluated more than 300,000 residents 66 years of age and older who had new prescriptions for antihypertensive therapy between 2000 and 2009. Angiotensin receptor blockers (ARBs), calcium-channel blockers, and thiazide diuretics were also included. Patients were excluded if they were being treated with these drugs for conditions other than hypertension.

In the previous year, 3% of patients had fallen and 6% had experienced a hip fracture. During an overall observation period of 450 days before and after initiation of antihypertensive therapy, there were 1,463 hip fractures. The 45-day high-risk period was associated with an elevated fracture risk for all patients, although the incidence rate ratio estimates were not statistically significant for ARBs, calcium-channel blockers, or diuretics.

The study was limited by a lack of information on specific drugs, dosages, and the time of day when falls occurred.

Sources: ASBMR meeting; MedPage Today, October 14, 2012.

Benefits of Beta Blockers Questioned

Beta blockers are considered helpful in reducing the risk of a second heart attack, but for some patients, the drugs might increase the risk of cardiac events. In a large observational study from New York University School of Medicine that enrolled patients with a history of myocardial infarction (MI), the primary outcome of composite rate of cardiovascular death, nonfatal MI, or nonfatal stroke did not differ statistically between those taking these drugs and those not taking them. Similar findings were noted in patients with coronary artery disease (CAD) but with no history of MI. However, when
patients had risk factors only for CAD, beta blockers conferred a higher risk of cardiovascular death, nonfatal MI, or nonfatal stroke.

Older studies did not have the benefit of modern reperfusion techniques or medical therapy. In the new study, more than 80% of patients taking beta blockers were also taking aspirin or statins, and more than half were using an angiotensin-converting enzyme (ACE) inhibitor.

The long-term use of beta blockers for patients with coronary or other vascular disease has also been downgraded to a class IIb recommendation, the authors noted. However, some experts emphasized that this was not a randomized, controlled trial and that guidelines should not be changed for this reason. The current guidelines recommend beta blockers for patients with a recent MI and those with heart failure. It is unclear how long patients should continue taking these drugs after having a heart attack.

Some experts suggest that beta blockers might be overused for hypertension without strong evidence for their benefits. In Europe, these drugs, when used to treat hypertension, are classified as a fourth-line therapy.

Although the drugs might provide benefits for angina, other medications carry fewer adverse effects. Statins and antiplatelet therapy might be better at preventing cardiovascular events. Limitations of the study included the lack of data about the type of beta blocker used, the dosage, the type of MI before beta blocker use, and the reason for taking the drug.


Mexitil, a Heart Drug, Relieves Rare Muscle Disorder

An antiarrhythmic drug improved muscle stiffness in patients with a rare disorder called nondystrophic myotonia in a phase 2 trial conducted in Kansas. In a two-stage crossover trial, patients taking mexiletine (Mexitil) reported less stiffness compared with when they took placebo over a period of 4 weeks.

Nondystrophic myotonia, caused by mutations in skeletal muscle ion channels, are characterized by delayed muscle relaxation, which causes stiffness and pain. Mexiletine is a class 1b antiarrhythmic medication with a high affinity for muscle sodium channels. It is widely used in an off-label fashion to treat nondystrophic myotonias, but its value had not been confirmed in clinical trials, largely because of the difficulty of conducting a study.

To overcome that hurdle, the Rare Disease Clinical Research Network organized a double-blind, placebo-controlled study in the U.S., Canada, Italy, and the United Kingdom. Fifty-nine patients received a 200-mg dose of mexiletine three times per day or placebo for 4 weeks. After a 1-week washout period, they were switched to the opposite assignment for another 4 weeks.

In both study periods, mexiletine resulted in less stiffness. Adverse gastrointestinal effects and transient cardiac effects occurred. The only serious adverse event was a case of narcotic withdrawal, which was not thought to be related to the study drug.


RESEARCH NEWS
Lonafarnib Slows ‘Untreatable’ Progeria

The American Society for Cell Biology (ASCB) has reported positive results for a drug used to treat progeria, a rapid-aging disorder in children. An infant born with progeria, up to now considered to be incurable, stops growing by 16 to 18 months and quickly develops signs of old age (e.g., hair loss, thin skin, osteoporosis, and arteriosclerosis). By 10 years of age, children with progeria appear to be 80.

The new trial grew out of the identification of a defective gene, LMNA, in 2003. Later research found a link between progeria and defective proteins (lamins) that make up the envelope surrounding the cell nucleus. Further research revealed that a greasy tag molecule, farnesyl, accumulates on defective lamin A proteins. The identification of the defective LMNA gene transformed progeria into a “laminopathy”—a growing class of diseases caused by problems with nuclear lamins. Normal aging is thought to involve many of the same processes as laminopathies.

With the discovery of the lamin link, researchers began looking at farnesyl transferase inhibitors (FTIs) for the treatment of progeria. They focused on lonafarnib (Merck), an FTI drug that was found to be safe for use in children but was ineffective against its brain cancer targets.

In the new clinical trial, physicians at Boston Children’s Hospital observed a significant slowing of bone loss and blood vessel blockage after giving lonafarnib to 26 children with progeria for 2½ years.


Advances in Drug Delivery
Simple Insulin Device for Diabetes

In a study by CeQur SA, a Swiss company, patients with type-2 diabetes replaced daily insulin injections with the PaQ device. Researchers in Austria completed the study in 6 months.

PaQ is a discreet, wearable device that provides 3 days of consistent, basal insulin delivery along with on-demand bolus insulin. According to CeQur, half of all patients who need multiple daily injections of insulin skip doses because they consider the injections inconvenient, painful, or disruptive to their daily activities.

Initial results are expected next year. Source: CeQur SA, September 26, 2012, http://cequrcorp.com
Ultrasound for Transdermal Therapy

Using ultrasound waves, engineers at the Massachusetts Institute of Technology have found a way to enhance the permeability of the skin to drugs, making transdermal drug delivery more efficient and less painful.

Ultrasound can increase skin permeability by lightly wearing away the top layer of the skin, an effect that is transient and pain-free. Applying two separate beams of ultrasound waves—one of low frequency and one of high frequency—uniformly boosted permeability across a region of skin more rapidly than using a single beam of ultrasound waves. Such a system may someday be used to replace capsules, possibly allowing the dose to be increased; enhancing the activity of skin patches already in use; and providing non-invasive needle-free insulin and vaccines.


ThermoDox (Doxorubicin) Trial in Liver Cancer

Celsion Corporation has announced that the independent data monitoring committee for the company’s HEAT study has completed a review of all 701 patients enrolled in the trial and has unanimously recommended that the trial continue. HEAT is a double-blind, placebo-controlled, pivotal phase 3 trial of ThermoDox for hepatocellular carcinoma (primary liver cancer). The company expects to report top-line results in the fourth quarter of 2012. The HEAT study received an FDA fast-track designation and was designated as a priority trial for liver cancer by the National Institutes of Health (NIH).

ThermoDox was granted an orphan drug designation in the U.S. and in Europe. The drug is a heat-activated liposomal encapsulation of doxorubicin, a cancer drug. In the HEAT study, ThermoDox is injected in combination with radiofrequency ablation. Localized mild hyperthermia (39.5°C to 42.0°C), created by the ablation, releases the entrapped doxorubicin from the liposome, allowing high levels of doxorubicin to be deposited preferentially in a targeted tumor.


Ultrasound Therapy For Metastatic Bone Pain

ExAblate (InSightec Ltd.), a magnetic resonance imaging (MRI)-guided device, is used to treat pain from bone metastases in patients who do not respond to or cannot undergo radiation treatment for their pain. ExAblate was approved in 2004 as a noninvasive, outpatient therapy for uterine fibroids. The new technique combines therapeutic acoustic ultrasound waves, continuous guidance, and treatment monitoring with MRI. The focused ultrasound acoustic energy destroys the nerves that are causing the pain.

Source: InSightec Ltd., October 22, 2012

Neptune System Recalled

Stryker Instruments has recalled Neptune 1 Silver and two models of its Neptune 2 Ultra Waste Management Systems. These mobile vacuum devices are used to dispose of surgical fluid waste in operating rooms. A fatality occurred when a customer incorrectly connected the Neptune 2 system to a patient’s chest drainage tube after surgery.

Sources: Drugwatch.com, October 8, 2012; MedPage Today, October 5, 2012

NEW MEDICAL DEVICES

Marvin Goldenberg PhD, RPh, MS

Name: Reliance 4-Front Implantable Defibrillator Lead


Approval Date: September 24, 2012

Purpose: This implantable lead is used in patients with atrial fibrillation.

Description: Defibrillation leads are insulated wires that connect an implantable cardioverter defibrillator or cardiac resynchronization therapy defibrillator to the heart to treat patients with heart failure and sudden cardiac arrest.

Benefit: The lead body is modestly reduced in size to improve handling and maneuverability while maintaining insula-
tion thickness and reliability. Irox, a fractal coating, enhances electrical properties and lowers pacing thresholds. The secured Gore coating helps to prevent tissue ingrowth into the defibrillation coils. Adhering the Gore coating to the lead simplifies implantation by eliminating steps.

Sources: www.cxvascular.com; http://bostonscientific.mediaroom.com

Name: Subcutaneous Implantable Defibrillator (S-ICD) System
Manufacturer: Cameron Health, San Clemente, Calif.
Approval Date: September 28, 2012
Purpose: The S-ICD System is a small battery-powered device that monitors and restores heart rhythm in patients at risk for ventricular tachyarrhythmias.
Description: A therapeutic dose of electricity is delivered to restore cardiac rhythm when the device senses tachycardia or sudden cardiac arrest. A lead is implanted just under the skin along the bottom of the rib cage and breastbone.
Benefit: The Cameron device is less invasive than previous models, allowing the patient’s blood vessels or heart to be bypassed. The system can accommodate the challenging anatomy of some patients.

In a study of 321 patients, the device restored all detected abnormal arrhythmias to normal. During the 6 months following implantation, the defibrillator detected and recorded 78 spontaneous arrhythmias in 21 patients; all arrhythmias were either successfully converted back to normal with the device or were restored to normal on their own.

Contraindications and Precautions:
The device is approved only for patients who do not need a pacemaker or pacing therapy. In the study, because the SICD System memory stores data from only the 22 most recent arrhythmic episodes, there could have been other detected episodes. Complications included inappropriate shocks, discomfort, system infection, and electrode movement, continued on page 650
which required repositioning the patient. Eight patients died, although the deaths could not be directly attributed to the device. The system had to be removed in some patients, and others experienced discomfort. At the end of 6 months, more than 90% of patients had no complications.

Cameron Health is required to conduct a postmarketing study to assess the long-term safety of the system and assess any sex differences in effectiveness.

Sources: www.fda.gov; http://physician.cameronhealth.com