TRENDS-in-MEDICINE

December 18, 2011

by Lynne Peterson

Quick Takes

…Highlights from this week's news relating to drugs and devices in development that are not covered in other *Trends-in-Medicine* reports…

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SHORT TAKES

- **ABBOTT LABORATORIES** is licensing the rights to antioxidant inflammation modulators being developed by **Reata Pharmaceuticals** to treat chronic conditions, such as rheumatoid arthritis, multiple sclerosis, Parkinson's disease, and chronic obstructive pulmonary disease (COPD).

- **ALLERGAN's Lap-Band –** The FDA warned consumers about misleading weight-loss claims about this gastric band. The FDA sent warning letters to eight surgical centers and the marketing firm 1-800-GET-THIN in California about misleading advertising of Lap-Band, but it also wants consumers to know some of the advertising is misleading not only about the benefits but also about the side effects.

- **AMGEN's Enbrel (etanercept) –** A study published in the ***International Journal of Dermatology*** found this psoriasis therapy may be associated with an increased risk for multiple squamous cell carcinomas (SCCs). The Mayo Clinic researchers examined four case studies and performed a literature review that detected another four cases of SCC following Enbrel therapy for psoriasis.

- **BAXTER INTERNATIONAL** is buying **Synovis Life Technologies** to acquire its line of soft-tissue repair products. The acquisition is expected to be completed in 1Q12.

- **BERLIN HEART's Excor pediatric ventricular assist device (VAD)**, a mechanical pulsatile device, was given a Humanitarian Device Exemption (HDE) approval by the FDA as a bridge-to-transplant. It was already approved in Europe and Canada.

- **CELLADON's Mydicar**, an investigational gene therapy for heart failure, was given fast track status by the FDA.

- **COVIDIEN** plans to spin off its pharmaceuticals business (e.g., bulk acetaminophen, opioids, and generic drugs) into a public company that will operate independently of Covidien. The new company may take the name **Mallinckrodt**. Covidien will then focus on its medical device business and other operations.

- **FUJIFILM** made a bid to acquire compact-ultrasound developer **SonoSite**.

- **GE HEALTHCARE –** In an alliance with the M+W Group, GE plans to build two biopharmaceutical plants in Latin America and another in the Middle East to produce lower-cost drugs and vaccines.

- **GILEAD's Truvada (tenofovir + emtricitabine) –** A supplemental new drug application (sNDA) was submitted to the FDA for this HIV antiviral therapy as a pre-exposure prophylaxis (PrEP) to reduce the risk of HIV infection in men who have sex with men (MSM) and heterosexual men and women.

- **GLENMARK PHARMACEUTICALS and NAPO PHARMACEUTICALS** ended their collaboration on **Provir** (crofelemer), which is used to treat chronic diarrhea in HIV patients.

- **NEOPROBE** (soon to be renamed **Navidea Biopharmaceuticals**) bought the worldwide rights to **AstraZeneca's AZD-4694**, a radiopharmaceutical imaging drug in development to help in the diagnosis of Alzheimer's disease. Neoprobe plans to start a pivotal trial in early 2013.

- **NOVARTIS' Gilenya (fingolimod)** – One patient reportedly died within 24 hours of taking this oral multiple sclerosis drug. The company said Gilenya's role in the patient's death "can't be excluded or confirmed," but the case was reported to the FDA.

- **ONYX PHARMACEUTICALS' carfilzomib** was accepted by the FDA for standard, not accelerated, review. Onyx said the FDA determined that the company didn't do the necessary clinical trials for expedited review of this investigational multiple myeloma drug. The PDUFA date is July 27, 2012.

- **ORION's Comtan (entacapone)** – A 25-patient study presented at the American Academy of Addiction Psychiatry (AAAP) meeting suggested that this COMT inhibitor, which is approved to treat Parkinson's disease, may help alcoholics stay sober. Researchers reported that 88% of outpatients given the drug had a decrease in craving for alcohol.

- **SALIX PHARMACEUTICALS' crofelemer** was submitted to the FDA to treat HIV-related diarrhea.

- **ST. JUDE MEDICAL's Riata defibrillator lead** – The FDA raised the recall to Class I, saying there is a potential for injury or death from inappropriate shocks or a failure to deliver an appropriate shock. The lead was taken off the market last year. About 79,000 Americans currently have the lead implanted, and experts are not recommending (yet) that these be removed unless a problem develops.

- **SYGNIS PHARMA's AX-200** – A Phase II trial of this investigational protein-based drug for stroke treatment failed, showing no statistically significant difference from placebo on the primary endpoint.

- **TROPHOS' olesoxime** missed the primary endpoint in a pivotal Phase III trial in amyotrophic lateral sclerosis (ALS), so **Actelion** is not exercising its option to acquire the company.

- **VALEANT PHARMACEUTICALS** – The Federal Trade Commission (FTC) approved Valeant's takeover of the skin-care businesses of **Sanofi** and **Johnson & Johnson**. However, the FTC said Valeant has to sell all rights to generic **BenzaClin** (clindamycin and benzoyl peroxide) and generic **Efudex** (fluorouracil) to **Mylan Pharmaceuticals** and to sell **Refissa** (tretinoin) to **Spear Pharmaceuticals**. The FTC is expected to issue a final decision after the 30-day comment period ends on January 12, 2012.

- **VERTEX PHARMACEUTICALS' Kalydeco (ivacaftor, VX-770)** – The FDA granted priority review for this treatment for cystic fibrosis in patients who carry a mutated G551D gene. The PDUFA date is April 18, 2012.

NEWS IN BRIEF

ALEXZA PHARMACEUTICALS' Adasuve (loxapine inhalation powder) – FDA panel vote too close to be definitive

The FDA's Psychopharmacologic Drugs Advisory Committee was split on whether this once-daily inhaled antipsychotic for bipolar disorder and schizophrenia should be approved, voting 9-8 (with one abstention) to recommend approval – provided a risk evaluation and mitigation strategy is implemented. The panel was concerned the drug may put some patients at risk for respiratory failure (potential fatal bronchospasms). *The FDA usually considers such a close panel vote as neutral, not positive.*

Adasuve was rejected by the FDA in October 2010 because of concerns about pulmonary toxicity, but the company resubmitted the drug in August 2011 with a proposed REMS. The PDUFA date for this submission is February 4, 2012.

CRT – substantial benefit in heart failure after all

The European CRT Survey, which was published in the ***European Journal of Heart Failure***, suggested that cardiac resynchronization therapy (CRT) reduces death and re-hospitalization in heart failure patients. Based on data from <2,000 patients at 141 sites in 13 European countries, the researchers found that with one year of follow-up:

- Nearly 25% of patients died or were re-hospitalized, a rate consistent with clinical trial data.
- The patients who died or were re-hospitalized tended to have more severe heart failure and pre-existing atrial fibrillation.
- Patients rated their symptoms better with the device than pre-implant.
- Mortality was higher in patients who got a CRT rather than a CRT-D.

One of the researchers, Nigussie Bogale, MD, from Stavanger University Hospital in Norway, said: "Unless [patients] have contraindicating co-morbidities, it is now our belief that these patients should be considered for CRT-D implantation." The survey was a joint project of the Heart Failure Association and the European Society of Cardiology's European Heart Rhythm Association.

Dengue fever
– clue that could lead to drug development

A report published in the journal ***mBio*** discussed a discovery about how the body fights the dengue virus, a finding that could explain differences in the ability to fight off the virus and help in developing a drug to boost this response.

Researchers from Washington University, Walter Reed Army Institute of Research, and the University of Copenhagen said mannose-binding lectin (MBL), a part of the immune system, is involved in targeting dengue viruses for destruction. MBL recognizes sugar molecules present on the outsides of many different kinds of viruses and bacteria. When it finds these sugars, MBL activates the complement system, which targets foreign materials in the body for destruction in any of a number of cruel ways.

This is an important discovery in terms of human health because different people naturally make different levels of MBL, and high levels were associated with better neutralization of the dengue virus, providing a clue that may help in the development of an antiviral.

Electronic health records (EHRs)

■ **ALLSCRIPTS' MyWay.** Costco plans to sell this cloud-based EHR system through a value-added reseller, Etransmedia Technology. The product is aimed at small physician practices.

■ **Changes in EHR vendor rankings.** No. 1 in the small physician practice (1-10 doctors) space this year is Amazing Charts. Tops in practices with 11-75 physicians is athenahealth, and the leader in practices with >75 physicians is Epic.

Last year the leaders were all different, except for Epic in the large practice category. e-MDs led in the 2-5 physician category, Greenway Medical Technologies in the 6-25 physician space, and eClinicalWorks in the 26-100 category.

The leading vendors in other KLAS categories include:

- **Cardiovascular image management and reporting:** DigiView from DigiSonics.
- **Speech recognition:** eScription from Nuance.
- **Acute care electronic medical records:** EpicCare Inpatient Clinical System from Epic.
- **Radiology:** Epic Radiant from Epic.

■ **More time before penalties.** The Department of Health and Human Services (HHS) is giving physicians more time before penalties for not using EHRs goes into effect. Doctors meeting the meaningful use criteria can still earn incentive payments starting next year, but requirements to comply with stage 2 does not go into effect until 2014 instead of 2013.

Hospital procedure volume down
– especially for hip replacements and valve surgeries

Wells Fargo's monthly Hospital Volume Report found that in October year-over-year:

- Inpatient admissions were down 3.75% overall. Commercial inpatient volumes were down 2.3%, but down 5.03% for Medicare and down 11.3% for Medicaid.
- Outpatient admissions dropped 2.2%, while inpatient surgeries declined 7.7%, with neurological surgery down 6.57%.
- Overall cardiovascular surgeries were down 11.15%, with drug-eluting stents down 9%, ICDs down 13%, and pacemakers down only 0.3%. Heart valve procedures were down 10.6%.
- Overall orthopedic surgery was down 5.51%, with knees off 16.8%, hips down 2.7%, shoulders down 5.3%, and spine procedures down 3.3%.

INTERMUNE's Esbriet (pirfenidone)
– German reimbursement in question

In Germany, the Institute for Quality and Efficiency in Health Care (IQWiG) issued a negative opinion on this therapy for idiopathic pulmonary fibrosis. The IQWiG questioned the clinical benefits of the drug, saying it did not have additional benefits, did not affect mortality, and did not improve quality of life. This raises concerns that the German government will deny reimbursement.

The IQWiG has similarities to the U.K.'s NICE, but it isn't the same, and historically most of its decisions are unfavorable to the drug or device in question. Only rarely does it support use of something.

LABORATOIRES SERVIER's Mediator (benfluorex) – at the center of French scandal

This diabetes drug appears to be at the center of a public health scandal in France, according to an article in the ***New York Times***. French health officials estimated that ≥2,000 people died and thousands more were hospitalized due to cardiac valve damage and pulmonary hypertension believed to be linked to Mediator. French government investigators have accused Servier of licensing Mediator as a diabetes drug to avoid scrutiny but urging doctors to prescribe the pills as a diet aid to bolster sales – a practice that greatly expanded the pool of those potentially harmed by the drug.

The article goes on to describe inherent conflicts of interest present at the regulatory body known as AFSSAPS, which oversees drug safety in France, and how they may have led to the current situation.

MERCK AND ROCHE – first HCV trial collaboration under way

Merck, in collaboration with **Roche**, initiated the first in a series of planned trials of combinations of marketed and investigational drugs in HCV-1, the 12-week Phase II DYNAMO-1 trial of **Victrelis** (boceprevir) and **Roche's mericitabine** (RO-5024048), an oral NS5B nucleoside polymerase inhibitor, plus **Pegasys** (pegylated interferon alfa-2a) and **Copegus** (ribavirin) in null responders to interferon/ribavirin therapy.

Opioids – CMS takes new steps to crack down on fraud

HHS hopes to cut Medicare fraud by telling Medicare prescription drug plans to withhold payment when they see signs of suspicious activity related to **Purdue Pharma's OxyContin** (oxycodone), **Endo Pharmaceuticals' Percocet** (acetaminophen + oxycodone), and other opioids. The Centers for Medicare and Medicaid Services (CMS) will ask the drug plans to "use every tool at their disposal" to prevent fraud. Specifically:

- The plans will be told to withhold payment on suspicious claims, including when enrollees use multiple doctors to obtain painkillers and narcotics. While HHS generally requires prompt payment, the new guidance clarifies that if a plan sees signs of suspicious activity, it should withhold payment to pharmacies until it verifies the claim is valid.
- Plans will be told how they can use tools like prior authorization, retrospective medical review, and prescribing for less than 30 days (with the cooperation of prescribing practitioners).

PHARMASSET's PSI-938 – dropped for toxicity

The company is amending the design of the Phase IIb QUANTUM trial of this ***purine*** nucleotide for hepatitis C virus (HCV) and discontinuing all treatment arms with a regimen containing PSI-938. Pharmasset is ending all trials of this agent, monotherapy as well as combination therapy with PSI-7977 (a ***pyrimidine*** nucelotide) ± ribavirin, due to liver enzyme elevations.

The company carefully pointed out that it has not seen ALT elevations in patients on PSI-7977 + ribavirin in that study or in other studies. The 12- and 24-week PSI-7977 and ribavirin arms in QUANTUM will continue unchanged, and the company plans to use that data to support the 12-week, interferon-free, Phase III NEUTRINO trial of PSI-7977 + ribavirin in HCV-1. The liver toxicity with PSI-938 does not affect **Gilead**'s purchase of Pharmasset.

PHARMAXIS' Bronchitol (inhaled dry powder mannitol) – missed primary endpoint in CF study but researchers still believe it has value

A study published in the American Thoracic Society's **American Journal of Respiratory and Critical Care Medicine** found long-term use of this product improves lung function in cystic fibrosis patients, with an 8.22% (106.5 mL) improvement in FEV_1 with Bronchitol vs. 4.47% (52.4 mL) for control, but the difference was not statistically significant ($p=0.059$). Forced vital capacity increased 136.3 mL in the treatment group vs. 65.0 mL with control. Bronchitol patients also had fewer pulmonary exacerbations than controls. However, during the 26-week open-label extension phase of the study, improvements in FEV_1 were maintained in the treatment group.

The researchers speculated that the failure to show a significant effect on FEV_1 with Bronchitol "may have been due to use of a single baseline visit to establish baseline FEV_1 values." They found that when baseline FEV_1 values were calculated as an average of FEV_1 values over two baseline visits, as in prior clinical intervention studies, the overall increase in absolute FEV_1 was significantly greater in the treatment group ($p=0.0008$). A 50 mg dose of mannitol was used in the control group, and that also may have limited the difference between the two groups.

The researchers concluded: "Our results support the use of inhaled mannitol [Bronchitol] for the daily management of cystic fibrosis."

SSRIs – pregnancy safety still uncertain

The FDA told OB/GYNs, psychiatrists, and family practice doctors there is no clear link between women taking selective serotonin reuptake inhibitor (SSRI) antidepressants during pregnancy and an increased risk of Persistent Pulmonary Hypertension of the Newborn (PPHN) in their babies. After reviewing new study results, the FDA concluded that it is premature to draw the conclusion that SSRIs cause PPHN, but SSRI labels will be updated to add the new data and the conflicting results.

Transcranial magnetic stimulation – may help stroke patients

A 20-patient, sham-controlled study supported by the Italian Ministry of Health and published in the American Academy of Neurology's journal, ***Neurology***, suggests that external transcranial magnetic stimulation may speed recovery from a stroke. Patients receiving the magnetic stimulation improved on tests that measure information processing ability by 16% by the end of treatment and by 22% two weeks later. Sham patients did not improve. In an accompanying editorial, Heidi Schambra, MD, of Columbia University Medical Center called the study "an important step forward in the effort to find ways to help people rehabilitate from hemispatial neglect after stroke."

VIROPHARMA's Vancocin (vancomycin) – new approval may give 3 more years exclusivity

The FDA approved an sNDA for this antibiotic, probably giving the company three additional years of exclusivity before any generic versions can be approved.

How is exclusivity determined for sNDAs? The FDA has a checklist of critical conditions that must be met. The decision is posted electronically in the Orange Book; the sponsor is not notified by the FDA. FDA officials said the key points are that:

- The applicant must have all rights to the drug; non-exclusive rights are not sufficient.
- Any labeling change that required review of clinical data may potentially be eligible for exclusivity.
- Exclusivity requires a clinical trial that is not just a pharmacokinetic (PK) or bioequivalence study. At least one trial is necessary to support the indication, and it must be ***new*** clinical investigations "conducted or sponsored by the sponsor that were essential to approval of the application."
- If the sNDA approval was based on historic literature and not a clinical trial, exclusivity is typically not granted. It needs to be based on ***new*** clinical data. Typically, this is a sponsor study that the FDA has not received before.
- If a company buys/licenses a product from another company, whether or not trials done by that original company can be used for exclusivity purposes depends on what the purchase agreement says. Exclusivity can apply if the buyer now "owns" the data (which is what ViroPharma claims) rather than just a "right of reference" and provided the data had not already been reviewed by the FDA.
- *Did the sponsor pay a user fee to the FDA?* In this case, ViroPharma did. Apparently, some sNDAs are approved without requiring a payment, but then the product is not eligible for exclusivity.

REGULATORY NEWS

CMS conference call on Medicare audit plans

On December 21, 2011, CMS is holding a conference call Special Open Door Forum (ODF) to discuss the recently approved Recovery Auditor Prepayment Review Demonstration that will begin January 1, 2012. This program is designed for Medicare Fee-For-Service providers who may be subject to Recovery Auditor review in the 11 approved demonstration states: CA, FL, IL, LA, MI, MO, NC, NY, OH, PA, and TX. This is the program under which Recovery Auditors will review claims – particularly orthopedic and cardiology procedures – ***before*** they are paid to ensure the provider complied with all Medicare payment rules. On the conference call, CMS will provide an overview of the project, addressing why it is being implemented, how it will impact providers in the affected states, operational details, etc. Participants will have an opportunity to ask questions. On December 19, 2011, discussion materials for this Special ODF will be available to download at **http://go.cms.gov/cert-demos**.

CMS sets new disclosure requirements

Under the Affordable Care Act, CMS proposed a rule that would require manufacturers of drugs, devices, biologicals, and medical supplies covered by Medicare, Medicaid, or the Children's Health Insurance Program to report to CMS payments or other transfers of value they make to physicians and teaching hospitals. The proposed rule also would require manufacturers and group purchasing organizations (GPOs) to disclose to CMS physician ownership or investment interests.

The proposed rule is designed to increase transparency and help reduce the potential for conflicts of interest that physicians or teaching hospitals might face due to their relationships with manufacturers. It applies to drug and biologic manufacturers,

medical device or supply manufacturers, and GPOs. Data collection would begin when final regulations are issued, and the first reports will probably be due on March 31, 2013. After collecting all the data, CMS would allow manufacturers, physicians, and teaching hospitals 45 days to review them, then would make the data publicly available by September 30, 2013.

Public comments will be accepted until February 17, 2012.

Dialysis centers do well on CMS P4P program

The first results from CMS' new pay-for-performance (P4P) or "value-based purchasing" program for dialysis facilities – the End-Stage Renal Disease Quality Incentive Program (ESRD QIP) – was released, and it showed that:

- 69.1% of dialysis facilities evaluated met the criteria so they will ***not*** see a reduction in their payment for payment year (PY) 2012.
- 30% will have payment reductions: 16% a 0.5% reduction, 6% a 1% reduction, 8% a 1.5% reduction, and 0.6% a 2% reduction. About 11% of the facilities did not receive a Total Performance Score due to insufficient data. These facilities will not receive a payment reduction.

For this first year, facilities were rated on three things with respect to care of Medicare dialysis patients:

1. The percentage with an average hemoglobin <10 g/dL (low best)
2. The percentage with an average hemoglobin >12 g/dL (low best)
3. The percentage of patients with an Urea Reduction Ratio (URR) of ≥65% (high best)

FDA clarifies drug supply disruption notification

The FDA issues an interim final rule clarifying what a "discontinuance" of production of a drug is and what "sole manufacturer" means when it comes to a pharmaceutical company's duty to inform federal officials about a potential drug shortage. A **discontinuation** is now defined as either a permanent *or temporary* disruption in the supply of a product. Previously, companies had to inform FDA only when they stopped making a drug completely and permanently.

FDA proposes guidelines on women in device trials

The FDA issued draft guidance aimed at addressing the historic under-representation of women in clinical trials. The FDA recommends that investigators and manufacturers strive to enroll representative proportions of both women and men in their device studies and outlines what it recommends in terms of the quality and consistency of sex-specific data on devices.

The FDA believes certain medical products elicit different responses in women than in men, due to genetics, hormones, body size, diet, sociocultural issues, etc. In the new guidance, devices intended for single-sex use would, of course, not be expected to address potential sex differences.

A 2001 report by the U.S. Government Accountability Office (GAO) found 52% of trial participants were women, but 30% of studies did not report outcomes by sex. A 2009 study of cardiovascular device pre-market applications (PMAs) found that pivotal studies reporting findings by sex enrolled only an average of 34% women.

The FDA will accept public comment for 90 days.

IOM says chimp studies no longer necessary

A report by the National Institute of Health's Institute of Medicine (IOM) concluded that the use of chimpanzees is no longer needed for research in NIH-funded biomedical studies because sufficient non-chimpanzee models and new technologies are available today instead.

The IOM is not recommending a complete ban on using chimps but set criteria for when they could be used for research:

- If no other suitable model, including *in vitro* and non-human *in vivo* methods, is available.
- If a study can't ethically be carried out in humans.
- If foregoing chimp use would substantially slow or prevent work on agents to treat severe or life-threatening conditions.
- If the study would provide otherwise "unattainable insight" through minimally invasive techniques that do not cause excessive pain or distress.

NIH Director Francis Collins, MD, PhD, said ~37 research projects are under way using chimpanzees, and they will be reviewed to see if they meet the IOM criteria, but he expects about half will not meet the criteria and will be phased out.

Legislation to force medical device tracking

A bipartisan bill was introduced in the Senate by Sen. Herb Kohl (D-WI), Sen. Richard Blumenthal (D-CT), and Sen. Charles Grassley (R-IA) that would allow the FDA to require companies to track implanted devices, such as hips and knees, that do not require human testing before approval.

Physician Medicare payments

A bill – the Middle Class Tax Relief and Job Creation Act (HR 3630) – would once again fix the sustainable growth rate (SGR) formula used by CMS to compute physician payments. The bill would give doctors a 1% raise instead of the 27% cut in Medicare payments that will occur without an SGR fix. However, the bill does not address the 25% reduction in professional imaging fees going into effect on January 1, 2012.

FDA approval/clearances

- **ENDO PHARMACEUTICALS' Opana ER (extended-release oxymorphone)**, a painkiller. The company expects a transition to the new crush-resistant formulation next year.
- **HOLOGIC's Cervista High Throughput Automation (HTA) system**, which is used to automate the company's Cervista HPV HR for cervical cancer screening test, was cleared.
- **INFRASCAN's Infrascanner Model 1000**, a hand-held device that uses near-infrared spectroscopy to help detect life-threatening intracranial hematomas in patients with traumatic head injuries, was cleared under the FDA's de novo pathway. It is an adjunct, not a replacement, for CT.
- **INTUITIVE SURGICAL's Single-Site Instrumentation kit** to enable single-incision cholecystectomy procedures with the da Vinci surgical robot.
- **JOHNSON & JOHNSON/DEPUY ORTHOPAEDICS' AOX antioxidant polyethylene material** received premarket approval (PMA) clearance for use in knee replacement systems to enhance long-term oxidative stability and wear resistance.
- **MERIDIAN BIOSCIENCE's illumigene** molecular diagnostic assay to detect Group B *Streptococcus*.
- **SOTEIRA's Shield Kyphoplasty System** received 510(k) clearance to treat osteoporotic vertebral compression fractures.

FDA warning letters were issued to:

- **EUSA PHARMA's ProstaScint (capromab pendetide)** – for overstating the efficacy and underplaying the risks of this diagnostic imaging agent used in prostate cancer.
- **NEUROGESX's Quetenza (capsaicin patch)** – for making unproven efficacy claims and failing to adequately describe the risks for this pain medication at an exhibit booth at the American Academy of Nurse Practitioners meeting in June 2011.
- **SUNOVION PHARMACEUTICALS' Latuda (lurasidone)** – for a sales rep discussing off-label use of this schizophrenia drug in bipolar disorder and minimizing its risks.

Canadian regulatory actions

- **AMAG PHARMACEUTICALS and TAKEDA's Feraheme (ferumoxytol)** was approved to treat anemia in adults with chronic renal disease.
- **GUIDED THERAPEUTICS' LuViva Advanced Cervical Scan** was approved for detecting precancer of the cervix.

European regulatory actions

- **GILEAD SCIENCES' Vistide (cidofovir)** – The European Medicines Agency (EMA) recommended a precautionary recall on one batch of this HIV drug, which was produced at Ben Venue Laboratories, because of possible contamination. *So, now it isn't only J&J that is affected by the Ben Venue problems.*
- **OPTIMER PHARMACEUTICALS and ASTELLAS' Dificlir (fidaxomicin)** – Dificid in the U.S. – was approved to treat *Clostridium difficile* infection.
- **ROCHE's Zelboraf (vemurafenib)** – The Committee for Medicinal Products for Human Use (CHMP) recommended that Zelboraf be granted full marketing authorization as monotherapy in BRAF V600 mutation-positive unresectable or metastatic melanoma. A European Commission decision on Zelboraf is expected in February 2012.
- **Contamination warning.** The EMA warned healthcare professionals to inspect vials of **Pfizer's Torisel** (temsirolimus) for kidney cancer and **EpiCept's Ceplene** (histamine dihydrochloride) for leukemia because of contamination and other problems at manufacturer Ben Venue's Ohio facility. The EMA also urged a precautionary recall of 14 batches of **Pfizer's Ecalta** (anidulafungin), an antifungal drug, and one batch of **Lantheus' Luminity**, a diagnostic agent.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	December 2011	
December 21	**Medicare Recovery Auditor Prepayment Review Demonstration** that starts January 1, 2012	CMS Special Open Door Forum (ODF) conference call
	January 2012	
January	**Pfizer's Prevnar13** (PCV13), a pneumococcal vaccine for adults	PDUFA date
January 3	**Medical device labeling** feedback is sought	FDA deadline for public comment
January 11	**Torax Medical's LINX Reflux Management System** to treat the symptoms associated with gastroesophageal reflux disease (GERD)	FDA's Gastroenterology and Urology Devices Advisory Committee
January 20	Efficacy of **Columbia Laboratories' progesterone gel 8%** to reduce the risk of preterm birth in women with short uterine cervical length	FDA's Reproductive Health Drugs Advisory Committee
January 28	**Bristol-Myers Squibb and AstraZeneca's dapagliflozin**, a first-in-class SGLT2 inhibitor for Type 2 diabetes	PDUFA date
January 28	**Eli Lilly, Amylin Pharmaceuticals and Alkermes' Bydureon** (weekly exenatide XR), an injectable drug for Type 2 diabetes	FDA decision date
	February 2012	
February	**Alcon's tandospirone** for dry AMD – Phase III final data expected	Company announcement or medical conference presentation
February 4	**Alexza Pharmaceuticals' Adasuve** (loxapine inhalation powder) for the acute treatment of agitation associated with schizophrenia/bipolar I disorder	PDUFA date
February 9	**NeurogesX' Quetenza** (transdermal capsaicin) for HIV-related neuropathic pain	FDA's Anesthetic and Analgesic Drug Products Advisory Committee
February 10	Possible reclassification of **cranial electrotherapy stimulator (CES) devices** to Class III (requiring a PMA)	FDA's Neurological Devices Advisory Committee
February 17	**Corcept Therapeutics' Corlux** (mifepristone) for Cushing's syndrome	PDUFA date
February 27	Review of evidence needed for approval of **anti-inflammatory ophthalmic drugs post-ocular surgery** and appropriateness of marketing a single bottle for use in both eyes post-surgery	FDA's Dermatologic and Ophthalmic Drugs Advisory Committee
February 28	**Pfizer's axitinib** for advanced renal cell carcinoma	PDUFA date (*approximate*)
	March 2012	
March tba	**Anti-nerve growth factor (NGF)** drug class safety review	FDA's Arthritis Advisory Committee – originally scheduled for September 13, 2011, but postponed indefinitely, now March 2012
March 6	**Discovery Labs' Surfaxin** (lucinactant) for infant respiratory disease	PDUFA date
March 7	**NeurogesX' Quetenza** (transdermal capsaicin) for HIV-related neuropathic pain	PDUFA date
March 8	**Roche/Genentech and Curis' vismodegib** for advanced basal cell carcinoma in adults for whom surgery is not an option	PDUFA date
March 27	**Affymax and Takeda's peginesatide** for anemia	PDUFA date
March 28	**Bristol-Myers Squibb's Eliquis** (apixaban) to prevent strokes in AFib	PDUFA date
March 28	**Chelsea Therapeutics' Northera** (droxidopa) for symptomatic neurogenic orthostatic hypotension with primary autonomic failure	PDUFA date
March 28	**Edwards Lifesciences' Sapien** transcatheter aortic valve	CMS expected to publish NCD decision memo
	April 2012	
April 17	**Vivus' Qnexa** (phentermine + topiramate) for weight loss	PDUFA date for resubmission
April 18	**Vertex Pharmaceuticals' Kalydeco** (ivacaftor) for cystic fibrosis	PDUFA date
April 24	**Cell Therapeutics' pixantrone** for aggressive non-Hodgkin's lymphoma	PDUFA date
April 25	**Takeda's alogliptin**, a DPP-4 for Type 2 diabetes	PDUFA date
April 26	**Amgen's Xgeva** (denosumab) for prevention/delay of bone metastases in prostate cancer	PDUFA date
April 27	**Salix Pharmaceuticals and Progenics Pharmaceuticals' Relistor** (methylnaltrexone injection) for opioid-induced constipation	PDUFA date
April 29	**Vivus' avanafil** for erectile dysfunction	PDUFA date
April 30	**Baxter and Halozyme's HyQ** for immunodeficiency	PDUFA date

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	Other 2012	
May 1	**Protalix Biotherapeutics' taliglucerase alfa**, an investigational Gaucher disease drug	PDUFA date
June	**Forest Laboratories and Ironwood Pharmaceuticals' linaclotide** for IBS-C	PDUFA date
June 25	**QRxPharma's MoxDuo** (morphine + oxycodone)	PDUFA date
June 26	**Edwards Lifesciences' Sapien** transcatheter aortic valve	CMS final NCD expected
July 26	**Amarin's AMR-101** (omega-3 fish oil EPA) to treat hypertriglyceridemia	PDUFA date
July 26	**Horizon Pharma's Lodotra** (low-dose prednisone) for rheumatoid arthritis	PDUFA date
July 27	**Onyx Pharmaceuticals' carfilzomib** for multiple myeloma	PDUFA date
July 30	**Regeneron's Arcalyst** (rilonacept) for gout	PDUFA date
August	**Pfizer's tofacitinib,** an oral JAK2 inhibitor for rheumatoid arthritis	PDUFA date