Trends-in-Medicine

Quick Takes

by Maude Campbell and Lynne Peterson

Trends-in-Medicine
Stephen Snyder, Publisher
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409 Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

March 21, 2010

…Highlights from this week's news affecting drugs and devices in development…

SHORT TAKES

- **ISTA PHARMACEUTICALS** received a warning letter from the FDA telling the company to stop misleading advertisements for Xibrom (bromfenac ophthalmic solution) which, the FDA complained, suggest the drug is superior to others in its class.
- **OSI PHARMACEUTICALS** rejected an unsolicited offer from Astellas Pharma to purchase the company for $3.5 billion.
- **SIRION THERAPEUTICS** received an FDA warning because a sales aid card for Durezol (difluprednate ophthalmic emulsion) 0.05% promotes an unapproved dose, overstates the efficacy of the drug, and makes unsubstantiated claims.
- **TIGENIX** faces what may be a 5-year delay before it can market its cartilage repair product, ChondroCelect. The FDA has instructed the company to conduct another trial before it can submit for approval.

NEWS IN BRIEF

ALPHARMA – agrees to $42.5 million fraud settlement

Alpharma reached a $42.5 million settlement with the U.S. Department of Justice over allegations that the company made fraudulent or false safety and efficacy claims about its pain drug, Kadian (morphine sulfate extended-release), in an effort to increase prescribing. According to the Department of Justice, Alpharma also funded training programs, consulting forums, research grants, and speaker's bureaus to illegally promote the drug. Terms of the settlement include an $8.9 million payment to state Medicaid programs throughout the country.

BOSTON SCIENTIFIC – recalls all ICDs and CRT-Ds

Boston Scientific notified the FDA early last week that it became aware of two production changes that had not been submitted for FDA approval, and therefore was recalling all affected devices. The recall applies to all implantable cardioverter

defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds) in the company's Cognis, Confient, Livian, Prizm, Renewal, Teligen, and Vitality product lines. The FDA is advising that these devices not be implanted until it reviews and approves changes made to them, meaning Boston Scientific will need to submit premarket approval supplements for each ICD and CRT-D. As for already-implanted models, the FDA said it is "not aware of new safety concerns and, therefore, does not recommend that any of the devices subject to the recall be explanted."

FDA questions third-party device reviews

As part of its reevaluation of the device-approval process, the FDA is taking another look at third-party reviews of medical devices submitted for approval. Proposed changes to the current policy are expected later this year. Measures being considered include terminating the third-party system, limiting the types of devices the third-party policy covers, or giving outside reviewers more information on devices in an effort to improve their review quality all are being considered. Leading to the concern over third-party review are FDA data indicating that more than 80% of radiological device reviews from outside companies were accepted without additional action, and that 300 third-party device reviews were submitted in 2008 vs. only 185 in 2003. The program is a popular way for manufacturers to bring devices to market earlier. Approximately a third of the devices in the third-party program are imaging machines.

Hospital marketing

Worried about long waits in hospital emergency rooms? A Florida hospital has found a new marketing gimmick. It is advertising the current wait time for its ER on a billboard on a major interstate. The time is updated electronically, just like a temperature chart. At 9:30 pm on a recent Tuesday night, the wait time was listed in big red letters as 11 minutes. The question is: If you were on the way to the hospital and the wait time was three hours, should you turn around and go home, stop at the store and get a snack and a book first, or get to the hospital as quickly as you could?

LILLY/AMYLIN PHARMACEUTICALS/ALKERMES' Byetta-LAR – gets complete response letter from FDA

The FDA failed to approve the long-acting version of Byetta (exenatide), known as Byetta-LAR injectable, for diabetes, asking that the company provide more information on its proposed risk management plan, product label, and manufacturing process. The good news was that the FDA did not request additional clinical trial data or additional analysis of existing clinical trial data. This indicates that the issues will fall under a Class 1 resubmission, not requiring advisory committee review, and significantly decreasing the delay until approval, the company said. Byetta-LAR can be injected once a week vs. the BID version currently available.

MANNKIND's Afrezza (inhaled insulin human [rDNA origin]) – FDA requests more data

The FDA has requested more information, including additional ***clinical*** data, on the company's inhaled insulin product, formerly called Technosphere, intended for treatment of both Type 1 and Type 2 diabetes. The FDA also has questions about the MedTone inhaler that will be marketed with the drug because an earlier version of the inhaler was used in the Afrezza clinical trials. The FDA said it has completed its review of Afrezza and had no safety concerns but asked for updated safety data as well as changes to the proposed labeling.

MEDTRONIC/CORE VALVE – international trials begin

An international clinical program for the CoreValve transcatheter aortic valve system has started enrolling patients worldwide (outside the U.S.). The clinical program, CoreValve Advance, is a prospective, observational, postmarket study to evaluate outcomes in patients with severe aortic stenosis treated with the CoreValve system. The program will enroll ~1,000 patients at about 90 clinical trial sites. The system offers a minimally-invasive approach for aortic valve replacement in patients with severe aortic stenosis.

MEDTRONIC's Deep Brain Stimulation (DBS) Therapy – FDA panel recommends approval, with conditions

The FDA's Neurological Devices Panel voted 7 to 5 to recommend FDA approval of DBS as an adjunct for partial-onset seizures in adults with refractory epilepsy, with two conditions: (1) a post-approval study be required to track patient safety for five years and (2) product labeling should contain warnings about the potential for depression and memory loss with treatment. The device already is approved for treatment of movement disorders, including Parkinson's disease.

MEDTRONIC's Revo MRI SureScan – panel recommends FDA approval

The Circulatory System Devices panel of the FDA's Medical Devices Advisory Committee voted unanimously on March 19, 2010, to recommend approval of what would be the first pacemaker considered MRI-safe. Currently, MRIs are avoided in patients with a pacemaker because the scan can interfere with the operation of the pacemaker. Revo would allow MRIs of most – but not all – of a patient's body.

MERCK's Zocor (simvastatin) – receives FDA warning

The FDA issued a warning for a potentially increased risk of muscle injury, including the development of rhabdomyolysis, among patients taking higher doses (80 mg) of the drug. Zocor is sold alone, combined with ezetimibe in Merck's Vytorin, and combined with extended-release niacin in Abbott

Laboratories' Simcor. The warning is the result of an "ongoing FDA effort to evaluate the risk of statin-associated muscle injury and provide that information to the public as it becomes available," the FDA said. In addition, the FDA is reviewing muscle injury data from the SEARCH trial comparing cardiovascular event outcomes in patients taking 80 mg vs. 20 mg of the agent.

NEC Display Solutions – cautions against diagnostic use of consumer-grade displays

NEC Display Solutions of America is recommending that radiologists ***not*** use consumer-grade LCD displays for diagnostic purposes. The practice is becoming more common with increasing hospital budgetary constraints and the boom in telemedicine, specifically teleradiology. Teleradiology practices allow the radiologist to practice outside of a traditional hospital, lab, or office. Budget constraints also are leading many institutions to consider commercially-available, consumer-grade LCD displays for in-hospital use.

According to the American College of Radiology, >70% of radiology errors are perceptual, and perceptual diagnostic errors can lead to lawsuits. Medical-grade displays offer the resolution needed to observe small details and display an adequate range of shades of gray and a uniformly bright image. NEC notes that while many consumer-grade LCD displays may appear to be good enough for diagnostic work, medical-grade displays offer better return on investment in several ways:

- A typical medical-grade display has a product life four times that of a consumer-grade display.
- Medical-grade displays typically offer longer warranties and some even come with overnight replacement.
- Medical-grade displays include integrated front sensors and backlight sensors that automatically hold calibration steady over a period of time.

SBS/ALA – to vote on merger

The memberships of the Society for Biomolecular Sciences (SBS) and the Association for Laboratory Automation (ALA) will vote by proxy on whether to approve a merger of the two groups. The organizations have been strategizing a merger for the past 18 months. If approved, both the SBS and ALA will retain their individual identities but will provide a single international community dedicated to advancing scientific research and discovery through laboratory technology.

Vertebroplasty – efficacy continues to be debated

Presentations given during the Society of Interventional Radiology (SIR) meeting indicate that vertebroplasty ***does*** confer benefit, specifically in the alleviation of pain. This news is in contrast to recently published trials which found similar outcomes between patients undergoing vertebroplasty and those having a sham procedure.

- In a new study of 202 patients with compression fracture randomized to vertebroplasty or conservative therapy, vertebroplasty resulted in significantly better pain relief, and the benefit was sustained at one year ($p=0.014$). Although use of pain medications was reduced during the first month after surgery, there was no significant difference between vertebroplasty and sham procedure in pain medication use at later follow-ups.
- A second, uncontrolled trial of 1,542 patients undergoing the procedure showed that 96.9% had significantly improved pain and disability scores at Month 3 vs. baseline ($p<0.0005$). Investigators for both studies emphasized the need for proper patient selection and effective treatment of the underlying osteoporosis.
- On the other hand, Mayo Clinic investigators presented a subgroup analysis of INVEST, which included 131 randomized patients, comparing pain relief over time between vertebroplasty and a sham procedure, and there was no difference between the groups in either pain severity or disability.