Trends-in-Medicine

Quick Takes

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

SHORT TAKES

BOSTON SCIENTIFIC's Taxus Element – The paclitaxel-eluting Taxus Element stent received a CE Mark for use in diabetics and could be available in Europe as early as June 2010. Boston Scientific is hoping for FDA clearance in 2011.

CLEARSTREAM TECHNOLOGIES – has signed a 5-year contract to purchase and globally distribute Advanced Vision Medical Technologies' SilkenFlex line of self-expanding stents for use in peripheral vascular disease. The stents are expected to be marketed in 4Q10.

GE HEALTHCARE will invest $5 million in a partnership with genetic test manufacturer CardioDx, whose lead product is Corus CAD for detecting a patient's potential for developing obstructive coronary artery disease.

HANSEN MEDICAL – The FDA has granted an investigational device exemption (IDE) allowing Hansen to conduct a clinical trial including 300 patients to assess the safety and efficacy of its Sensei X robotic catheter system and Artisan control catheter in atrial fibrillation.

MAP PHARMACEUTICALS' Levadex (dihydroergotamine) – clinical trials of this inhaled migraine therapy are completed, and the company will seek FDA approval during the first half of 2011.

PFIZER – has acquired rights to Ergonex's investigational pulmonary arterial hypertension (PAH) drug terguride, which is in Phase II clinical trials.

NEWS IN BRIEF

AVEXA's apricitabine – trials stopped for lack of licensing partner

Although Phase III safety and efficacy trials for apricitabine, a nucleoside analog reverse transcriptase inhibitor (NRTI), in previously treated HIV patients showed promising results, Avexa has closed its study program because it has been unable to secure a licensing partner. Apricitabine would have required BID dosing, making it an unattractive competitor to established NRTIs, including Bristol-Myers Squibb/Gilead's once-daily combination Atripla (tenofovir + emtricitabine + efavirenz) and Gilead's Truvada (tenofovir + emtricitabine).

BECKMAN COULTER – expects troponin test filing next year

Beckman Coulter will conduct a prospective clinical trial with its troponin test to satisfy FDA guidance and expects to file a 510(k) application for troponin tests for both its Dxl and Access automated immunoassay systems in 1H11. Earlier this year, the company recalled troponin tests for the Dxl system because of faulty results, and the FDA told the company that modifications had been made to the tests without FDA clearance.

BOSTON SCIENTIFIC – bars media from shareholders' meeting

With no explanation and several media outlets reporting they received a "no comment" response when asking for an explanation, Boston Scientific closed its annual meeting to the media. The company previously allowed reporters to attend. This was the first annual shareholders' meeting held with Boston Scientific under the direction of new president/CEO J. Raymond Elliot, who took over in July 2009.

Could this be because of all the negative news lately?

- Boston Scientific reported 1Q10 losses of almost $1.6 billion.
- In March 2010, it suspended sales of its defibrillators for a month because of failure to obtain prior FDA clearance for manufacturing changes.
- In February 2010, Boston Scientific agreed to pay Johnson & Johnson $1.7 billion over patent disputes.
- In April 2010, a U.S. Federal District Court judge rejected a $296 million settlement between Boston Scientific and the U.S. Department of Justice for defective Guidant defibrillators that caused several deaths during the past 10 years.
- In May 2010, it was revealed that the Department of Justice is investigating the company's ICD reimbursement policies.

GLAXOSMITHKLINE's Promacta (eltrombopag) – new safety concerns

GSK alerted the FDA that it terminated the randomized, placebo-controlled ELEVATE trial using this thrombopoietin receptor agonist in patients with idiopathic thrombocytopenic purpura (ITP) because of increased incidents of portal venous thrombosis. In the trial, six patients (4%) receiving Promacta had a thrombotic event of the portal venous system, and five of the six patients had portal venous thrombosis. One patient (1%) receiving placebo experienced a thrombotic event. Promacta is currently approved for use in thrombocytopenia, and GSK plans to work with the FDA on labeling revisions. Meanwhile, GSK said Promacta should be administered with caution to patients with hepatic disease or known risk for thromboembolism. In addition, Promacta treatment should not be used in an attempt to normalize platelet count but should be administered to achieve a platelet count that minimizes bleeding.

Insulin-degrading enzyme (IDE) inhibitor developed

Researchers at the Mayo Clinic in Florida have developed small molecules that prevent IDE from devouring insulin, allowing the hormone to remain in the body longer for glucose control. The research was partially funded by the National Institutes of Health (NIH) and was reported in the May 2010 issue of ***PLoS ONE***. Because insulin is involved in a wide range of processes, including memory and cognition, IDE inhibitors may eventually have uses beyond treatment of diabetes, the researchers said.

Insurance company rate increases targeted

A new report released by Health Care for America Now (HCAN) says the five largest for-profit health insurance companies recorded huge profits in 1Q10 while covering fewer people and offering fewer benefits. Sen. Dianne Feinstein (D-CA) and Rep. Jan Schakowsky (D-IL) have introduced a bill – the Schakowsky-Feinstein Health Insurance Rate Authority Act of 2010 – would give Health and Human Services Secretary Kathleen Sebelius the authority to ***block or modify insurance rate increases deemed unreasonable*** and the ***authority to order insurance companies to pay rebates to consumers***.

In a teleconference with reporters, Sen. Feinstein, Rep. Schakowsky, and HCAN executive director Ethan Rome roundly criticized the insurance industry in general and WellPoint/Anthem in particular. Sen. Feinstein explained that the bill would give the Secretary of Health and Human Services (HHS) the "authority to assure Americans that rates are reasonable, and it sets up a methodology by which it can be achieved. If a state already has an insurance commissioner which can do the investigations and make the findings, then it is not affected…But it establishes a federal floor to ensure that rates don't go up 39% a year, which right now could happen."

Outlook in the Senate: Sen. Feinstein candidly said this legislation will ***not pass*** in the Senate unless some Republicans vote for it, and she was not optimistic about that, "I think that it's clear that there is support…We will not have every Democrat. I doubt that Sen. Ben Nelson will support it, so we'd need to pick up some Republicans, and that is the difficult part…This is hard, and I'm not sure [that we can pass it]. We've been working on it. Someone I thought would be for it is now against it, and there is a staunch view [among Republicans in the Senate] that this is a state issue and that the states should take care of it."

Outlook in the House: Rep. Schakowsky predicted that the bill would pass the House quickly, especially in light of recent bad publicity for WellPoint/Anthem and other insurance companies. She said that she is hopeful the House will pass the bill before the mid-term elections, "The insurance companies have been helpful in moving this bill along [with all the bad publicity]. People are astonished at the increases being proposed, and I do understand that this is about greed and not necessity…I'm optimistic about this legislation because it will take care of these unconscionably rising rates. There is wide consensus that this is something that needs to be done."

Sen. Feinstein said the bill will help states that don't have the ability to regulate insurance premiums, "The problem is that some states have the legislation to take care of it (regulating insurance premiums), and others don't. About 20+ states do have insurance commissioners who can regulate. California does not. What the legislation would do is set up a federal floor, and I think that is a guarantee for consumers that they will be protected. The loophole is that there is nothing in healthcare reform that would stop this from happening. Many people think that once the [healthcare insurance] exchanges are in play, which is 2014, this [huge increases in rates] won't happen because there will be competition among exchanges and among plans. I don't know whether it's true or not, but let's say it is. You still have a period of time where you can have really high rate increases."

The insurance industry was accused of making outrageous profits at the expense of consumers. Sen. Feinstein said, "The driving force in this sector is profits for shareholders. It isn't good coverage for beneficiaries, and that's a problem...We know that from 2000 to 2008 premiums have increased some 97% for families, and in view of the profit that's made, I think that is really unacceptable. Over the last two years two million people in California have lost their healthcare coverage, and at the same time Anthem, a subsidiary of WellPoint, is increasing [premiums]. Its profits have gone up quarter-over-quarter some 51%, and yet their non-medical costs generally average 19%, and the medical loss ratio in a year is about 1%, so clearly this is a hugely profit-driven industry. I'm concerned because we have until 2014 when exchanges go online. There is nothing to stop these companies from raising premiums further."

The insurance industry's exemption from antitrust legislation was also lambasted. Sen. Feinstein said, "All of these companies have been exempted from antitrust. Other than Major League Baseball, no one is exempted from antitrust [laws]. This means that they (the insurance companies) can merge and acquire, which is happening."

Sen. Feinstein explained why the language was not included in the healthcare reform legislation that already passed, "When President Obama heard of the WellPoint/Anthem situation, he put our bill into the reconciliation package. The reconciliation package came over to the Senate, but it failed the Byrd Point of Order of 60 votes, and the budget implications weren't as high as the policy implications. The Parliamentarian ruled that point of order would rest against it, and it fell from the bill."

Rep. Schakowsky called the bill "really just a follow-up on to what would have been in the bill in the first place. We're already seeing healthcare insurers trying to wrangle out of the provisions [of the healthcare reform legislation], especially as it relates to medical loss ratio…WellPoint is the poster child for unbridled greed…In Illinois, I have constituents who are facing a 60% rate hike this year…Someone in California reviewed its 39% rate increases, and they were able to catch the faulty math, and that rate increase isn't going through. So, you have to wonder about miscalculations. And Americans need the protection of tough regulation in the name of their health and financial security."

Asked if she would offer the bill as an amendment on financial regulatory services or an extenders bill, Sen. Feinstein said, "We can't add it [in the Senate] on the extenders bill. It has to be added in the House. It is a possibility. I wouldn't add it on the regulatory bill, though I thought that might be worth a try in the beginning. But it gives people too many excuses to vote against it, such as it being not pertinent to the subject at hand."

HCAN's Rome said the results his organization found were "stunning." He said, "In the worst economy since the Great Depression, the five largest for-profit health insurance companies recorded huge profit gains in the first three months of 2010 compared with a year earlier. Combined net income was $3.2 billion, a 31% leap from the same period in 2009. This came after they set a profit record for the full year of 2009. So the real question is how do they do it? They do it through greed…Our report shows that the top five insurers made record profits by covering fewer people, offering worse benefits, providing less care, and charging consumers and employers more. It is an obscene business model. They sell people a product, make it worse, and deny people the healthcare they pay for when they need it the most…What this all adds up to is skyrocketing premiums that businesses and families can't afford…From 2000 to 2008, family premiums for the big insurers grew twice as fast as medical inflation, five times faster than general inflation, and three times faster than wages. As we have all recently learned, it gets worse. WellPoint's rate request was based on faulty numbers. Maybe

WellPoint had bad intentions, or maybe they're just bad at math."

MERCK – will seek five approvals, halts anemia drug

Merck plans to file for FDA approval for five drugs in 2010.

1. The contraceptive NOMAC/E2, which combines natural estradiol with the progestogen, nomegestrol acetate.
2. An extended-release form of Janumet (metformin + sitagliptin) for diabetes treatment.
3. A combination of Zocor (simvastatin) and Januvia (sitagliptin) for patients with diabetes and dyslipidemia.
4. Boceprevir, a treatment for hepatitis C.
5. Ridaforolimus for sarcoma treatment.

Meanwhile, Merck has halted clinical trials with a long-acting version of erythropoietin for anemia, which would have competed with several similar agents already on the market.

NICOX's naproxcinod (naproxen nitric oxide donor) – fails to gain FDA advisory committee support

Members of the FDA's Arthritis and Drug Safety and Risk Management Advisory Committee voted 17 to 1 ***against*** recommending approval of this anti-inflammatory for pain relief in patients with osteoarthritis. This would have been the first-in-class cyclooxygenase-inhibiting nitric oxide donor. It consists of naproxen bound to a nitric oxide moiety and was designed to provide the anti-inflammatory effects of naproxen while lessening the gastrointestinal side effects and increased blood pressure often observed with other Cox-inhibiting agents. NicOx plans to conduct additional safety and efficacy studies for naproxcinod.

NOVARTIS/VECTURA's Onbrez (indacaterol) + NVA-237 – Phase III trials begin

Phase III trials have begun with the combination of Onbrez and NVA-237 in patients with severe chronic obstructive pulmonary disease (COPD). One trial will include 2,000 patients and compare the combination to NVA-237 alone, and another will evaluate safety and tolerability of the combination in 339 patients. Novartis is not expected to file for regulatory approval for the combination before 2012. Phase III trials of NVA-237 alone began in June 2009, and the company plans to seek approval for monotherapy in 2011. Onbrez is currently available in Europe for treatment of asthma and COPD.

PATHWAY GENOMICS' Insight – Walgreens postpones genetic test kit sales

Walgreens will postpone selling Insight saliva testing kits in any of its 7,500 U.S. retail stores until it receives "further clarity" from the FDA. Walgreens had planned to make the kits available this month for $20-$30. Consumers would then mail in a saliva sample and make a further purchase online for an ancestry and health report for about $199. The test kits are also available online and claim to detect carrier status and genetic markers for more than 70 health conditions. On May 10, 2010, the FDA issued a letter to Pathway saying the Agency "had been unable to identify any Food and Drug Administration clearance or approval number" for the test kit and advising the company to "provide the basis of the determination" on which the company may believe FDA clearance or approval is not required.

PFIZER's neratinib – moving into Phase III clinical trials

Phase III clinical trials using the anti-HER2 agent in combination with Taxol (paclitaxel) are planned after Phase II study results reported at the IMPAKT Breast Cancer Conference showed promise. In one Phase II trial, 69% of patients with metastatic breast cancer responded. In a second trial of women treated with neratinib and GSK's Navelbine (vinorelbine), there was a 25%-43% overall response rate. The most common adverse event associated with neratinib was diarrhea. Neratinib inhibits the ErbB-1, -2, and -4 receptors. Currently available anti-HER2 drugs include Genentech's Herceptin (trastuzumab), which inhibits ErbB-1, and GSK's Tykerb (lapatinib), which blocks ErbB-1 and -2.

Late tPA administration – causes "significant harm"

U.K. researchers reported in the ***Lancet*** that administering tissue plasminogen activator (tPA) 4.5 hours after onset of stroke symptoms causes "significant harm" and increases the likelihood of death and a poor recovery. They analyzed data from eight clinical trials including 3,670 stroke patients and found that those receiving tPA within 3 hours of stroke onset were most likely to have a full recovery. Those receiving the anticoagulant within 90 minutes had double the chance of a full recovery vs. those not receiving it within 3 hours. Patients who had tPA at 4.5 hours after stroke onset were only 22% more likely to go on to a full recovery than were stroke patients who never received tPA.

ST. JUDE MEDICAL's Epicor – receives off-label use warning

The FDA issued a warning letter because some St. Jude marketing statements, including one on the company's website, imply that the Epicor surgical ablation device can be used to treat atrial fibrillation. Epicor is FDA cleared for cauterizing tissue during surgery but is not cleared for cardiac ablation. However, marketing statements included the wording, "safely, effectively, and reproducibly create a classic box lesion in a single step," which describes a lesion typically used during ablative procedures for atrial fibrillation. St. Jude said it is "working diligently to address the points in the warning letter and to resolve the FDA's concerns."

FDA NEWS

➢ Radiation device public meeting

A public meeting will be held June 9-10, 2010, during which the FDA will seek feedback from radiation therapy device manufacturers on how best to prevent misadministration of radiation treatments. The meeting is part of the FDA's initiative to better regulate radiation therapy devices due to previous reports of overdoses. Radiation device makers also will be asked to suggest methods for improving clinician training in the use of their devices.

➢ Rotavirus vaccines recommendations revised

The FDA has determined that it is appropriate for healthcare professionals to resume the use of GSK's Rotarix and to continue the use of Merck's RotaTeq. The Agency said the decision was based on "a careful evaluation of information from laboratory results from the manufacturers and the FDA's own laboratories, a thorough review of the scientific literature, and input from scientific and public health experts, including members of the FDA's Vaccines and Related Biological Products Advisory Committee which convened on May 7, 2010, to discuss these vaccines.

The FDA said it also considered the following in its decision:

- Both vaccines have strong safety records, including clinical trials involving tens of thousands of patients as well as clinical experience with millions of vaccine recipients.
- The FDA has no evidence that either contaminant in the vaccines – PCV1 or PCV2 – poses a safety risk in humans, and neither is known to cause infection or illness in humans.
- The benefits of the vaccines are substantial, and include prevention of death in some parts of the world and hospitalization for severe rotavirus disease in the U.S.
- The benefits outweigh the risk, which is "theoretical."

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