GENERIC LINE®

Vol. 25, No. 15
Aug. 6, 2008

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Lawmakers Blast Drugmakers for High Prices, Look to Biosimilars

Lawmakers outraged by what they call extraordinary drug price increases have asked the Government Accountability Office to see if the increases are justified and directed the Federal Trade Commission (FTC) to investigate a drug firm's potential anti-competitive conduct for one product.

Acknowledging that the Orphan Drug Act provides incentives to recoup R&D costs of drugs for niche markets, "at least a handful of drug companies have used this 'status' of orphan drugs to keep increasing costs — well beyond the costs of research, development and manufacturing," Sen. Amy Klobuchar (D-Minn.) said as she opened a hearing on egregious price increases in the pharmaceutical drug industry.

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Congress Questions FDA in Wake Of Ranbaxy Justice Probe

Two congressmen have launched an investigation into whether the FDA allowed drugs made by Ranbaxy to be sold in the U.S. despite knowing it had approved them based on fraudulent information and were made in violation of good manufacturing practices.

Reps. John Dingell (D-Mich.), chairman of the Committee on Energy and Commerce, and Bart Stupak (D-Mich.), chairman of the Subcommittee on Oversight and Investigations, sent a letter to FDA Commissioner Andrew von Eschenbach requesting information on each drug for which Ranbaxy has FDA approval.

The letter came roughly a week after India-based Ranbaxy defended itself against allegations in a Justice Department motion that it and consultant Parexel had withheld subpoenaed documents and thwarted an investigation over alleged fraud and conspiracy involving generic applications.

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She singled out some drugmakers. For example, Ovation Pharmaceuticals increased the price of Indocin IV (indomethacin sodium), a drug used to repair a heart problem in some premature infants, from $100 to $1,875, she said, noting she had asked the FTC to investigate the firm's conduct for the product.

"Yet Indocin is an old drug," Alan Goldbloom, president and CEO of Children's Hospitals and Clinics of Minnesota, testified at the Joint Economic Committee hearing. "It has been on the market for more than three decades, so this dramatic price increase cannot be attributed to the high cost of research and development." Ovation did not respond to a request for comment by press time.

Klobuchar also singled out Questcor Pharmaceuticals, which she said increased the price of H.P. Acthar Gel (corticotrophin) from about $1,600 per vial to $23,000. The drug is indicated to treat multiple sclerosis but is used off-label as standard treatment for infantile spasms, a disorder that affects about 2,000 U.S. patients, she said.

Questcor raised Acthar's price "to the level required to ensure its availability," it says in a prepared statement regarding the hearing. It "struggled for years to keep the drug financially viable" and is "not aware of any patients who need the drug but have not been able to access it," the company adds.

Follow-on Biologics Pathway

Acknowledging benefits from pharmaceutical innovation, Sen. Chuck Schumer (D-N.Y.), the committee's chairman, said, "The testimonies today are disturbing and show that much greater oversight and, perhaps, even significant action by the Congress is needed."

He noted that he had introduced a bill to create a way to approve generic versions of biologics and was "pleased that the National Organization for Rare Diseases touted the passage of a pathway for follow-on biologics in their submission for the record of this hearing."

His bill, the Access to Life-Saving Medicine Act, H.R. 1038, was introduced last year by Rep. Henry Waxman (D-Calif.). HHS Secretary Mike Leavitt has endorsed Schumer's suggestion that the FDA and Congress work together to formulate proposed legislation for creating a follow-on biologics approval pathway, and President Bush included user fees for such a pathway in his proposed fiscal 2009 budget for the FDA (*Generic Line*, Feb. 20).

According to the Generic Pharmaceutical Association (GPhA), several studies have shown that the availability of biogenerics would save the health care system billions of dollars each year. A study by Insmed, a biotech company, estimated $67 billion to $108 billion in savings over 10 years, with $236 billion to $378 billion in savings over 20 years for generic versions of the top 12 categories of biologics with patents that either have expired or are soon to expire.

A study conducted on behalf of the Pharmaceutical Care Manufacturers Association estimated $14.9 billion in savings over a standard 10-year scoring period for certain biopharmaceuticals in the top 200 Medicare Part B reimbursed categories. Express Scripts estimated $71 billion in savings over 10 years for products in four therapeutic categories — interferons, erythropoietin, growth hormone and insulin, GPhA said.

"Countless patients in need of life-saving biopharmaceutical treatments are struggling to afford their high costs. For patients facing serious conditions such as cancer and heart disease, safe and affordable biogenerics would allow them to improve their lives while reducing their health care costs," said GPhA President and CEO Kathleen Jaeger said.

The senators' opening statements and witnesses' written testimony are available at jec.senate.gov/index.cfm?FuseAction=Hearings.HearingsCalendar&ContentRecord_id=4b40a6a9-9445-145b-51f4-492c9a16b85b. Questcor's statement is available at www.questcor.com/pdf/Quesctor_Statement.pdf. — David Grant

Teva, Par Face Lawsuit Over RLS Drug

Teva Pharmaceuticals and Par Pharmaceutical are facing a lawsuit in which the plaintiff alleges the companies' generic versions of pergolide, a treatment for Parkinson's disease and restless leg syndrome (RLS), caused her valvular heart disease.

The companies "misrepresented the safety and efficacy of pergolide and concealed or understated [these] dangerous side effects," plaintiff Leigh Ann Karnell alleges in court documents. A generic version of Valeant's Permax (pergolide mesylate), the drug is a member of a class of ergot derivatives, which have been associated with certain cardiovascular conditions.

Karnell claims to have taken pergolide from February 2003 until March 2007 for RLS and suffered "serious and permanent injuries including, but not limited to, valvular heart disease" as a result, according to court documents.

She has asked the court for compensatory damages in excess of $75,000, a full refund of costs associated with her purchase of the drug, pre- and post-judgment interest, attorney's fees and other costs related to the litigation.

In March 2007, Valeant withdrew Permax after two studies showed patients taking it increased their chance of serious heart damage compared with patients taking other Parkinson's drugs, according to the FDA. Par and Teva also withdrew their generic versions of the drug from the market at that time.

The two studies were published in the Jan. 4, 2007, *New England Journal of Medicine*. They showed the use of either Permax or Pfizer's Dostinex (cabergoline), a drug indicated to treat hyperprolactinemia, was associated with an increased risk in heart valve damage not seen in patients taking non-ergot-derived dopamine agonists.

Teva said it was unable to comment on the lawsuit, and Par did not respond to a request for comment by press time. — Elizabeth Jones

Actavis Recalls Products After FDA Inspection

Actavis Totowa, a U.S. subsidiary of Icelandic generic drug firm Actavis, is recalling all drug products manufactured at its plant in Little Falls, N.J., after an FDA inspection revealed the products were not made according to GMP standards.

"A recent inspection revealed operations which did not meet the FDA's or Actavis' standards," the company said. "This action is not prompted by product complaints or health hazards associated with the products, which are all prescription medications."

Approximately 55 different products are being recalled, ranging from anti-viral drug amantadine HCl to painkiller oxycodone. Tuberculosis antibiotic rifampin also is affected, as well as Type 2 diabetes drug glyburide and antidepressant mirtazapine.

According to the FDA's July 30 Enforcement Report, the company is recalling 117,469 amantadine HCl 100- and 500-count bottles because they contained product found to be subpotent after 18-month stability tests.

The firm also is recalling 42,024 glyburide 100- and 1,000-count bottles and 89,201 mirtazapine 30-unit blister packs because the drugs exceeded impurity specifications, the report says.

Products made at other U.S.-based Actavis facilities, including sites in Sunrise, Fla., Baltimore, and Elizabeth, N.J., are not affected by the recall, the company said.

Last year, Actavis received a warning letter for the Little Falls facility. The plant was cited for various quality control deficiencies, including inadequate cleaning validation studies and manufacturing equipment maintenance, as well as for failures to investigate out-of-specification test results.

"We are in the process of implementing corrective actions at the Little Falls facility and are working quickly and carefully to return products to the market," Actavis said. — Christopher Hollis

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Justice, through the U.S. State Attorney's Office for the District of Maryland and the Civil Division, Office of Consumer Litigation, maintains the company submitted false information about stability and bioequivalence to support ANDAs for anti-retrovirals distributed by the President's Emergency Plan for AIDS Relief, a five-year, $15 billion program aimed at combating HIV and other diseases in 114 countries.

The government is probing whether Ranbaxy used active pharmaceutical ingredients (API) from unapproved sources, blended approved with unapproved API and put less API in drugs than approved by the FDA. It had subpoenaed certain documents, some of which the company refused to provide.

Ranbaxy subsequently said it would turn over all requested documents (*Generic Line*, July 23). Under an order issued July 29, Justice's motion to enforce subpoenas is being held in abeyance for 60 days to give Ranbaxy enough time to produce the documents and the government time to confirm they have been produced.

According to Justice's motion, the FDA was aware of the alleged "pattern of systematic fraudulent conduct" for at least 18 months but did not remove the products from the market.

"If true, these statements would call into serious question whether the leadership of the Agency, including your office, the Center for Drug Evaluation and Research, and the Office of Regulatory Affairs, have met even the minimum requirements of due diligence with respect to the FDA's primary mission under the Federal Food Drug and Cosmetic Act," the congressmen's letter says.

In light of the agency's alleged inaction in the Ranbaxy case, the lawmakers have requested the FDA provide the following for each drug the company markets in the U.S., and any "for cause" inspections:

- All documents relating to preapproval inspection assignments;
- All documents detailing the tasks undertaken and investigators' findings during the preapproval inspections, including Form 483s or establishment inspection reports (EIRs);
- All documents relating to any "for cause" inspection of Ranbaxy or its API suppliers;
- A list of all API suppliers and any 483s, EIRs and other documents detailing the tasks undertaken and findings resulting from inspections of those suppliers;
- A list of all laboratories that performed bioequivalence studies, noting which Ranbaxy drug substances were tested, when they were tested and the test results;
- Any 483, EIR or comparable document that would describe inspections (if any) of the laboratories that performed bioequivalence testing for Ranbaxy; and
- A list of FDA personnel who conducted or reviewed each inspection listed above.

The lawmakers plan to interview investigators involved in the Ranbaxy inspections by the end of August. — Elizabeth Jones

Teva's Sales Surge In Second Quarter

Teva Pharmaceuticals had record net sales of $2.82 billion in the second quarter, up 18 percent from the same period last year, the firm said in a conference call.

Net income for the quarter was $539 million compared with $515 million for the same period of 2007 — an increase of 5 percent, the company added.

North American pharmaceutical sales were roughly $1.5 billion — an increase of 12 percent compared with the second quarter last year. Quarterly sales were boosted by the launches of generic antidepressant Wellbutrin XL (bupropion HCl) 150 mg and anti-psychotic Risperdal (risperidone), as well as sales of other new generic products in the previous two quarters.

The company also saw strong sales of multiple sclerosis drug Copaxone (glatiramer acetate), which had quarterly global in-market sales of $563 million, reflecting a 29 percent increase over the second quarter of 2007, Teva said. In the U.S., in-market sales increased by 17 percent to reach $332 million, and sales outside the U.S. increased by 53 percent to $231 million.

News of Copaxone's strong sales comes a few weeks after the FDA accepted Momenta and Sandoz's ANDA for a generic version of the drug. Teva said it expects to receive Paragraph IV certifications on the '098, '161, '430, '476, '539, '589 and '847 patents covering Copaxone's chemical composition, pharmaceutical compositions and methods of use. The patents are listed in the Orange Book and expire May 24, 2014 (*Generic Line*, July 23).

Pharmaceutical sales in Europe in the second quarter totaled $762 million, up 25 percent over the same period last year. The increase is a result of strong generic sales in France, Hungary, Poland and the Czech Republic, and increased sales of Copaxone and Azilect (rasagiline mesylate), a treatment for Parkinson's disease.

In June, Teva announced results of a Phase III study of Azilect 1 mg that showed the drug can slow the progression of Parkinson's disease — a finding that could allow it to be the first Parkinson's treatment to receive a label for disease modification.

As of July 23, Teva had 149 product applications awaiting final FDA approval, including 41 tentative approvals. Collectively, the brand products covered by these applications had annual U.S. sales of approximately $93 billion. Of these applications, 88 included Paragraph IV certifications challenging patents of branded products. Teva says it is the first to file on 50 of the 88 applications.

News of Teva's financials comes on the heels of its announcement that it will acquire Barr Pharmaceuticals, the fourth-largest generic drug company in the world. The firm also just closed its purchase of Bentley Pharmaceuticals for roughly $360 million — a move that will boost its presence in Spain. — Elizabeth Jones

Taro: Sales Up Despite Sun Dispute

Despite facing legal costs associated with its attempt to terminate a merger agreement with Sun Pharmaceutical, Israeli drugmaker Taro Pharmaceutical has reported gross profit of about $91.5 million for the first half of the year.

For the six months ending June 30, Taro estimates that it had net sales of roughly $166 million, operating income of about $29.2 million and net income of roughly $20.6 million.

The net income nearly matches the $21.1 million the company achieved during all of 2007, Barrie Levitt, Taro's chairman, said. "Results for the first two quarters indicate dramatic financial and operational improvements and show that the turnaround, to which we referred several months ago, is clearly taking place," he added.

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Taro noted that its success came despite having to spend roughly $10 million to maintain its Irish facility, as well as pay professional and legal fees associated with the termination of a merger agreement with Indian drugmaker Sun.

Since May, the two companies have been involved in a dispute over whether Taro can terminate the merger agreement because of its improved financial situation. Taro also wants to sell its Irish operation, an action to which Sun objects.

In a letter sent to Taro in early June, Sun Chairman Dilip Shanghvi says he "will not stand by idly" if the sale of the Irish operations goes through. Because Taro knows the strategic importance of the Irish facility, Sun regards the attempt to divest the operation as part of an effort to discourage the merger, he says.

If the divestiture moves forward, Shanghvi says Sun will hold Taro's directors liable for breach of fiduciary or other duties.

However, Sun recently has reaffirmed its commitment to maintaining and enhancing Taro's facilities in Israel and reassured Taro's employees that it has no plans to lay anyone off once the merger is complete.

The drugmaker cites newspaper articles reporting that the mayor of Haifa sent a letter to the Minister of Industry expressing concern that "after completing the purchase and merger process, Sun intends to close the production lines in Israel and transfer them to India."

"We believe that the current management of Taro is significantly underutilizing its facilities and has considerably reduced its investment in R&D, which is so vital for the future of a pharma company. Sun Pharma will reverse this. When some of the world's largest and most respected companies, including pharmaceutical companies, manufacture and conduct research for global markets in Israel, and compete effectively, I see a good opportunity for Sun Pharma doing the same using these facilities," said Dilip Shanghvi, Sun's chairman and managing director. — Elizabeth Jones

Endo, Penwest Sue Impax Over Generic Opana

Endo Pharmaceuticals and Penwest Pharmaceuticals are suing Impax Laboratories for amending an ANDA to include the manufacture of generic 7.5-, 15- and 30-mg strengths of the pain drug Opana extended release (ER).

In a June 13 notice, Impax informed the plaintiffs that it had amended its ANDA for generic Opana ER (oxymorphone HCl) with Paragraph IV certifications on the drug's '456 and '933 patents, both of which expire Sept. 9, 2013.

The plaintiffs subsequently filed suit in the U.S. District Court for the District of Delaware. Penwest is the owner of the patents, and Endo, as the exclusive licensee, launched the three strengths earlier this year. The drug also is available in 5-, 10-, 20- and 40-mg strengths.

The plaintiffs sued Impax last November in the same court, alleging it wrongfully sent them a series of Paragraph IV certification notices after the FDA rescinded its acceptance of Impax's ANDA (*Generic Line*, Nov. 28, 2007).

The plaintiffs alleged that Impax had no right to issue the notice, or subsequent notices, without a complete ANDA on file. "Endo and Penwest have asked Impax to withdraw its improperly served Paragraph IV notices, but Impax has refused to do so," they wrote.

After the FDA deemed Impax's ANDA acceptable for filing, the company asserted that its original application met all the requirements for acceptance it would pursue its administrative remedies with the FDA to reinstate its original June 29, 2007 filing date (*Generic Line*, Dec. 12, 2007).

Endo and Penwest also are suing Actavis South Atlantic in the U.S. District Court for the District of New Jersey over a proposed generic version of Opana ER.

Combined net sales for Opana were $40.3 million for the first quarter of this year compared with $29.2 million for the first quarter of 2007, according to Endo. — Elizabeth Jones

Teva, Dr. Reddy's Settle Coreg Suit

Teva and Dr. Reddy's have settled a patent case involving the active pharmaceutical ingredient in GlaxoSmithKline's (GSK) heart drug Coreg.

The suit was one of several Teva filed beginning in June 2007 to protect its '997, '184, '942 and '008 patents relating to Coreg's active ingredient carvedilol. Teva also sued Ranbaxy Laboratories, Watson Pharmaceuticals, Lupin, Orchid Chemical & Pharmaceuticals, Cadila Pharmaceuticals and others in the U.S. District Court for the District of New Jersey.

The defendants in the cases had either received tentative approval from the FDA to market generic Coreg or submitted drug master files indicating they planned to supply carvedilol, according to Teva's complaint.

Teva said it had tried in a May 8, 2007 request to get information on the composition and processes the companies intended to use, but they did not provide the information or samples Teva requested.

As a result, Teva asked the court to declare that its patents were valid and would be infringed on by the products. It also requested a permanent injunction against the companies to prevent them from supplying carvedilol.

The court dismissed the case against Dr. Reddy's without costs and without prejudice, and it may be reopened within 60 days if the settlement is not carried out, according to court documents.

Teva continues carvedilol litigation in the New Jersey court with Apotex and Zydus.

Coreg had U.S. sales of roughly $85 million during the second quarter, according to GSK. — Elizabeth Jones

KV Gets Double the Bad News In Ritalin Suit

KV Pharmaceutical lost its counsel when a New Jersey court disqualified the drugmaker's law firm due to conflict of interest in a patent case against Celgene involving long-acting (LA) Ritalin, a treatment for attention deficit hyperactivity disorder.

KV has 30 days from the date of the opinion to retain new counsel.

Celgene asked that Buchanan Ingersoll & Rooney be removed from the suit before the U.S. District Court for the District of New Jersey because its representation of KV constitutes a conflict of interest prohibited by the New Jersey Rules of Professional Conduct. The rules state, "A concurrent conflict of interest exists if: (1) the representation of one client will be directly adverse to another client," according to court documents.

Buchanan has represented Celgene since 2003 in a securities case in the Superior Court of New Jersey. Although the firm argued that it could continue to represent KV because Celgene had given it two waivers of future conflicts of interest — one in 2003 and another in 2006 — the district court disagreed. It ruled that Buchanan is disqualified from representing KV because it failed to prove Celgene had given truly informed consent.

Celgene and Novartis, which licensed the product from Celgene, filed the lawsuit in October 2007 after KV informed them it had filed an ANDA for generic Ritalin LA (methylphenidate HCl) with Paragraph IV certifications on the 1998 '284 patent and 2003 '284 patent, both of which expire Dec. 4, 2015.

Novartis holds the NDA for Ritalin LA capsules 10, 20, 30 and 40 mg.

The ruling comes days after the court denied KV's motion to dismiss the suit on the basis that Celgene and Novartis had failed to make a reasonable inquiry about its infringement claims, as required by law, before they filed suit.

KV had alleged that the plaintiffs' attorneys had not conducted a reasonable and competent prefiling inquiry as required under Federal Circuit law. But the district court disagreed, stating that the 45-day period in which the Hatch-Waxman Act requires patent owners to bring suit is too short for Celgene and Novartis to have conducted the analysis KV requested in its motion to dismiss.

The Ritalin family of products had worldwide sales of $375 million last year, according to Novartis. — Elizabeth Jones

Barr Sued After Submitting ANDA For Pain Drug

Cephalon and Cima Labs have filed a patent infringement suit against Barr Laboratories after it submitted an ANDA to market generic versions of the pain drug Fentora.

The lawsuit, filed Tuesday in the U.S. District Court for the District of Delaware, came roughly five months after Barr filed an application with Paragraph IV certifications on the '590 and '604 patents to market several strengths of generic Fentora (fentanyl citrate) tablets. The plaintiffs asked the court to enjoin Barr from selling the generic version before the two patents expire in March 2019.

Cima, which Cephalon bought in 2004, owns the patents and has granted Cepahlon a license to market fentanyl buccal tablets in the U.S.

Cephalon and Cima also are suing Watson in the same court for after the drugmaker filed an ANDA for generic Fentora (*Generic Line*, June 11).

The FDA approved Fentora in September 2006 to manage breakthrough pain in cancer patients who tolerate opioid therapy. The drug had annual sales of approximately $142 million in the U.S., based on IMS sales data for the 12-month period ending in May, according to Barr. — Elizabeth Jones

Teva, Barr Face Suit Over Generic Sensipar

Barr Laboratories and Teva Pharmaceuticals are facing a patent infringement lawsuit after filing ANDAs to market generic 30-, 60- and 90-mg strengths of Sensipar tablets, a treatment for secondary hyperparathyroidism in dialysis patients with chronic kidney disease.

The Brigham and Women's Hospital, NPS Pharmaceuticals and Amgen filed the lawsuit in the U.S. District Court for the District of Delaware after receiving notices that Teva and Barr planned to make generic versions of Sensipar (cincalcet HCl). Both firms' generic Sensipar ANDAs contained Paragraph IV certifications on the '244, '146, '068 and '003 patents. The '244 patent expires in October 2015, and the others expire in December 2016.

NPS is the sole owner of the '244 patent and owns the other patents with the Brigham and Women's Hospital. Amgen holds exclusive licenses for each of the patents.

The three plaintiffs asked the court to order that the effective date of any FDA approval of generic Sensipar be no earlier than the expiration of the patents or any later date of exclusivity.

Based on IMS data, Sensipar had annual sales of approximately $377 million in the U.S. for the 12-month period ending in May, according to Barr. The drug was approved in March 2004 by the FDA after a priority review.

News of the lawsuit comes a little more than a week after Teva announced it was buying Barr (*Generic Line*, July 23). — Elizabeth Jones

AstraZeneca Files Suit to Protect Seroquel Patents

AstraZeneca is suing Handa Pharmaceuticals and an unnamed co-defendant for infringing on patents covering schizophrenia drug Seroquel extended release (XR) in 200-, 300- and 400-mg strengths.

The plaintiff brought the lawsuit in the U.S. District Court for the District of New Jersey after receiving notices that Handa had submitted an ANDA for generic Seroquel (quetiapine fumarate) XR with a Paragraph IV certification on the drug's '437 and '288 patents. The '288 patent expires in September 2011, and the '437 patent expires in May 2017.

Handa initially notified AstraZeneca in a July 10 letter that it planned to manufacture the 200- and 300-mg strengths before the patents expire. Then it sent a July 23 letter notifying AstraZeneca that it had amended its ANDA to include a 400-mg dose.

In its letters, Handa alleged the '288 patent is invalid and unforceable and the '437 patent is invalid.

AstraZeneca's suit also claims that a John Doe Entity "initiates, directs and controls the activities of Handa" with regard to the ANDA, has provided financial or technical support in the ANDA's preparation and would profit from its approval.

AstraZeneca has asked the court to declare that the defendants infringe on the patents and enjoin them from selling their product before the patents expire.

U.S. second-quarter sales of Seroquel were $733 million. Total prescriptions were up 6.4 percent, with 40 percent of the growth attributable to Seroquel XR, according to AstraZeneca. — Elizabeth Jones

Eisai Gets Win In Aciphex Suit

A federal appeals court has affirmed a ruling in favor of Eisai in a patent infringement case over proposed generic versions of its proton pump inhibitor Aciphex, a treatment for gastroesophageal reflux disease.

Japan-based Eisai filed the lawsuit in November 2003 in the U.S. District Court for the

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Southern District of New York after Teva Pharmaceuticals and Dr. Reddy's Laboratories submitted separate ANDAs with Paragraph IV certifications to market generic Aciphex (rabeprazole sodium) before the May 2013 expiration of the '552 patent.

Eisai also sued Mylan in the same court in January 2004 after the company submitted an ANDA for the product. The proceeding was stayed, and Mylan agreed to be bound by the final judgments and appeals in that case.

Although Dr. Reddy's stipulated the validity of the patent, both defendants took the position that it should be found unenforceable because Eisai committed inequitable conduct when it applied for the patent. They alleged that Eisai misled the examiner reviewing the '552 patent by not disclosing the existence of a pending application for an '013 patent, which claimed the ethyl homolog of rabeprazole.

Because the compounds in the applications for the two patents were substantially similar, the defendants held Eisai should have told the examiner about the '013 application to avoid double-patenting, according to court documents.

In October 2006, the district court granted partial summary judgment to Eisai, upholding the validity of the '552 patent. The following May, the court ruled that Eisai had established that the defendants had infringed on the patent, a ruling they subsequently took to the U.S. Court of Appeals for the Federal Circuit (*Generic Line*, May 16, 2007).

In their appeal, Teva and Dr. Reddy's reiterated their claim that Eisai had committed inequitable conduct when it obtained its '552 patent. The court disagreed, finding that while the disclosure of the '013 patent application "would have been prudent," Eisai's failure to do so was "by no means fatal," according to court documents.

Aciphex was launched in the U.S. in 1999 and is marketed in more than 90 countries. It was discovered and developed by Eisai and is co-promoted in the U.S. with PriCara, a division of Ortho-McNeil-Janssen Pharmaceuticals. — Elizabeth Jones

Barr Subsidiaries Challenge Xyzal Patents

Sepracor and UCB have filed suit against Barr Pharmaceuticals and two of its subsidiaries for filing an ANDA for a generic version of Xyzal, an allergy treatment.

The plaintiffs filed their suit in the U.S. District Court for the Eastern District of North Carolina after Barr Laboratories and Pliva-Hrvatska submitted an ANDA with a Paragraph IV certification on the '558 patent for Xyzal (levocetirizine dihydrochloride) 5 mg. The patent expires in September 2012.

Barr and Pliva maintain that the patent is invalid, unenforceable or will not be infringed on by the commercial manufacture, use or sale of the product described in the ANDA, according to court documents.

The plaintiffs also are suing Sun Pharmaceutical, Synthon and Sandoz in the North Carolina court for filing applications for generic Xyzal. In both cases, Sepracor and UCB have asked the court to enjoin the defendants from selling generic versions of the drug before the '558 patent expires (*Generic Line*, June 11).

The FDA approved Xyzal in May 2007 to treat symptoms associated with seasonal and perennial allergic rhinitis and uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children age 6 years and older. The drug is distributed and marketed by UCB and sanofi-aventis in the U.S.

Xyzal had annual sales of roughly $74 million in the U.S., based on IMS sales data for the 12-month period ending in May, according to Barr. — Elizabeth Jones

Drugmakers File Lawsuit To Protect Flomax

Astellas and Boehringer Ingelheim have filed a patent infringement suit against Impax Laboratories for submitting an ANDA to market a generic version of Flomax capsules, 0.4 mg, a treatment for benign prostatic hyperplasia.

The firms filed the lawsuit in the U.S. District Court for the Northern District of California, claiming Impax infringed on the ’063 patent covering Flomax (tamsulosin HCl) when it submitted an ANDA for the drug. They have asked the court to issue an order delaying the approval date of Impax’s ANDA until after the patent expires in October 2009, according to Astellas.

According to Wolters Kluwer Health, U.S. sales of Flomax capsules were approximately $1.5 billion in the 12 months ending in May, Impax said. — Elizabeth Jones

Counterclaims to Stand In Naropin Case

A New Jersey judge has refused to dismiss counterclaims asserted by Navinta against Abraxis Bioscience in a patent case involving the anesthesia Naropin.

Abraxis filed its lawsuit in March 2007 in the U.S. District Court for the District of New Jersey after Navinta submitted an ANDA for generic Naropin (ropivacaine HCl monohydrate) with a Paragraph IV certification on the ’086 patent, which expires in September 2010. However, Navinta did not attach a certification on the ’524 and ’489 patents, both of which expire in May 2014, because they were not listed in the Orange Book at the time, according to court documents.

Abraxis amended its complaint in November 2007, alleging that the defendant’s proposed use of ropivacaine HCl as described in the ANDA would infringe on the ’086, ’524 and ’489 patents. Navinta filed its answer the following month, asserting several counterclaims.

Navinta based its counterclaims on allegations that Abraxis conspired with one or more AstraZeneca entities to purposefully delay and manipulate the Orange Book listing of the ’524 and ’489 patents to impede the approval of the ANDA.

Abraxis asked the court to dismiss the counterclaims on various grounds, but it also moved for the bifurcation of the claims from the rest of the action and a stay for discovery as an alternative. Navinta did not oppose this motion, and the court agreed to the bifurcation and stay. — Elizabeth Jones

Teva Forays Into Spain With Bentley Acquisition

Israeli drugmaker Teva Pharmaceutical will boost its presence in Spain after completing its roughly $360 million purchase of Bentley Pharmaceuticals.

New Hampshire-based Bentley manufactures and markets about 130 pharmaceutical products, primarily in Spain. It also sells generics in other parts of the EU through its subsidiaries — Laboratorios Belmac, Laboratorios Davur, Laboratorios Rimafar and Bentley Pharmaceuticals Ireland. Bentley also manufactures and markets active pharmaceutical ingredients through its subsidiary, Bentley API.

Bentley’s generic pharmaceutical operations generated revenues of about $114 million for the year that ended Dec. 31, 2007, and Teva expects to recognize revenue from its acquisition within 12 months of closing.

Following a June spin-off of its drug delivery business into an independent company known as Cpex Pharmaceuticals, Bentley’s generic pharmaceutical operations were its sole business.

Teva initially established a presence in Spain — one of the fastest-growing markets in Europe — in 2004, according to the company. Since then, Teva Genericos Espanola has introduced

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FDA Gives OK For Generic Depakote

The FDA has approved the first generic versions of Abbott's Depakote delayed-release tablets, 125, 250 and 500 mg.

The generic tablets will have the same safety warnings as Depakote (divalproex sodium), including a boxed warning that cautions about the risk of liver damage and pancreatitis, according to the FDA. The warning also will highlight the risk of birth defects.

Sun Pharmaceutical, Genpharm, Nu-Pharm, Upsher-Smith Laboratories, Sandoz, Teva Pharmaceuticals USA, Dr. Reddy's Laboratories and Lupin Limited all received approval to market the generic drug.

Depakote is approved by the FDA to treat seizures, bipolar disorder and migraine headaches. Sales of the drug were strong in the second quarter, bringing in $414 million worldwide, according to Abbott. — Elizabeth Jones

Mylan Launches Generic Hypertension Drug

Mylan Pharmaceuticals has received final FDA approval for generic versions of Sciele Pharma's anti-hypertensive Sular extended release (ER) in 20-, 30- and 40-mg strengths.

Mylan's nisoldipine ER is the first generic version of Sular ER (nisoldipine) to be launched in the U.S., the firm said. The '741 patent protecting the brand drug expired June 8, according to the Orange Book.

In January, the FDA approved formulations of Sular in 8.5-, 17-, 25.5- and 34-mg strengths. The new Sular formulation uses SkyePharma's Geomatrix technology, which is designed to provide a lower dose of the drug for each of its previously marketed doses.

The brand drug had annual U.S. sales of approximately $94 million for the 12 months ending March 31, according to Mylan.

Mylan has 93 ANDAs pending FDA approval, 21 of which are potential first-to-file opportunities, according to the company. — Elizabeth Jones

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more than 60 products and is the fourth-largest generic company in the Spanish hospital market. The combined generics operations will offer more than 170 products and has more than 45 products pending registration.

The closing comes on the heels of Teva's announcement that it is acquiring Barr Pharmaceuticals, the world's fourth-largest generic company.

Teva has agreed to pay $7.46 billion in cash and stock and to assume Barr's net debt of approximately $1.5 billion. The Israeli company expects that transaction to close later this year (*Generic Line*, July 23). — Elizabeth Jones

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