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Teva Is Blocked From Introducing Generic Formulation of Evista

A federal judge in Indiana has issued a preliminary injunction delaying the introduction of Teva Pharmaceuticals USA's generic version of Eli Lilly's osteoporosis drug Evista.

Judge Sarah Evans Barker of the U.S. District Court for the Southern District of Indiana said Teva hadn't proven that the '086 patent covering Evista (raloxifene HCl) is invalid. The patent expires in July 2012.

Barker also ruled that Teva couldn't start a limited launch of its proposed generic product as it would "likely result in the same type of displacement of Evista in the marketplace as would a broader launch," according to court documents.

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New Democrat Coalition Endorses Eshoo's Biosimilars Bill

A group of moderate Democrats has declared its support for a biosimilar bill introduced by Reps. Anna Eshoo (D-Calif.) and Jay Inslee (D-Wash.).

The New Democrat Coalition said H.R. 1548, the Pathway for Biosimilars Act, strikes an appropriate balance between patient safety and creating a pathway for timely approval of follow-on biologics. Eshoo introduced the bill with Inslee and Rep. Joe Barton (R-Texas) March 17 (*Generic Line*, April 1).

"This bill puts in place necessary measures to ensure the United States remains an attractive place for innovators to develop new pharmaceutical treatments," Rep. Adam Smith (D-Wash.) says in a statement. "It also opens the door to get more affordable bio-similar versions of biologic drugs on the market."

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Teva had submitted a voluntary agreement in March to limit its generic Evista launch to no more than 1 million bottles between April 23 and Dec. 12, according to court documents. The company argued that this limited launch would effectively eliminate the irreparable harms Lilly had alleged.

Teva's offer to limit the amount of the release is a potentially unique strategy, according to Chad Landmon, a patent litigator and partner at Axinn, Veltrop & Harkrider, LLP.

If the court were to allow Teva to launch and later found the company infringed the patent after a full trial, the damage inflicted on Lilly would be limited, Landmon added.

"At the preliminary injunction stage, Teva quantified this damage to the brand company and argued that it would not be irreparable, i.e., not only would it be in an amount that Teva could pay back, but it wouldn't damage the brand company by so much that the brand company would be forever harmed," Landmon told *Generic Line*.

However, Barker disagreed with Teva's reasoning:

"Even if, as Teva contends, Lilly were able to fully recover its position in the market, we find that there would nonetheless likely be irreparable damage to Lilly's relationship with physicians and customers in addition to causing a significant disruption or loss of research that otherwise would have been sponsored or completed by Lilly as well as a scaling back of investment in research and development that otherwise would not have occurred," Barker says in her April 22 ruling.

"We believe Teva's challenges to Lilly's Evista patents are without merit and we expect to prevail in this litigation," Robert Armitage, Lilly's senior vice president and general counsel, says in a statement.

"We have taken and will continue to take all appropriate actions needed to protect our intellectual property rights as they relate to Evista," Armitage concludes.

Teva notified the court that it intends to appeal the ruling. If the company prevails, the injunction against its launch would be dissolved and Teva would be able to go to market. However, the decision is preliminary, and the court still needs to hold a full trial. The District Court ultimately would have to hold that trial and consider the evidence on a full basis, Landmon told *Generic Line*.

Ongoing Litigation

Teva notified Lilly in May 2006 that it had filed an ANDA for generic Evista with Paragraph IV certifications. Lilly subsequently sued Teva, saying the ANDA infringed on the '968, '049, '050 and '086 patents covering the drug.

It later amended its complaint, asserting Teva also infringed on the '811, '719 and '064 patents.

Teva received tentative approval for the Evista ANDA in April 2008 (*Generic Line*, April 30, 2008).

Teva amended its ANDA last July to include a new particle-size measuring methodology. It informed Lilly of this amendment and provided three batch samples.

This action prompted Lilly to ask the court to extend the statutory 30-month stay of approval because, by waiting so long to amend the ANDA, Teva had prejudiced its preparations for trial.

Lilly also moved for a temporary restraining order and preliminary injunction to prevent Teva from marketing its product after the expiration of the original 30-month stay. Barker granted this request.

Teva appealed, contending that an extension of the stay was unnecessary because it had

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Report: Generic Drug Prices Fall In 2008, Specialty Costs Soar

The average annual increase in manufacturer prices charged to wholesalers for the most widely used brand drugs was 8.7 percent last year — much higher than the increases during the previous six years, according to a new AARP report.

Prices for most of the generic drugs didn't increase, the "Rx Watchdog Report" found. On average, prices for the 185 generic products most widely used by Medicare beneficiaries fell 10.6 percent last year — the largest average decrease since at least 2003, according to the report.

The prices of 83 percent of generic drugs didn't change last year, despite an increase in general inflation. Drug prices that did fall dropped dramatically. For example, the manufacturer price for Teva Pharmaceutical Industries' generic version of Pfizer's antidepressant Zoloft (sertraline HCl) plunged 45.1 percent, according to the report.

Last year, prices increased for all but seven of the 219 brand products examined in the study, and almost 93 percent of the increases exceeded the rate of general inflation.

"A person taking three brand name prescription drugs could see his or her annual costs climb by more than $550 in just one year," says AARP Public Policy Director John Rother. "Switching to generic drugs whenever possible is one of the quickest and easiest ways to drastically reduce your health care bills."

The report also examined the manufacturer prices of widely used specialty prescription drugs to treat cancer, multiple sclerosis and rheumatoid arthritis. These drugs had higher price increases than traditional brand drugs, rising an average of 9.3 percent in the last year.

The average annual increase in the cost of therapy with a specialty drug grew from $2,297 in 2007 to $2,860 last year. Thirty-one of the widely used specialty drugs were biologics, which are made from living organisms.

There currently is no FDA pathway for the approval of generic versions of biologic drugs, leaving manufacturers free to continue charging the same or even higher prices, the report says.

AARP has urged Congress to address the rising cost of prescription drugs, particularly through policies that will bring more generic competition to the marketplace. Cost-saving measures include allowing Medicare to negotiate directly with drugmakers, closing loopholes that allow brand-drug makers to pay off generic-drug producers to delay competition, allowing for the legal importation of safe prescription drugs from abroad and creating a pathway for the approval of generic biologics.

Lowering Drug Prices

The Generic Pharmaceutical Association (GPhA) urged Congress to take action. "It's time to do right by our seniors and all Americans struggling with health care costs by approving legislation that brings safe, effective and affordable biogeneric medicines to patients sooner," GPhA President and CEO Kathleen Jaeger says in a statement.

"GPhA also strongly believes that increasing funding for FDA would ensure the more timely approval of generic medicines," Jaeger adds.

Not everyone agrees with the report's findings. PhRMA Senior Vice President Ken Johnson calls the report "one-sided" in a statement.

"While AARP focuses on selected brand medicines, the government's consumer price index is the best measure of the prices consumers pay for medicines. It shows that since the beginning of this decade prescription drug prices grew at an average annual rate of 3.6 percent, while prices for medical goods and services grew at a rate of 4.3 percent. From 2007 to 2008, average prescription drug prices increased 2.5 percent while overall medical prices rose 3.7 percent," Johnson adds.

The complete AARP "Rx Watchdog Report" is available at www.aarp.org/research/health/drugs/rx_watchdog.html. — Elizabeth Jones

Biosimilars, *from Page 1*

Rep. Melissa Bean (D-Ill.) says in the statement that U.S. pharmaceutical leadership is critical to worldwide healthcare. "This legislation proposed by Reps. Inslee and Eshoo recognizes the necessary risk-reward balance to foster the continued innovation of new drug development and resulting patient benefits," she adds.

Competing legislation introduced by Reps. Henry Waxman (D-Calif.) and Nathan Deal (R-Ga.), Promoting Innovation and Access to Life-Saving Medicine Act, H.R. 1427, provides for five years of data exclusivity — a provision that brand-drug makers say is insufficient.

The lawmakers introduced H.R. 1427 March 11, and a bipartisan companion bill was introduced in the Senate by Sen. Charles Schumer (D-N.Y.) March 26.

Under Eshoo's bill, the HHS secretary wouldn't be allowed to approve a biosimilar application for 12 years after a biologic product was first licensed. Companies also wouldn't be able to submit biosimilar applications until four years after the reference product was approved.

Stakeholder Reactions

Generic Pharmaceutical Association (GPhA) President and CEO Kathleen Jaeger doesn't agree with many of the provisions in Eshoo's bill, calling it "the wrong road for patients looking for safe and affordable biogeneric medicines, particularly during these difficult economic times." The needless roadblocks in the legislation will keep patients from getting needed medicines in a timely manner, she added. GPhA supports Waxman's and Schumer's bills.

The Biotechnology Industry Organization (BIO) doesn't support the Waxman bill and its Senate companion legislation, which follows H.R. 1427 "through the looking glass to a world of biosimilars that would jeopardize patient safety and undermine future medical breakthroughs," President and CEO Jim Greenwood says in a statement. BIO has joined innovator companies like Johnson & Johnson in supporting the "balanced, landmark" Eshoo bill (*Generic Line*, April 15).

Eshoo's legislation, which has 66 co-sponsors, is available at frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:h1548ih.pdf.

Waxman's competing legislation, Promoting Innovation and Access to Life-Saving Medicine Act, H.R. 1427, has 10 co-sponsors and is available at frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:h1427ih.txt.pdf.

The Senate companion bill introduced by Schumer, Promoting Innovation and Access to Life-Saving Medicine Act, S. 726, has six co-sponsors and is available at frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:s726is.txt.pdf. — Elizabeth Jones

Hatch, Kennedy Oppose Bill To Limit Biogeneric Exclusivity

Sen. Orrin Hatch (R-Utah) opposes the limited data exclusivity provisions in Rep. Henry Waxman's (D-Calif.) generic biologics bill and says Sen. Edward Kennedy (D-Mass.), chairman of the Health, Education, Labor and Pensions (HELP) Committee, agrees with him.

Hatch, former chairman of the Senate HELP committee, told reporters last week at the Food and Drug Law Institute (FDLI) & FDA 52nd Annual Conference that Kennedy said he supports Hatch's views on granting innovators longer exclusivity periods for biotechnology products.

Legislation for generic biologics could be incorporated into a larger healthcare reform package in the Senate — a possible route to win approval of the longer data exclusivity provisions, Hatch told reporters.

Sen. Max Baucus (D-Mont.), chairman of the Senate Finance Committee, is seeking to hold mark-up hearings on healthcare reform legislation in the second week of June, Hatch said.

However, the Senate does not yet have a healthcare reform bill, Hatch added. He supports providing universal access to health insurance, promoting innovation, curbing the growth of costs, modernizing healthcare infrastructure and addressing entitlement reform. — Christopher Hollis

Senators Introduce Bill to Increase Foreign Drug Plant Inspections

The FDA would get fees for conducting inspections of generic and other foreign drug plants and new subpoena powers under legislation introduced by Sens. Chuck Grassley (R-Iowa) and Edward Kennedy (D-Mass.).

Grassley and Kennedy, chairman of the Health, Education, Labor and Pensions Committee, introduced the Drug and Device Accountability Act of 2009 last week, according to a statement issued by the minority staff of the Senate Finance Committee.

The bill's introduction follows problems at foreign plants that produce generic drugs. Last year, the FDA issued two warning letters and an import alert for drugs produced at generic-drug maker Ranbaxy's Indian plants in Dewas and Paonta Sahib. In the letters, the agency identifies deviations from good manufacturing practices (*Generic Line*, Oct. 1, 2008).

"An increasing number of drugs and ingredients for pharmaceuticals are being manufactured in other countries, yet studies show the FDA doesn't know how many foreign plants are subject to inspection, and the FDA conducts relatively few foreign inspections each year," Grassley says in a statement.

The bill also allows the agency to prevent distribution of a drug when an inspector has reason to believe the product is adulterated, Grassley said in a floor statement about the legislation.

Separately, Rep. John Dingell (D-Mich.), the former chairman of the House Energy and Commerce Committee, is urging Congress to act on his bill — the FDA Globalization Act — that includes provisions for inspection user fees (*Generic Line*, Feb. 4). Dingell's bill would require FDA inspections of generic- and brand-drug facilities and device plants in the U.S. and abroad every two years, unless the agency decides a facility's record requires fewer reviews.

The FDA Globalization Act, H.R. 759, also would require the agency to conduct preapproval inspections of foreign plants in countries such as India and Brazil, which export generic drugs. Additional funding for preapproval inspections of generic drug plants would come from a new fee imposed on the manufacturers who, unlike their brand-name counterparts, do not currently pay Prescription Drug User Fee Act fees.

The FDA Globalization Act is available at frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:h759ih.txt.pdf. The Drug and Device Accountability Act, S. 882, is available at www.fdanews.com/ext/files/KER09202_xml.pdf. — Christopher Hollis

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disclosed all information to Lilly and provided batch samples from its amended ANDA product in a timely manner.

In February, the U.S. Court of Appeals for the Federal Circuit ruled 2–1 that Barker hadn't abused her discretion in extending the stay after Teva altered its Evista ANDA late in the litigation — an action that "adversely affected Lilly's infringement case and trial preparation," according to court documents.

However, Judge Sharon Prost dissented, maintaining that the majority misapplied the law and misapprehended the facts, according to court documents.

Prost asserts the District Court never determined whether Teva reasonably cooperated in expediting the litigation.

The lower court had ordered Teva to produce various documents before Aug. 18, 2008, but Teva did not complete production until Sept. 5, 2008. The court did not determine whether this 18-day delay was unreasonable.

After Teva's loss in the Appeals Court, Barker dealt the company another blow when she granted Lilly a temporary restraining order barring the introduction of Teva's generic product.

"Teva's launch will remove Lilly's marketing exclusivity with respect to Evista, which will result in a rapid loss of market share that will be difficult if not impossible for Lilly to recover even if the court were to later rule in favor of Lilly and Teva's generic raloxifene product was removed from the market," Barker wrote in her opinion.

Evista is indicated to prevent and treat osteoporosis in postmenopausal women, reduce the risk of invasive breast cancer in postmenopausal women with osteoporosis; and lower the risk of invasive breast cancer in high-risk postmenopausal women.

The product had first-quarter sales of $256.9 million, down 2 percent from $261.1 million during the same period last year, according to Lilly. — Elizabeth Jones

Trial Reporting Gains Momentum, Amid Stakeholders Concerns

Mandatory reporting of clinical trial results under the FDA Amendments Act (FDAAA) is picking up steam, but generic- and brand-drug stakeholders have voiced potential concerns about the system.

The NIH held a meeting April 20 to consider how to expand the database as required by the law. The Generic Pharmaceutical Association (GPhA), Taro Pharmaceuticals USA, the Biotechnology Industry Organization (BIO) and PhRMA offered their perspectives on what kinds of studies should be posted at ClinicalTrials.gov.

FDAAA's Mandate

The data-reporting requirement took effect Sept. 27, 2008, one year after the FDAAA was signed into law by then-President George W. Bush.

Sponsors generally are required to submit results within 12 months of a trial's completion. The requirement to register ongoing trials, excluding Phase I trials, took effect Dec. 26, 2007.

Gordon Johnson, vice president of regulatory sciences at GPhA, opposes the release of results from clinical bioequivalence studies.

"In these studies, the drug is already available. We are concerned about increasing obstacles to the approval of generic drugs. This just gives competitors a road map," he said at the meeting.

Howard Rutman, Taro's group vice president and medical director, says in written comments that generic drug development allows multiple manufacturers to work independently on their products.

"Forced public disclosure of development plans through the registry mechanism would have the negative consequence of deterring other potential competitors from pursuing development plans," Rutman adds.

He proposed that the study design as well as safety and efficacy results should be available to the public only after the FDA approves an ANDA.

"Based on this draft document, it appears that trials conducted outside of the U.S. and not conducted under an IND will be exempt from registration requirements provided that the drug product is also manufactured outside of the U.S.," Johnson writes in comments submitted before the meeting.

"GPhA is concerned that this exemption will disadvantage U.S. companies and provide an incentive to move operations outside of the U.S.," he adds.

PhRMA also expressed reservations that the NIH "is applying FDAAA to voluntary submissions of clinical trial information, including Phase I studies, in a manner that is likely to dissuade sponsors from utilizing ClinicalTrials.gov to disseminate information about early stage research," Jeffrey Francer, assistant general counsel of the trade group, says in prepared comments.

BIO recommends that results of pivotal confirmatory clinical trials be submitted after development of a product has been discontinued for safety reasons.

The NIH should consider carefully what results to disseminate, as there are instances in which posting information about unapproved products "may restrain our member companies' ability to conduct research into new treatments that will help patients in the future, for example, by releasing information that undermines a company's competitive position," the organization says in prepared comments.

Interested parties may submit comments on the docket until June 22. — Martin Berman-Gorvine, Elizabeth Jones

Actavis Resumes Production Of Oxycodone in New Jersey

Actavis has restarted production of 15- and 30-mg oxycodone tablets at its facility in Little Falls, N.J., which was closed last year for alleged good manufacturing practice (GMP) violations.

The painkiller tablets are the first products to be produced at the facility since a recent FDA inspection cleared the plant to reopen, Actavis says in an April 17 statement.

"Actavis requalified all equipment and utilities for production and packaging — and we requalified and revalidated all methods used to release products from our Totowa facilities," Nasrat Hakim, vice president of quality compliance and technical services for Actavis, says in the statement.

Actavis entered into a consent decree with the FDA last December following inspections that found that the Little Falls facility and two other facilities in Totowa, N.J., did not meet current GMP requirements (*Generic Line*, Jan. 7).

All of the drug products made at the Little Falls plant were subject to a recall last August due to GMP violations (*Generic Line*, Aug. 6, 2008).

The reopened plant could help ease the current shortage of the oxycodone painkiller. The FDA said last month that there was a shortage of 5-, 15- and 30-mg oxycodone tablets and mentioned a separate GMP-related recall by KV Pharmaceutical (*Generic Line*, April 1). — David Belian

Sanofi Snubbed as Supreme Court Refuses Lovenox Case

The U.S. Supreme Court has refused to hear Sanofi-Aventis' appeal in its patent dispute over the blood-thinner Lovenox.

The court declined to hear the Lovenox (enoxaparin sodium) appeal without comment Monday. In bringing the case to the high court, Sanofi-Aventis had sought a reversal of a May 2008 ruling by the U.S. Court of Appeals for the Federal Circuit that the company had obtained the '618 patent covering Lovenox through inequitable conduct, thus making the patent unenforceable (*Generic Line*, May 28, 2008).

The Appeals Court's decision upheld a ruling in the U.S. District Court for the Central District of California that Sanofi-Aventis intended to deceive the PTO by withholding information when it filed an application covering the drug.

The '618 patent, which was reissued as the '743 patent, was set to expire in 2012. Amphastar Pharmaceuticals and Teva Pharmaceutical Industries each have filed ANDAs with Paragraph IV certifications to gain approval for generic versions of Lovenox, and both await a decision on whether the FDA will approve their products.

Sandoz and Momenta Pharmaceuticals also are working on a generic copy of the drug (*Generic Line*, May 14, 2008).

Currently, there are no approved generic versions of the blood-thinner, which had sales of about $3.6 billion last year, according to Sanofi-Aventis. — Elizabeth Jones

Omnitrope Is Approved As First Canada Biosimilar

Sandoz Canada has received market authorization for the human growth hormone replacement Omnitrope — the first subsequent-entry biologic (SEB), or biosimilar, to be approved in the country.

Omnitrope (somatropin recombinant) is similar to Pfizer's Genotropin and has been approved in the U.S. and the EU. It was the first medicine to be approved as a biosimilar in the EU, according to a Sandoz statement.

"Subsequent Entry Biologics, known as biosimilars in Europe and follow-on proteins in the U.S., are a key part of the Sandoz strategy to focus on difficult-to-make products that provide added patient benefits," said Pierre Frechette, president and CEO of Sandoz Canada, says in a statement. "Due to the rising cost of health care and the growing need for more complex treatments, they will play an increasingly important role in ensuring access to medicines."

The Canadian Generic Pharmaceutical Association (CGPA) urged Health Canada to complete its SEB guidance as soon as possible. The draft guidance was released March 27 and was published with notices describing amendments to existing guidances on data protection and patents to address SEBs.

Canada's existing legislative and regulatory framework for pharmaceuticals and biologics provides the legal basis for approving SEBs. Health Canada is working to clarify its submission and approval requirements by developing a related guidance. Consultations on the second draft of the guidance will conclude at the end of May, according to CGPA.

"This approval demonstrates that generic companies can develop safe and effective biologic medicines, and clearly demonstrates that a sound scientific and legal environment already exists in Canada to support the approval of subsequent entry biologics," CGPA President Jim Keon says in a statement.

Health Canada began work on biosimilars in January 2008, when it issued the "Draft Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics." However, work on the guidance was delayed when the Canadian Parliament was dissolved late last year, forcing the agency to start over.

The draft guidance is available at www.hc-sc.gc.ca/dhp-mps/consultation/biolog/2009-03-seb-pbu-eng.php. Interested parties may comment on the draft until May 26. — Elizabeth Jones

Apotex Barred From Selling Generic Pulmicort

A federal judge granted AstraZeneca a temporary restraining order to stop Canadian drugmaker Apotex from selling a generic formulation of its asthma treatment Pulmicort.

The U.S. District Court for the District of New Jersey barred Apotex from selling the drug until April 27, when the court will hold a hearing to determine whether the order should be extended, AstraZeneca says in a statement last week.

The FDA approved Apotex's generic of Pulmicort Respules (budesonide) last month. AstraZeneca says it has patents covering the drug until 2018, with pediatric exclusivity until 2019. The company "has full confidence in the strength of its intellectual property rights protecting Pulmicort Respules," the company says in a statement.

Last November, AstraZeneca reached a settlement with generic-drug maker Teva that will allow Teva Pharmaceutical to begin exclusively marketing a generic version of Pulmicort Respules this December (*Generic Line*, Nov. 26, 2008).

AstraZeneca had alleged in a patent dispute that Ivax Pharmaceuticals, which was later acquired by Teva, had filed an ANDA for a generic version of the drug before the expiration of patent protection. — David Belian

Watson Seeks to Market Generic Mucinex, May Be First to File ANDA

Watson Pharmaceuticals has filed two ANDAs for versions of the decongestant Mucinex before patent protection expires.

Reckitt Benckiser, which owns the '252 and '821 patents on Mucinex (guaifenesin), sued Watson to prevent it from commercializing its generic 600- and 1,200-mg tablets and Mucinex DM (dextromethorphan hydrobromide/guaifenesin) tablets — 30 mg/600 mg and 60 mg/1,200 mg.

Watson may be the first applicant to file an ANDA for a generic version of Mucinex DM and could be entitled to 180 days of market exclusivity.

Reckitt Benckiser filed *Reckitt Benckiser, Inc. v. Watson Laboratories, Inc. – Florida and Watson Pharmaceuticals, Inc.* April 20 in the U.S. District Court for the Southern District of New York.

For the 12 months that ended Dec. 31, 2008, Mucinex and Mucinex DM products had total U.S. sales of about $106 million and $85 million respectively, Watson says in a statement, citing IMS Health data. — Elizabeth Jones

Teva, Glenmark Resolve Coreg Patent Dispute

Teva Pharmaceutical Industries and Glenmark Generics have reached an agreement to resolve patent infringement litigation related to GlaxoSmithKline's (GSK) heart drug Coreg.

Judge Garrett Brown of the U.S. District Court for the District of New Jersey signed off on the settlement, effectively dismissing the parties' claims and counterclaims.

The dispute centered on alleged infringement of Teva's '997 and '008 process patents relating to carvedilol, the active ingredient in Coreg. The patents were issued in March 2004 and October 2006, respectively, according to the PTO.

Teva's '067 patent covering carvedilol had pediatric exclusivity through Sept. 5, 2007. After that date, the FDA started approving ANDAs for generic Coreg. Glenmark was one of a number of applicants that won approval at the time.

Teva sued Glenmark because the active ingredient it was going to use in its product would have infringed Teva's '997 and '008 process patents. Teva asked the court to find that Glenmark had willfully infringed the patents, which would entitle Teva to treble damages, according to court documents.

Teva Pharmaceutical Industries, Ltd., et al. v. Glenmark Generics Inc., USA, et al. was one of several suits Teva filed beginning in 2007 to protect its patents related to carvedilol. Teva also sued Ranbaxy Laboratories, Watson Pharmaceuticals, Lupin Pharmaceuticals and Orchid Chemicals & Pharmaceuticals in the New Jersey court.

The Coreg franchise had sales of about $73 million in the first quarter, which ended March 31, according to GSK. — Elizabeth Jones

Par, Reliant to Settle Dispute Over Rythmol Patent

Par Pharmaceutical has agreed to a settlement with Reliant Pharmaceuticals to resolve litigation related to Reliant's heart drug Rythmol SR.

The agreement in *Reliant Pharmaceuticals, Inc, v. Par Pharmaceutical Inc.* will give Par the right to introduce a generic version of Rythmol SR (propafenone HCl) Jan. 1, 2011, or earlier under certain circumstances.

Reliant sued Par in December 2006 in the U.S. District Court for the District of Delaware after Par filed an ANDA with a Paragraph IV certification on Reliant's '588 patent. Par alleged the patent, which expires Oct. 28, 2014, was invalid, unenforceable or not infringed by the sale of its generic product.

Rythmol SR capsules are indicated to prolong the time to recurrence of symptomatic atrial fibrillation in patients without structural heart disease. — Elizabeth Jones

Vectura Receives Milestone Payment For Asthma, COPD Drug Candidate

Sandoz has made a milestone payment of about $3.2 million to UK-based Vectura Group related to the development of VR315, a combination therapy for asthma and chronic obstructive pulmonary disease (COPD).

VR315 is being developed as a generic product delivered with Vectura's GyroHaler dry powder inhaler. Vectura licensed the European and U.S. rights for VR315 in 2006 to Sandoz, Novartis' generic unit.

"VR315 is a major opportunity and this payment is indicative of the progress we are making," Chris Blackwell, Vectura's chief executive, says in a statement last week.

The companies also have an agreement for another asthma/COPD candidate, VR632. Sandoz exercised an option to license the product in Europe in December 2007.

Combination therapies for asthma and COPD have annual sales of more than $10 billion, Vectura says in the statement. GlaxoSmithKline's blockbuster asthma/COPD product Advair Diskus (fluticasone propionate/salmeterol xinafoate) had U.S. sales of about $4.4 billion last year, according to IMS Health data. Pediatric exclusivity for the drug expires in 2011. — Elizabeth Jones

Glenmark Gets Tentative OK To Market Generic Zetia

The FDA has given Glenmark tentative approval to market generic Zetia 10-mg tablets to treat high cholesterol levels.

The brand drug is sold through the partnership between Merck and Schering-Plough. The generic Zetia (ezetimibe) clearance is the first granted by the FDA, potentially giving Glenmark 180 days of marketing exclusivity, according to a company statement.

Glenmark filed its ANDA for the product Oct. 25, 2006, with a Paragraph IV certification on Zetia's '721 patent, which has pediatric exclusivity through April 25, 2017. Schering-Plough and Merck sued Glenmark, and the lawsuit *Schering Corporation and MSP Singapore Company LLC v. Glenmark Pharmaceuticals Inc., USA et al.* is pending in the U.S. District Court for the District of New Jersey.

Final approval of Glenmark's ANDA depends upon resolution of the case.

Zetia had sales of about $1.5 billion last year, according to a Glenmark statement. — Elizabeth Jones

Teva Pulls EU Plavix Application, Gets Good News on Two Drugs

Teva Pharmaceuticals Europe has withdrawn its marketing authorization application for a generic version of Plavix 75-mg, film-coated tablets, citing marketing strategy.

The application was under review by the European Medicines Agency's (EMEA) Committee for Medicinal Products for Human Use (CHMP) when the application for generic Plavix (clopidogrel bisulfate) was pulled, according to a committee statement. Teva submitted its application last July. The EMEA will post more information about Teva's product and the company's withdrawal letter after the next CHMP meeting May 26–29. Plavix is co-promoted by Bristol-Myers Squibb and Sanofi-Aventis.

Separately, Teva has received positive opinions from CHMP for generic versions of a Type 2 diabetes drug and a chronic hepatitis C treatment. The diabetes product is a generic version of Novo Nordisk's NovoNorm (repaglinide), which is sold as Prandin in the U.S. There are no approved generic equivalents to Prandin yet, but Caraco Pharmaceutical Industries won tentative approval to market the drug in 2007, according to the FDA.

Teva also received a positive opinion for its ribavirin 200- and 400-mg film-coated tablets, a generic version of Schering-Plough's chronic hepatitis C infection treatment Rebetol. — Elizabeth Jones

Generic Rivals Take Toll on J&J As Company Awaits Approvals

FDA action on several Johnson & Johnson (J&J) pipeline drugs is expected over the coming months as the company tries to offset the loss of some of its blockbuster drug sales, including the migraine treatment Topamax, to generic competition.

Seventeen generic competitors for Topamax (topiramate), which had sales of $2.2 billion last year, have entered the market (*Generic Line*, April 1).

The antipsychotic drug Risperdal (risperidone) also became subject to generic competition last year (*Generic Line*, July 23, 2008). The brand product had annual U.S. sales of about $78 million for the 12 months ended Sept. 30, 2008.

J&J is starting to report sales of Invega (paliperidone), the company's follow-on to Risperdal. During the first quarter this year, the drug had sales of $66 million in the U.S. and $25 million in the rest of the world. That does not come close to Risperdal's sales of $2.6 billion for the 12 months ended March 31, 2008, according to IMS Health.

The company expects FDA action on its monthly tumor necrosis factor inhibitor golimumab at the end of the month. The BLA submitted to the agency last June is seeking indications to treat rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis.

Stelara (ustekinumab), another important product for the company, is an interleukin-12 and interleukin-23 drug under FDA review for the treatment of chronic, moderate-to-severe plaque psoriasis. J&J received a complete response letter for the biologic, asking it for a risk evaluation and mitigation strategy. FDA action on J&J's response is expected in July, Louise Mehrotra, vice president of investor relations, said last week.

J&J submitted its reply in early February to a complete response letter for paliperidone palmitate, a monthly, long-acting injectable form of Invega. The FDA considered the submission a Class II response, which has a six-month review cycle, Mehrotra said. — Christopher Hollis

Teva Sued Over Generic Proposed for Lovaza

Norwegian drugmaker Pronova BioPharma has filed a lawsuit against Teva Pharmaceuticals USA for infringing patents covering the heart drug Lovaza.

Teva notified the plaintiff in March 9 letter that it had filed an ANDA for generic Lovaza (omega-3-acid ethyl esters) with a Paragraph IV certification on the '077 and '667 patents, which expire in 2013 and 2017 respectively.

Teva says in the letter the patents are not valid, unenforceable or will not be infringed by the commercial manufacture of its proposed product (*Generic Line*, March 18).

Pronova filed the suit *Pronova Biopharma Norge AS v. Teva Pharmaceuticals USA et al.* April 23 in the United States District Court for the District of Delaware. — Elizabeth Jones

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