

GENERIC LINE®

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Bill Would Allow Price Negotiation, Encourage Medicare Generics Use

The Centers for Medicare & Medicaid Services (CMS) would gain the right to negotiate prices for Medicare Part D drugs directly with pharmaceutical companies and potentially increase the use of generics if a new bill becomes law.

“This would allow the HHS secretary to negotiate and would encourage the use of more affordable generics. The Veterans Administration currently has that power,” Rep. Jan Schakowsky (D-Ill.) said in a conference call with reporters last Tuesday.

Drugmakers pushed for Congress to add a provision to the Medicare Prescription Drug, Improvement and Modernization Act of 2003 that kept the agency from negotiating lower prices, said Schakowsky, a sponsor of H.R. 684, the Medicare Prescription Drug Savings and Choice Act of 2009.

(See Medicare Part D, Page 2)

House Globalization Bill Includes Generic Plant Inspections

New legislation 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.

Reps. John Dingell (D-Mich.) and Bart Stupak (D-Mich.) introduced the legislation with Rep. Frank Pallone (D-N.J.). It would fund increased good manufacturing practice inspections

(See Globalization, Page 4)

Report: FDA's Oversight Of Drugs Needs Reform

The FDA should protect the public more effectively by improving its oversight of drugs and biologics, according to a government report that added the agency to a list of operations in need of change or at risk for mismanagement.

New laws, complex medical products submitted for approval and the globalization of the drug industry are testing the FDA's ability to ensure the safety and effectiveness of drugs, biologics and devices, according to the report produced by the Government Accountability Office (GAO), the investigative arm of Congress.

The FDA has announced plans to address resource challenges, including a multiyear hiring initiative and investment in an IT modernization effort, the report says. However, the report emphasizes that the proposals must be effective.

"Although such initiatives may hold promise, we nonetheless believe that FDA needs to enhance its oversight of medical products to better protect public health," the report says.

The GAO updated its list to include two other federal operations considered at high risk of waste, fraud, abuse and mismanagement or in need of change: the U.S. financial regulatory system and the Environmental Protection Agency's assessment and control of toxic chemicals.

Foreign Inspections, Safety

The FDA's ability to ensure the quality of products manufactured overseas is "an area of particular concern," the report says.

Agency management of its inspection programs for foreign medical products has been hampered by a lack of electronically integrated databases; the large, unknown number of foreign manufacturers that require inspections; and a lack of staff the agency has dedicated to conducting the inspections, according to the report.

The report also expresses concern over how the FDA monitors postmarketing safety of drugs and how it reviews promotional materials for medical products.

The GAO has asked the FDA to systematically prioritize and track promotional materials for review, but HHS has disagreed with these recommendations.

Finally, the GAO reiterates its concerns about FDA oversight of clinical trials, saying the agency has failed to address in its written reviews of NDAs the need to compare the effect of drugs on men with their effect on women. The FDA has yet to act on this recommendation, which the GAO says it made in 2001.

Rep. Darrell Issa (R-Calif.), ranking member of the House Oversight and Government Reform Committee, has promised that he and Chairman Edolphus Towns (D-N.Y.) would work together not only to target and expose the waste, fraud and mismanagement outlined in the GAO report but also to hold all agencies accountable to a new standard of transparency and accountability, according to a committee statement.

The GAO report, "High-Risk Series, An Update," is available at www.gao.gov/new.items/d09271.pdf. — Elizabeth Jones

Medicare Part D, from Page 1

The bill was introduced last week by Rep. Marion Berry (D-Ark.) and by Sen. Richard Durbin (D-Ill.).

"In creating Medicare Part D, we left out an important element — we didn't allow Medicare to create its own drug program to allow it to buy drugs in bulk," Durbin said. He blamed former President George W. Bush and congressional Republicans for the bill's failure in the last Congress.

The bill may save enough money to "fill the doughnut hole" coverage gap in Medicare Part D, Berry said. — Martin Gidron

ASK THE EXPERTS

Experts Discuss Effect of NJ Rules On Hatch-Waxman Litigation

Generic Line asked Chad Landmon, a partner with the law firm Axinn, Veltrop & Harkrider LLP, and Andrea Johnson, an associate in the firm's Hartford office, about changes the generic drug industry can expect from the recently enacted District of New Jersey local patent rules.

Landmon and Johnson discuss the potential impact of the new rules on Hatch-Waxman litigation, including whether they will encourage or dissuade patent holders from bringing actions in the District of New Jersey and whether there are any benefits — or detriments — to generic companies as a result of the rules.

Landmon practices primarily in the areas of food and drug law and patent litigation and counseling, focusing on the pharmaceutical industry. Johnson is a member of the firm's intellectual property group and focuses on patent lawsuits in general and Hatch-Waxman litigation in particular.

What do the New Jersey local patent rules say?

Landmon, Johnson: The New Jersey local patent rules took effect Jan. 1 as New Jersey Local Civil Rule 9.3. The rules were modeled after those that are applicable in the Northern District of California but have been adapted to New Jersey practice. Importantly, they add distinct provisions regarding Hatch-Waxman cases.

The rules include a number of provisions designed to reduce delays created by quarrels over the production of documents and disclosure of asserted claims, infringement and invalidity positions. For instance, local patent rule 2.2 provides that confidential information is to be produced immediately under an outside counsel-only basis until a discovery confidentiality order is in place. This provision will prevent parties from delaying production of documents while negotiating a discovery confidentiality order.

Provisions governing non-Hatch-Waxman patent cases also provide early deadlines for asserting infringement and invalidity contentions. Under local patent rule 3.1, the party asserting infringement must serve a disclosure of asserted claims and infringement contentions no later than 14 days after the initial scheduling conference. This disclosure should include the claims of each patent-in-suit allegedly infringed, each accused product or process of which the party claiming infringement is aware and a claim chart identifying each limitation of each asserted claim found within the accused product or process. It also must be accompanied by documents on which the party asserting infringement will rely, such as patent file histories, evidence of conception and reduction to practice and evidence of ownership.

In return, and no later than 45 days after service of the disclosure, the party opposing infringement must serve its invalidity contentions under local patent rule 3.3, along with a similar production of documents. This document production should include prior art and documents sufficient to show the operation, composition or structure of the accused product or process.

A different model for disclosure of infringement and invalidity contentions will be used in Hatch-Waxman cases. Under local patent rule 3.6, the alleged infringer must produce its ANDA at or before the initial scheduling conference. Then, no more than 14 days after that initial scheduling conference, the alleged infringer must provide both noninfringement and invalidity contentions, along with accompanying documents, prior to the patentee's submission of infringement contentions 45 days later.

Will this provision hurt or help generic companies?

Landmon, Johnson: The new rules will probably help generic companies in some respects but could hurt them in others. In the past,

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Globalization, from Page 1

for manufacturing sites by requiring companies to register plants annually, including foreign companies that export drugs or devices to the U.S., and pay fees for the registrations. The money would supplement the FDA's budget, according to a summary of the bill provided to *Generic Line*.

Other provisions of the bill that affect drug companies include ones that:

- Bar importation of products from foreign plants that lack safety documentation or that limit, delay or deny FDA inspections;
- Require manufacturers to provide documentation on their supply chain and the steps they have taken to secure it;
- Mandate that manufacturers that produce finished drugs or active pharmaceutical ingredients identify and mitigate supply chain risk, including written plans to identify and control risks, on-site audits of ingredient and raw material suppliers and testing for likely contaminants; and
- Require drugmakers to list on their websites the country of origin for all drug ingredients and finished products.

To enforce the new requirements, the bill would give the FDA the power to impose fines, order recalls, hold suspect drug shipments, subpoena records and destroy counterfeit or adulterated imports if they pose a risk of injury or death. Individuals who produce counterfeit drugs could face up to 20 years in prison instead of one year, as is now the case. If the counterfeit product kills someone, the penalty could be life in prison.

“Antiquated authorities and years of starving FDA of resources has put the public health at risk,” Dingell says in a statement, citing last year's massive heparin recall.

In response to calls from Congress and the Government Accountability Office to increase inspections abroad, the FDA has opened a number of international offices, in Costa Rica, as well as in New Delhi and Mumbai, India, for example, to help

improve oversight of the safety and quality of products shipped to the U.S. (*Generic Line*, Jan. 21).

The bill was introduced in the House last Wednesday. — Martin Gidron

Poll: Public Increasingly Prefers Generics

Between October 2006 and December 2008, the number of adults who would choose generics over brand drugs has increased 13 percent, according to a survey by Harris Interactive.

The poll, which was conducted online Dec. 9–15, 2008, surveyed 2,388 adults about their views of generic versus brand prescription drugs.

In response to the question, “If you had a choice between getting a brand name prescription drug or a generic drug, how often would you choose one over the other?” 81 percent of those surveyed said they were more likely to choose the generic over the brand drug. Of these respondents, 40 percent said they would always choose generics.

This number is up from 2006, when 68 percent of respondents said they would purchase a generic more often than a brand drug. At the time, only 23 percent said they would always buy the generic version.

Brand drug preference took a hit over the last two years. Of those surveyed, 19 percent said they preferred brand drugs — a 13 percent decrease since the October 2006 survey.

In addition, 49 percent said paying less than \$10 for a 30-day supply of generic drugs was reasonable. Roughly one-third agreed that between \$10.01 and \$25 was reasonable.

However, the number of those who said they were absolutely certain, very likely or likely to buy generic prescriptions from stores that offer 30-day supplies of the drugs for \$4 or a 90-day supply for \$15 declined slightly. Of those surveyed, 47 percent said they would buy from those stores, down 3 percent from 2006. — Elizabeth Jones

FDA Issues Its Draft Guidance On Citizen Petitions for ANDAs

Petitioners seeking a delay in FDA approval of an ANDA must submit specific certifications, verifications and other materials with their petitions, the agency says in a draft guidance.

The draft proposes specifications for citizen petitions that seek a stay of approval under section 505(q) of the Food, Drug and Cosmetic Act (FDCA) for an ANDA submitted under the law's section 505(j) or a drug submitted under section 505(b)(2).

Section 505(q) was added to the FDCA by the FDA Amendments Act. Drugs in section 505(b)(2) are those for which the petitioner does not have safety and effectiveness information and the studies in the drug application to the agency "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

The draft indicates that petitions to delay approval of drug applications filed under those sections should:

- Be submitted on or after Sept. 27, 2007;
- Meet FDA submission standards, including the provision that they may not rely on or cross-reference information not in the petition;
- Be filed to the FDA while the related ANDA is pending;
- Request an action that could delay approval of a pending ANDA; and
- Not fall within the exceptions described in Section 505(q)(4), which exempts petitions relating to 180-day exclusivity and those from an ANDA applicant regarding FDA actions with respect to that application.

The FDA can't delay an ANDA except in cases that protect public health, the draft says.

A petitioner seeking to stay an ANDA's approval must certify that its petition includes all information and views upon which the petition relies; includes representative data known to the

petitioner that are unfavorable to the petition; and take all reasonable steps to ensure that any information that is unfavorable to the petition is disclosed, the draft recommends.

In addition, the petitioner should verify that it has not intentionally delayed the submission of the petition or its contents. It also should provide the date when it became aware of the data that support the petition.

The draft guidance, "Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act," is available at www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2009-D-0008-gdl.pdf.

— Elizabeth Jones

Report: Biologics Need 14 Years Of Data Exclusivity

Without at least 14 years of data exclusivity for innovator biologic companies, fewer novel products will be introduced and less revenue will be generated, a report says.

Ted Buckley, the Biotechnology Industry Organization's (BIO) director of economic policy; Joseph Golec, associate professor of finance at the University of Connecticut; and John Vernon, assistant professor in the health policy and management department at the University of North Carolina, examined legislation introduced last year.

The Biologics Price Competition and Innovation Act of 2007, S. 1695, proposed a 12-year period of data exclusivity for innovator biologics. Adopting the legislation will speed introduction of follow-on biologics (FOB) and save the government about \$5.8 billion between 2009–2018 in healthcare spending, according to a Congressional Budget Office report released in June 2008.

However, the report contends the government will not save much more by shortening the exclusivity period to less than 14 years, according to the white paper released last week by BIO.

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Experts, from Page 3

brand companies have favored the District of New Jersey. However, the schedule provided under the new rules will speed up litigation, a situation that generally benefits generic companies, which may be able to obtain a favorable court decision prior to the running of the 30-month stay. The quicker court decision will terminate the 30-month stay, allowing the FDA to grant final approval to the pending ANDA.

On the other hand, the new rules flip the typical burdens of patentees and alleged infringers by requiring the ANDA filer to provide both noninfringement and invalidity contentions prior to their finding out which claims the patentee would otherwise assert in the litigations. As a result, ANDA filers will need to do even heavier lifting upfront to map out their invalidity and noninfringement arguments in their notice letters or soon thereafter. It remains to be seen whether this burden-shifting provision will further encourage brand companies to bring actions in the District of New Jersey.

How will this change how generic companies litigate Paragraph IV cases in New Jersey?

Landmon, Johnson: The burden-shifting aspect, coupled with the strict schedule, will require ANDA filers to be organized and diligent in formulating their litigation strategies early on.

In addition, local patent rule 3.7 provides that amendments to invalidity and noninfringement contentions may only be revised upon a showing of good cause. ANDA filers may no longer be able to set forth preliminary positions in notice letters and revise them as litigation continues, at least not without a showing of “good cause.” Although the majority of the noninfringement and invalidity analysis will now be performed during the early stages of litigation, this may prove to be a welcome change given that it will also force brand companies to stake out their positions early on and should help to move cases along at a quicker pace, potentially reducing overall litigation fees and allowing for a favorable court decision prior to the running of the 30-month stay.

FDA Grants Final Approval for Generic Risperdal

The FDA has granted final approval to Teva Pharmaceutical Industries’ ANDA for its generic version of Ortho-McNeil-Janssen Pharmaceuticals’ antipsychotic agent Risperdal 1-mg/mL oral solution.

As the first company to file an ANDA for generic Risperdal (risperidone) with a Paragraph IV certification, Teva has 180-day marketing exclusivity on the product, which it has begun shipping.

Risperdal is indicated to treat schizophrenia in adults and adolescents age 13–17 and to treat irritability associated with autistic disorder in children and adolescents age 5–16. It also is indicated for the short-term treatment of bipolar mania in acute manic or mixed episodes associated with bipolar I disorder, as monotherapy or in combination with lithium or valproate in adults, or as monotherapy in children and adolescents age 10–17.

The brand product had annual U.S. sales of about \$78 million for the 12 months that ended Sept. 30, 2008, Teva says in a statement citing IMS data. — Elizabeth Jones

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Caraco Changes Managers, Improves Quality Control

Generic-drug maker Caraco Pharmaceutical Laboratories has changed the managers, training and equipment in its manufacturing and quality control units after receiving a warning letter about its good manufacturing practices (GMPs).

The company took corrective action and is working to improve its quality control system, Caraco CEO Daniel Movens says in a third-quarter earnings statement. The company is now in substantial compliance with GMPs, he adds.

“We continue to invest in improved systems, equipment, training and personnel in quality and manufacturing,” Movens says. “In the last two years, we have added a considerable amount of infrastructure in our quality control laboratories.”

Caraco is expanding its primary facility in Detroit, adding manufacturing, quality control laboratories, raw material storage and administrative offices.

GMP Deficiencies

Caraco, which is majority-owned by Sun Pharmaceutical Industries, received the warning letter last October.

The letter reiterated concerns detailed in a Form 483 issued after a June 2008 inspection. The FDA cites the company’s compliance history, including several inspections that documented significant GMP deficiencies, and notes the serious nature of the observed violations. The agency expresses concerns about plans for expansion under the violative conditions and the risk to consumers associated with the GMP deviations involving potential product contamination.

If the company fails to correct the deficiencies promptly, it could face legal action, including seizure of products and an injunction. The letter might influence decisions by other federal agencies. Additionally, the FDA may withhold approval of requests for export certificates or approval of pending applications, Caraco says in the statement.

The letter also acknowledges Caraco’s multiple written responses and its efforts to correct deficiencies, make organizational changes, provide additional training, hire consultants and revise standard operating procedures.

The FDA has acknowledged it received Caraco’s response to the warning letter Dec. 22, 2008, adding that it will evaluate the company’s corrective actions during the next scheduled inspection of the Detroit facility, according to the Caraco statement.

It is unlikely that Caraco will receive any approvals for products from its Detroit facility until after the next inspection. However, the company does not anticipate further meetings with the agency, according to the statement.

Sales Down

Caraco experienced a sales decline in the fiscal 2009 third quarter compared with the same period of fiscal 2008 because of the loss of exclusivity for its generic version of Novartis’ epilepsy drug Trileptal (oxcarbazepine) during the first quarter.

For the third quarter that ended Dec. 31, 2008, Caraco had sales of roughly \$55.7 million, down from \$81.9 million in the same period in 2007.

Movens says Caraco intends to move aggressively to develop new products and hopes to file additional products with the FDA before the end of the fiscal year. It also has struck agreements with third parties to facilitate the development of products. — Elizabeth Jones

Generic Producers of Toprol-XL Hampered by Production Issues

AstraZeneca has no generic competition for its former blockbuster hypertension treatment Toprol-XL because good manufacturing practice (GMP) compliance issues have hindered other manufacturers.

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BIO, from Page 5

The authors of “Data Exclusivity Period Length and Federal Government Savings from Enactment of the Biologics Price Competition and Innovation Act of 2007” calculate that adopting either a 5- or 10-year period of data exclusivity would increase savings by \$400 million. Instituting a 14-year period of data exclusivity would mean a loss of \$1 billion in savings, according to the paper.

Adopting a shortened period of data exclusivity also would have an impact on R&D. The estimated break-even point for biologic drugs is 17 years, according to authors, who cite an unpublished study. A market exclusivity period that is less than 14 years would start generic competition before innovators have recouped R&D costs. That would slow the development of future biologic drugs, according to the document.

Innovator companies would lose \$117.4 billion in sales to generics under a 12-year exclusivity period, leading them to spend \$41.1 billion less on R&D, according to the BIO report. Biologics innovators will be less likely to develop breakthrough drugs, which are costlier and more risky to develop, because the products will attract FOB competition. Therefore, biologics makers probably will shift their R&D spending to more certain break-even products, the report concludes.

The Generic Pharmaceutical Association (GPhA) disagreed with the reports’ conclusions, citing reports that consumers can save billions through biogeneric competition. “BIO is seeking to delay these savings through excessive exclusivity provisions that unnecessarily preserve their profits to the detriment of consumers and true innovation,” GPhA President and CEO Kathleen Jaeger says in a statement.

Alex Brill, a research fellow at the American Enterprise Institute, told *Generic Line* that he estimates seven years of data exclusivity is more than enough to encourage investment in a portfolio of biologic drug research.

Brill authored a study last year, “Proper Duration of Data Exclusivity for Generic Biologics: A Critique,” which was commissioned by Teva Pharmaceuticals USA (*Generic Line*, Nov. 26, 2008).

He also calls the current report’s focus on federal cost savings “grossly misplaced,” adding that the writers adopt the narrow budget window of Washington insiders “instead of a more appropriate longer horizon.” More importantly, “they ignore all the other savings that will accrue from competition, particularly the savings that will be enjoyed by patients,” Brill adds.

Brill also told *Generic Line*, “It is wrong to equate data exclusivity with break-even point. While they are related concepts, the data exclusivity period should be less than the break-even point. This is because in the biologic drug industry, unlike small molecule, companies will continue to earn economic profits after the entrance of competition.” — Elizabeth Jones

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Ranbaxy US Production Expands Following Import Alert

The FDA's import alert for 30 generic drug products made at two Ranbaxy production facilities in India has spurred the company to expand its U.S. manufacturing operations and take an estimated \$50.8 million expense against earnings in 2008.

The FDA issued two warning letters and import alerts last fall (*Generic Line*, Oct. 1, 2008). The company submitted its response to the warning letter in November and has not yet heard back from the agency, Ranbaxy CEO Malvinder Singh said. He expects a regulatory meeting but will not speculate on timing.

The company's focus on resolving its compliance issues with the FDA has reduced the number of ANDAs it submitted last year, the company said.

"Because of the U.S. FDA ban, we are currently working on site switches to alternative sources in-house and also evaluating U.S. manufacturing capacity expansion in our existing facilities," Singh said during the company's year-end earnings call.

A good sign for the company might be recent inspections of plants in India conducted by Japan's Pharmaceuticals and Medical Devices Agency (PMDA).

The PMDA inspected three dosage-form facilities and one active pharmaceutical ingredient (API) plant, including those cited by the FDA, according to Ranbaxy. All the inspections were successful, leading to the Japanese approval of antibiotic levofloxacin and anti-androgen prostate cancer drug bicalutamide.

"This reaffirms Ranbaxy's position as a trusted supplier of generic medicines manufactured in line with the most stringent standards," the company says in a statement.

Getting the FDA warning letters and import alerts lifted is important to Ranbaxy's pipeline of ANDAs, specifically for generic versions of GlaxoSmithKline's (GSK) migraine treatment

Imitrex (sumatriptan succinate) and herpes medicine Valtrex (valacyclovir HCl).

Dr. Reddy's introduced the Imitrex authorized generic last November. Under an agreement with GSK, Ranbaxy was cleared to launch its generic last month. But the launch is being held up by the import alert, and Ranbaxy has filed an application with the FDA to switch the manufacturing plant for the product from a site in India to its U.S. Ohm Laboratories subsidiary in New Jersey.

It is not clear whether the FDA would approve other generic versions of Imitrex, which would affect Ranbaxy's exclusivity for the generic. During the earnings call, Singh said the company's window for exclusivity would expire this year.

A loss of exclusivity for Imitrex would hurt Ranbaxy because the brand product had U.S. sales of approximately \$1.12 billion in 2007.

Valtrex Timing

Ranbaxy still has time to get FDA approval of a manufacturing site change for its generic version of Valtrex. The company is the only FDA-approved manufacturer of the generic. Ranbaxy has agreed not to introduce it until late 2009 as part of an agreement previously made with GSK.

The company can't introduce the drug in the U.S. until the alert is removed or production is transferred to a site in the U.S. Singh said a filing the company made seeking to switch the manufacturing site for generic Valtrex is under FDA review.

The FDA compliance problems also caused the company to delay issuing financial guidance to investors for 2009. But Singh said Ranbaxy expects to start manufacturing Nexium's (esomeprazole magnesium) API for AstraZeneca under a supply contract.

The contract is part of an agreement the companies made to settle patent litigation (*Generic Line*, April 30, 2008). It calls for Ranbaxy to start supplying AstraZeneca with Nexium API in March. — Christopher Hollis

Toprol, from Page 7

KV Pharmaceutical and Novartis' Sandoz unit are the only companies that have FDA approval to manufacture generic Toprol-XL (metoprolol succinate). KV recently suspended almost all production because of GMP compliance issues (*see story, page 11*).

Sandoz received a warning letter last year questioning the validation process for its generic version of Toprol-XL (*Generic Line, Sept. 3, 2008*). The company subsequently recalled more than 6 million bottles of the drug. Sandoz told *Generic Line* it is still working with the FDA to have the warning letter lifted.

AstraZeneca, which manufactures the authorized generic Toprol-XL for Par Pharmaceuticals, has increased production to fill the void left by the generics companies, Tony Zook, vice president of global marketing, recently told analysts. "There was the pullback from KV and Sandoz," Zook said.

"We have been in discussions with FDA," Zook said. "We have ramped up our own manufacturing and supply, and we believe that we will be able to meet market demand — in the form of Toprol-XL and supply for Par — by the end of the quarter." — Christopher Hollis

Teva, Lonza Drugmakers Sign Biosimilars Agreement

Teva Pharmaceutical Industries and Lonza Group are establishing a joint venture to develop, manufacture and market biosimilars.

Teva President and CEO Shlomo Yanai says his company has been expanding its knowledge base and infrastructure to become a leader in the biosimilars market, and the partnership will bolster its biologics capabilities.

The companies expect to start operations during the first quarter of the year after the receipt of regulatory approvals. Financial details of the agreement were not disclosed.

This biologics agreement is not the first Switzerland-based Lonza has signed with a major drugmaker.

Last year, Lonza agreed to help Novartis develop its biologic pipeline. Under the terms of the agreement, Lonza provides development services from its Slough, UK, R&D center using its GS gene expression system, as well as large-scale manufacturing capacity from its operations in the U.S., Spain and Singapore. — Elizabeth Jones

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J&J Will Not Venture Into Biosimilars

Cash-rich Johnson & Johnson (J&J) is ready to take advantage of opportunities this year to purchase pharmaceutical or life science assets at distressed prices, but the company is not interested in biosimilars.

“The opportunities this year are going to be extraordinary,” CEO William Weldon told investors during J&J’s year-end earnings call. “This economic environment creates opportunities that we may never see again.”

However, the company doesn’t see biosimilars as an opportunity, Weldon told analysts. Clinical trials are still going to be required for such products, investments he called significant.

The company’s position is markedly different from that of rival Merck, which announced its intention last December to enter the biosimilar space. Merck’s new BioVenture division is planning to launch a biosimilar of an anemia drug by 2012 and estimates it will have five biosimilars in late-stage clinical development by that time.

However, unlike J&J, Merck does not market monoclonal antibodies. Its experience with biologics is in vaccines. — Christopher Hollis

KV, Subsidiaries Recall, Suspend Shipments of All Products

Two subsidiaries of KV Pharmaceutical have issued voluntary recalls of products following a Jan. 22 decision to suspend the manufacture and shipment of its products.

The latest recall by KV’s Ethex subsidiary of more than 125 drug products at the wholesale level and recalls of eight formulations of products at the wholesale level by its Ther-Rx subsidiary probably will contribute to KV’s inability to meet its credit obligations.

Failure to comply constitutes a default, meaning outstanding obligations immediately would become due and payable. Ethex also recalled seven drug products at the retail pharmacy level.

Both Ethex and Ther-Rx’s notices say the companies are unable to determine when distribution of the products will resume. One of Ther-Rx’s products, Gynazole-1 (butoconazole nitrate), was distributed in Eastern Europe, South America, Asia and Canada, according to the company’s recall notice.

The company’s shutdown of manufacturing and shipments of its products and its voluntary recall of most products are being conducted in the wake of an inspection of the company’s operations and inventory that began last December. That was when the drugmaker announced it would halt all shipments of its drug tablets, including generic Toprol-XL (metoprolol succinate), while it reviewed its manufacturing and quality system operations.

Company Faces Challenges

Numerous recalls have cost the company millions of dollars (*Generic Line, Jan. 7*). The recalls involved Ethex’s shipments of tablets, some of which might have been twice the appropriate thickness, combined with manufacturing interruptions and inefficiencies that caused losses in the beta blocker Toprol’s sales (*Generic Line, Nov. 26, 2008*).

The drugmaker reported \$159 million in revenue from the affected products in fiscal 2008, before production stopped. The deadline for resuming shipments depends on the time required to modify production processes, KV says in a statement. The company does not expect to release the hold on shipping all of the affected products by March 31.

The company will continue to ship products it distributes but does not manufacture, including Evamist (estradiol) transdermal spray, a treatment for moderate-to-severe vasomotor symptoms due to menopause, as well as ketorolac tromethamine and enteric-coated naproxen sodium tablets, according to a filing with the SEC.

Interim President and CEO David Van Vliet, who assumed command after former Chairman and CEO Marc Hermelin left the company in December, says the company’s new leadership is committed to resolving the issues and restarting production.

(See **KV**, Page 12)

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“We are committed, however, to resolving these issues and resuming production as soon as possible by working closely with the FDA and the independent experts from Lachman Consultant Services,” Van Vliet adds.

Lawsuit Cites Manufacturing

KV also has created a special committee in response to a shareholder lawsuit alleging violations of federal securities laws related in part to the company’s manufacturing difficulties, according to a Jan. 26 SEC filing.

Plaintiff Joseph Mas, who purchased KV securities, filed the suit, *Joseph Mas v. KV Pharmaceutical Company, Marc S. Hermelin and Ronald J. Kanterman*, Dec. 2, 2008, in the U.S. District Court for the Eastern District of Missouri on behalf of people who purchased the company’s class A and class B common stock and 7 percent cumulative convertible preferred stock between Feb. 15, 2008, and Nov. 12, 2008.

The suit alleges the company “made materially false and misleading statements about KV’s compliance with federal regulations concerning the manufacture and marketing of certain generic drug products as well as the Company’s current and future financial prospects,” according to court documents (*Generic Line*, Dec. 10, 2008).

The company says it is cooperating with all governmental matters, including the lawsuit and an informal inquiry by the SEC.

The Ethex recall is available at www.fda.gov/oc/po/firmrecalls/ethex01_09.html, and the Ther-Rx recall is available at www.fda.gov/oc/po/firmrecalls/therrx01_09.html. — Elizabeth Jones, David Grant

Boehringer Sues Mylan To Protect Mirapex

Boehringer Ingelheim is suing Mylan in a New Jersey court for infringing on a patent covering the Parkinson’s disease drug Mirapex.

Boehringer filed the suit, *Boehringer Ingelheim International GMBH, et al., v. Mylan Pharmaceuticals, Inc.*, in the U.S. District Court for the District of New Jersey Jan. 26 after Mylan filed an ANDA for a generic .75-mg Mirapex (pramipexole dihydrochloride) before the ’812 patent expired.

Boehringer sued Mylan in 2005 for infringing on the same patent in the U.S. District Court for the District of Delaware in the suit *Boehringer Ingelheim International GMBH, et al., v. Mylan Pharmaceuticals, Inc.*

Last September, the Delaware court entered a judgment in favor of Mylan that certain claims of the patent are invalid for nonstatutory double patenting. Boehringer is appealing that decision in the U.S. District Court for the Federal Circuit. Barr Laboratories also is named as a defendant in the case.

Boehringer claims in court documents in the current New Jersey case that Mylan has no defense against charges of patent infringement other than an assertion of nonstatutory double patenting, which was its defense in the Delaware suit. However, Boehringer has offered strong evidence in its appeal that the Delaware court erred in its decision. It has asked the New Jersey court to make the approval date of the ANDA no earlier than the expiration of the patent.

Mirapex is approved to treat Parkinson’s disease. — Elizabeth Jones

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