

Special Report Generic Drugs

Generics poised to ride wave of branded patent expirations

BY AMANDA BALTAZAR

Generics account for 60 percent of prescriptions, and the industry is poised to benefit from an unprecedented and prolonged wave of branded drugs coming off patent. A growing global market is creating opportunities for generics, while at the same time the U.S. pharmaceutical industry wrestles with the issue of biogenerics.

Biosimilars (also known as biogenerics and follow-on biologics) are gathering speed in Europe, with the most recent being approved late this summer. This means there now are four biosimilars available in Europe—three versions of Johnson & Johnson's anemia blockbuster Eprex, from companies Sandoz, Hexal Biotech and Medice Arzneimittel Putter, and human growth hormone Omnitrope, from Sandoz, which was approved in April 2006.

In the United States, however, the approval of biogenerics is just not happening—yet. There still exists no pathway to approve these drugs because, opponents say, they cannot be an exact match of a biotech drug. The battle continues to be waged, with supporters of the drugs, including the Generic Pharmaceutical Association, the Pharmaceutical Care Management Association and Rep. Henry Waxman, D-Calif., saying each one should be reviewed individually.

According to Waxman: "The uniqueness of biological products suggests only a case-by-case approach for evaluating each type of product. We can't afford to wait for a time when we have a universal test."

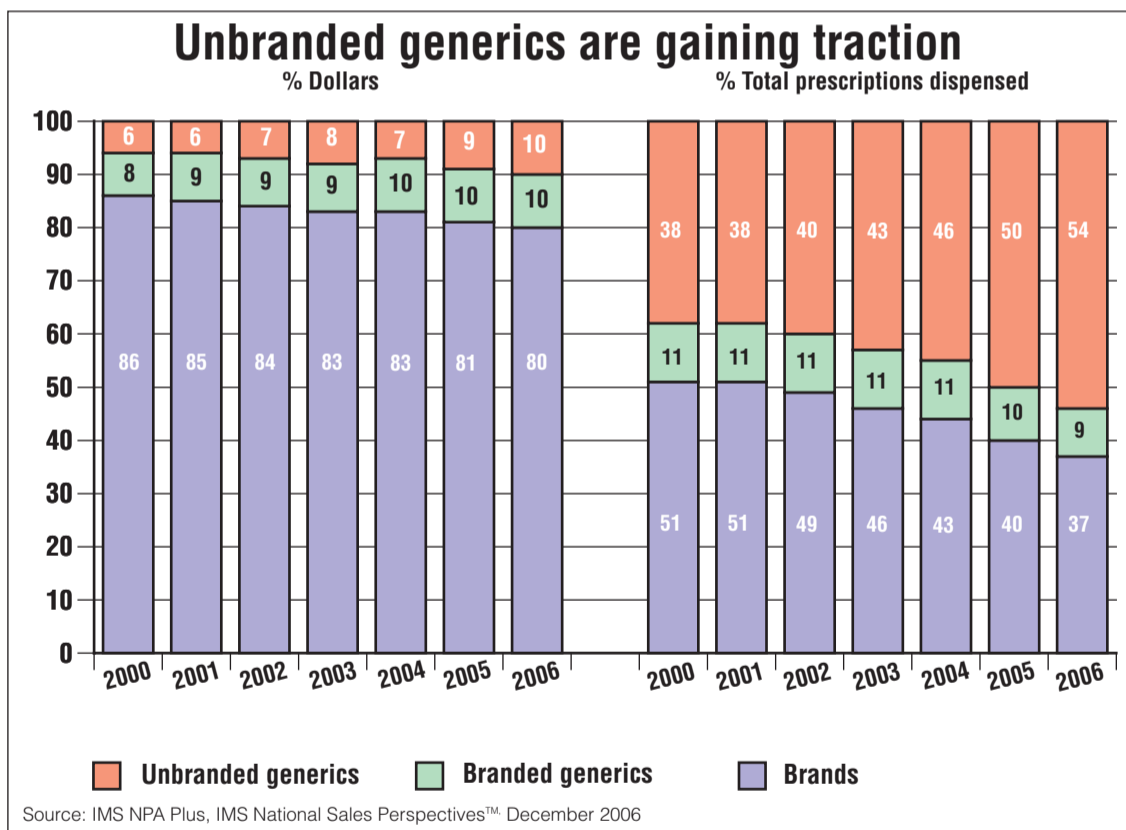
Biogeneric drug makers, together with a number of senators and Waxman, have been pushing legislation for the Food and Drug Administration to create a pathway to approve biogeneric drugs. However, it's now "extremely slim" that this will be added to a broader FDA bill that is now moving through Congress, Waxman said earlier this month. He added, however, that he was hopeful a generic biologics bill would pass before the current Congress closes at the end of 2008.

The U.S. generics industry also should keep its eyes on both India and China, two countries that are expected to become pharmaceutical powerhouses in the next 10 years.

These countries each have a strong medical infrastructure, cheaper manufacturing and labor, and an ease of recruiting patients with diseases for clinical trials. In the case of India, English also is predominant, negating the language barrier.

And there are other advantages: Much of these countries' populations are still very low-income, unable to afford branded pharmaceuticals even if they are available. And Western habits are starting to infiltrate on a broad basis. This means that along with a proliferation of fast-food chains, there also are more cars, video games and cigarettes, all of which add up to nations with a greater obesity problem and all the diseases that accompany it.

This news is good news for generic drug makers, and by 2010 foreign drug manufacturers could control half of China's pharmaceutical market, according to estimates



from Global Insight.

While keeping an eye on these emerging markets, U.S. generic drug firms also should be keeping check on the market at home.

These should be profitable times for generic drug makers. Generic drugs accounted for 60 percent of total drugs dispensed in 2006, and upcoming patent expirations make this the "golden age" of generics, said Ed Pezalla, vice president and medical director of Prescription Solutions, at the Pharmaceutical Care Management Association's Pharmacy Benefit Management & Generic Pharmaceutical Issues Symposium recently.

"We're just starting off on the biggest period of patent expirations we've ever seen," said Barath Shankar, research analyst with Frost & Sullivan. And it's not something that's going to end, he added, but there's

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Q&A



Outlook for generics legislation Kathleen Jaeger, GPhA

Drug Store News: What are the Generic Pharmaceutical Association's goals for the coming year?

Jaeger: We've had an extremely busy and productive year, and we anticipate that our agenda will be full in 2008 as well. Overall, our goal will be to continue to increase consumer access to safe, effective and affordable generics. This means we will be building on our successful efforts to move legislation forward to establish a workable Food and Drug Administration approval pathway for biogenerics, working to put an end to the practice of authorized generics, acting to increase funding for the FDA's Office of Generic Drugs and advancing legislation to address industry concerns with the Centers for Medicare and Medicaid Services' new pharmacy reimbursement rule. We also anticipate that congressional consideration will continue next year on pending legislation, including patent reform, patent settlements, anticounterfeiting/pedigree issues and free trade agreements.

DrSN: There has been a lot of talk about authorized generics in the past year. What is the outlook for them, and how are they affecting the generic drug industry?

Jaeger: When the Hatch-Waxman Act was created, Congress wisely granted a 180-day period of exclusivity to generic companies to spark competition and increase the availability of safe and affordable generics. However, brand companies are increasingly deciding to circumvent congressional intent by bringing authorized generics to market during the 180-day period. This blatant move to cut the legs out from under congressional intent only serves to harm consumers by stifling competition. Some members of Congress are taking action to close this loophole. Sen. John Rockefeller, [D-W.Va.], and Rep. JoAnn Emerson, [R-Mo.], have introduced legislation to block authorized generics from being marketed during the 180-day period. We strongly support that legislation and will work with its co-sponsors to help move the legislation forward in 2008.

DrSN: Four biosimilars have been approved in Europe, and legislation is attempting to push them through here. What do you expect to see in the next 12 months?

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Launches

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bons, are being replaced by ozone-friendly propellants, called hydrofluoroalkanes, which will be found in such brand-name inhalers as Key Pharmaceuticals' Proventil-HFA and Glaxo-SmithKline's Ventolin-HFA.

Pravachol recently saw the launch of its 80 mg strength to the generic market by Ranbaxy. The company, which also will be producing the 10 mg, 20 mg and 40 mg as well, received 180-day market exclusivity for the 80 mg dose from the Food and Drug Administration. Annual sales for all strengths of Pravachol were \$1.19 billion for 2006, according to IMS Health, with

\$209 million of that coming from the 80 mg strength.

Just recently, Teva began shipping the generic version of Novartis' herpes treatment drug, Famvir. The generic famciclovir will be available in all strengths. As the first company to file an abbreviated new drug application containing a paragraph IV certification for this product, Teva has been awarded an 180-day period of marketing exclusivity.

Lamisil was approved in a generic form to multiple generic drug manufacturers, including Amneal, Apotex, Dr. Reddy's, Genpharm, Mylan, Roxane, Teva, Watson and Wockhardt in 250 mg. The drug's patent expired June 30 and was approved quickly by

the FDA within three days.

Impax Pharmaceuticals will soon begin marketing the generic version of the branded hypertension drug Corzide (nadolol/bendroflumethiazide) in 40 mg/5 mg and 80 mg/5 mg. The drug had sales of about \$5.5 million for the 12-month period ended Feb. 28, according to Wolters Kluwer Health.

The beginning of 2007 saw such launches as generic Xanax and Seasonale.

As soon as Watson Laboratories announced that the FDA had approved its generic version of Barr Pharmaceutical's Seasonale (levonorgestrel/ ethinyl estradiol), Barr launched an authorized generic to go head-to-head.

Seasonale is an extended-cycle oral contraceptive. Barr's authorized generic has been launched under the name Jolessa, and Watson's is called Quasense.

Barr estimates Seasonale had U.S. sales of \$110 million over the 12-month period that ended in June.

Barr Pharmaceutical's generic response to Pfizer's Xanax (alprazolam) was approved last month. Barr received approval to market the product, alprazolam extended-release tablets, in 0.5 mg, 1 mg, 2 mg and 3 mg doses.

Xanax is approved to treat panic disorders, as well as anxiety disorder, and also can be used as an adjunctive treatment for anxiety associated with depression.

Generics poised

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a glut of expirations on the horizon—of both blockbuster pharmaceutical drugs and biotech medicines.

Last year, \$14 billion worth of branded drugs lost their patents and opened up the market to generic competition, and another \$63 billion worth of brand-name drugs are expected to go off patent between 2007 and 2012.

Even with branded drugs coming off patent and generics gaining a large share of prescriptions dispensed, there still are a number of hurdles, all of which are moving toward resolution at incredibly slow speed. These include:

Authorized generics

In an attempt to thwart the approval of generic versions of their brand-name drugs, big pharma continues to launch authorized generic drugs onto the market. Authorized generics basically are branded drugs disguised as generics. Branded companies supply their drug to a generic firm, or to their own subsidiary, to market the product as a generic in return for royalties. Many people say these are nothing but bad news for the generic drug industry because they cut into the 180-day exclusivity period that is granted to

the first generic on the market—and they are increasing. In the opposing camp, however, are the generic companies who contract with the brand companies to make their authorized generic products—and reap the financial rewards.

Citizens' Petitions

Threatening the approval of generic drugs also are citizens' petitions, which typically are launched by a brand company in an attempt to delay the launch of a generic and have been proliferating for years.

"These petitions have always been around," said Bill Rakoczy, a partner at law firm Rakoczy Molino Mazzochi Siwik, who represents generic companies. "But they're increasing because of the sheer number of generics [on the market now]. The brand companies have nothing to lose, and it costs them nothing."

"It's out of control and has almost become a knee-jerk reaction by the branded companies," he pointed out. For almost every generic that's launched these days, he said, there's an accompanying citizens' petition.

This has become such a problem, he said, that Congress has had to step in, and he expected that we may see some movement in Congress on this issue next year.

Funding at the FDA's Office of Generic Drugs

Behind the scenes, there's a huge backlog at the FDA's Office of Generic Drugs, which has seen the number of submitted applications increase by 150 percent, according to director Gary Buehler.

According to the FDA, fewer generics are being approved for two reasons: a shortage of personnel and the number of faulty applications that generic companies submit. To address the massive backlog, the FDA is reviewing some applications in 'clusters,' as it did for the recent approval of generic Ambien (from companies including Teva, Mylan, Dr. Reddy's and Watson). This method "can only be used when we get a number of applications on the same day," Buehler said.

Also attempting to improve the generic drug situation, Buehler said the agency has increased its staff "so we have benefited a lot from the increase in resources, but it hasn't kept pace with the increase in applications."

He said the Office of Generic Drugs needs up to 100 more employees over the next three years to eliminate the buildup—a move that would cost between \$16 million and \$19 million a year.

Generics flood

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Migraine medication Imitrex from GSK lost its patent in June. GSK has granted Dr. Reddy's authorized generic status for sumatriptan succinate, which is expected

to launch at the end of next year.

Next year will only be bigger for generics as more big name drugs lose their patents. Some of the big names that will lose their protection are Effexor XR (Wyeth), Fosamax (Merck), Depakote

(Abbott), Advair (GSK), Topamax (Ortho-McNeil), and Lamictal (GSK). Risperdal (Janssen) is set to lose its patent on Dec. 29, but because of their pediatric extension, Janssen will hold marketing rights until June 29, 2008.

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