

Generic glow dulls

Copycat drugs save money, but may not be the medicine you need

By MELISSA HEALY
Los Angeles Times

In the contentious debate over insuring Americans' health, the value of generic prescription drugs is a rare point of consensus. Patients, physicians, employers, politicians — all hail generics as powerful treatment for a swelling health-care tab. On average, these copycat medicines cost less than one-third as much as the brand-name drugs they mimic. In turn, the competition they provide drives down the cost of those first-to-market drugs.

Officials of the Food and Drug Administration insist this feat of economics comes without any compromise to a medicine's effectiveness. To be marketed in the United States, these low-cost medicines must be approved by the FDA, which ensures they are "bioequivalent" to their brand-name counterparts — the same dose of the same active ingredient, delivered in the same way, and manufactured according to the same standards of quality.

At odds with slogan

The Generic Pharmaceutical Association touts them with a slightly catchier slogan: "Same Medicine. Same Results." But sometimes patients and their doctors beg to differ.

A switch from a long-used brand-name drug to its generic equivalent can, on occasion, bring a shifting profile of side effects. In a number of cases documented in medical journals and recounted in interviews with physicians, a generic version of what is often called a "pioneer" drug simply doesn't appear to work as well for many patients.

"Everybody thinks generics are swell: To suggest otherwise is like saying you don't love your mother," said Dr. Peter R. Kowey, chief of cardiovascular diseases at the Philadelphia area's Main Line Health System, who reviewed the issue of generic substitution of certain heart drugs for the American Heart Association. But between some pioneer drugs and their generic imitators, Kowey said, "we are concerned that the margin of difference is large enough" to risk patients' health.

Last December, the American Epilepsy Society called on the FDA to approve a large clinical trial to determine "once and for all" whether the substitution of

brand-name drugs with generics increases the risk of "breakthrough" seizures or toxicity among patients with epilepsy. This type of research would probably take years. But until such a study is completed, the society declared, it would oppose measures by state, federal or private insurance programs that would limit physicians' choices in prescribing anti-seizure medicines.

Last fall, an independent laboratory, prompted by a flurry of consumer complaints, presented evidence that a generic version of the once-a-day antidepressant Wellbutrin XL may be

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less effective than the original at reducing some patients' symptoms. An agency spokeswoman said the FDA is investigating the matter and will make its findings public when the inquiry is complete.

In a report released March 17, the New York-based ConsumerLab.com, which conducted the Wellbutrin XL analysis, also urges the FDA to review the performance of a new generic for Toprol XL, a once-a-day version of a high blood pressure drug that is the fifth-most-prescribed medicine in the United States. That challenge comes after dozens of patients complained to the People's Pharmacy — a multimedia source of information about drugs and supplements — of erratic spikes in blood pressure and side effects after they had switched from Toprol XL to a new generic version of the drug.

Cardiologists concerned

Cardiologists, meanwhile, have been growing more vocal in their concern about "generic substitution" for newer, brand-name drugs. They have had long-standing worries about the effect of switching patients whose blood has been thinned with Coumadin to generic versions of the anticoagulant, including warfarin. Many have warned that patients with heart arrhythmias should be switched to generic drugs only when necessary. And many cardiologists view the swelling field of generic blood-pressure and cholesterol drugs with some distrust.

The American Association of Clinical Endocrinologists, the Endocrine Society and the American Thyroid Association joined voices in 2004 to warn that patients with hypothyroidism could be harmed by switching among the many generics used to treat the condition. And physicians who care for organ transplant recipients have opposed generic substitution of immunosuppressant drugs for their patients without a transplant specialist's prior approval. Societies that represent these doctors have been active in seeking state laws that would limit such switches.

Kathleen Jaeger, president and chief executive of the Generic Pharmaceutical Association, dismisses all of these debates as "misinformation campaigns" masterminded by brand-name pharmaceutical companies. As these companies' most profitable medicines face competition from generic upstarts, Jaeger said, they seek to "extend their monopoly" by sowing doubt in the minds of physicians, pharmacists and patients about the quality of the cheaper substitutes.

Those who would question generic drugs' equivalence to the brand-name drugs they mimic are calling into question a stringent FDA review process, Jaeger said. "They do a disservice to our health-care system," she added. "Consumers deserve better."

But many physicians and pharmacologists interviewed said that with some drugs, the FDA — an agency that has come in for harsh criticism on matters of drug safety in recent years — may be overlooking differences that could be important to patients' health.

FDA officials "have adopted a position that is in some respects quite brave," said Peter Meredith, a University of Glasgow pharmacologist who has written extensively about generic drugs and their regulation. "The FDA quite rigidly states that when they say a drug is substitutable, they mean that with no caveats, no qualifications. My concern would be that if you don't look for one, you don't see it."

With about 9,000 generic drugs on the U.S. market, concerns raised about a handful do not suggest a broad failure in the nation's formulary of low-cost medications. But many physicians and pharmacologists caution that with new generics entering the market at a rate of almost 500 per year, and millions of consumers switching to them, their safety and effectiveness will be increasingly critical.

"The reasonable people I know aren't pounding their fists saying all generics are bad," Kowey said. "They're saying to the FDA, 'C'mon guys, there may be some situations in which (these differences) may turn out to be important.'"

Almost two-thirds of all prescriptions filled in the United States are for generic medicines. That percentage is expected to rise steeply over the next several years.

Switch to generics with care

Don't just assume it's the same medication

By MELISSA HEALY
Los Angeles Times

Faced with stiff financial penalties when they opt for a more expensive drug insured patients rarely complain when their pharmacist dispenses the cheaper generic. Many patients do not even notice the switch until they open their pill bottle and see a tablet that differs in shape or color from the one they have been taking.

Mark Autrey was one of those patients. Since 2004, Autrey, 52, had controlled his high blood pressure with Toprol XL, a brand-name medication made by AstraZeneca. So had his elderly mother, for whom Autrey is a caregiver in Villa Rica, Ga. Last summer, Autrey came home from the pharmacy with a generic version of Toprol XL that both he and his mother took.

At first, the only change Autrey noticed was the price of the drug — a change he welcomed. Within a few weeks, though, he noticed unusual spikes in his mother's blood pressure. Feeling "a little off-key" and more tired than usual, he checked his own as well, and began noticing elevated levels he hadn't seen in years. His mother's physician was adamant that Autrey refill his mother's prescription with the brand-name product on which her blood pressure had been stabilized, and suggested Autrey switch back also.

Trust, but verify

Switching from a long-used brand-name drug to its generic counterpart — or from a generic made by one company to a generic made by another — patients should follow the same advice they receive when making any change to their medicines, says R. William Solter, a professor of pharmacology at the School of Pharmacy at the University of California, San Francisco.

To use one of Ronald Reagan's famous phrases, patients should "trust, but verify" that a new medicine is doing the job. That may mean checking blood pressure, blood-sugar levels or mood a bit more often for a few weeks, and alerting the prescribing physician of any changes.

There is little doubt that generic drugs save money. An increase of just 1 percent in Americans' use of generics would save consumers and taxpayers \$4 billion per year, according to the Generic Pharmaceutical Association.

Physicians have a warning

But the physicians who care for patients who jump — or are pushed — to generics are sometimes not as impressed with the resulting cost savings. They caution that extra blood tests or office visits that might be needed when a patient switches often offset some of the savings that come with taking a less expensive drug. And if the patient's generic substitute does not work as well as the pioneer drug that first brought the symptoms under control, physicians say they have major headaches: They face increased liability for the patient's worsened condition and, if they want to switch the patient back to a brand-name drug, a mountain of paperwork to justify their clinical judgment to insurance companies.

All that, and they have a sick patient whose condition must be stabilized all over again on a generic drug or restabilized on the brand-name medicine with which they began.

"Practicing physicians absorb the cost and liability of prescribing therapeutic substitutes at the whim ... of the health plan providers, whose sole motivation is to wring out every cent of cost savings possible for the benefit — i.e., the profit — of the plan," said Dr. Dean J. Kereiakes, chief executive and research director of the Ohio Heart & Vascular Center in Cincinnati. "I have never been harassed to the point where I currently am from insurance companies.... This is the most obnoxious racket that I've ever been involved in."

It's sometimes no picnic for patients either. As generic alternatives to a popular brand-name drug proliferate, patients face confusion, uncertainty and risk. Insurance companies and pharmacies may shift their preferred supplier of a given generic drug from month to month to reap cost savings. One month, a patient with high blood pressure may be dispensed a pink pill made by one generics manufacturer and the next month, a gray caplet made by another.

