If you or a family member have taken brand-name prescription drugs for such ailments as allergies, anxiety, heartburn, or high blood pressure, you can stop wondering why your bills have been so high. In many cases, cheaper generic equivalents have not made it to the marketplace as early as they could have after expiration of the typical 20-year drug patent.

Our interviews with consumers, federal regulators, and drug manufacturers and their trade groups, and our review of recent Federal Trade Commission (FTC) actions, paint a picture of a pharmaceutical industry busily engaged in stalling the entry of generic drugs to the marketplace. In April, the FTC filed the third complaint in a year charging drug makers with anticompetitive practices (see “Sweetheart Deals,” below).

The Bush administration recently gave the FTC a green light to begin an industry-wide investigation; the FTC has issued subpoenas to 100 pharmaceutical companies—brand-name and generic manufacturers alike. Investigators will focus on the business relationships between brand-name and generic-drug manufacturers, says outgoing FTC chairman Robert Pitofsky.

Consumers are bearing the financial brunt of tactics that delay the introduction of generic drugs, which typically cost 25 to 50 percent less than their brand-name equivalents. Consider David Hyams, 75, of Corte Madera, Calif., who began taking Hytrin (terazosin) to control his high blood pressure in 1992. With no drug insurance, Hyams paid the then $1-a-day cost of the brand-name drug himself. And the price kept going up. By 1999 it was up to $1.50 a day. In August of that year, a generic terazosin finally became available. “Of course, I made the switch,” says Hyams.

As more generic versions of the drug entered the market, prices were driven down. By spring 2001, Hyams was paying just 40 cents a day for his dose of the drug. But if it weren’t for a sweetheart deal, one of several tactics used to stall competition, generic versions of Hytrin could—and should—have been available months earlier, according to the FTC.

It’s a high-stakes game for drug manufacturers, their shareholders, and the public. Maintaining a monopoly on a product by delaying a generic introduction by even a day can mean millions in profits for the brand-name company. And the stakes will soon get higher. Patents on 21 best-selling drugs with annual U.S. sales approaching $20 billion will expire over the next five years.

“Brand-name pharmaceutical companies are using every possible tactic—legal or illegal—to rob Americans of billions of dollars over the next few years by delaying for as long as possible the entrance of generics to market,” says Sidney Wolfe, M.D., of the nonprofit Public Citizen Health Research Group, a Washington watchdog group. “It’s an economic and a health scandal. It prevents people who can’t afford the brand-name version—but might be able to afford the generic version—from getting the drugs they need.”

The Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, was designed to foster generic competition by
striking a balance between the interests of generic and brand-name companies. The legislation made it cheaper and easier for generic makers to win FDA approval for their drug. It gave some generic companies a six-month head start on the competition. And it rewarded makers of brand-name drugs with additional years of effective patent life to make up for market time lost awaiting FDA approval. True innovators who market first-of-their-kind drugs get up to five additional years of patent protection.

In recent years, companies have gone all out to evade the spirit of the 1984 law. They've been accused of the following:

**Legislative stealth.** Sneaking patent-extending riders into complex and unrelated legislative packages.

**Disabling competitors.** Paying chemical supply houses not to sell needed ingredients to rival drug manufacturers.

**Sweetheart deals.** Paying competitors to stay out of the market.

**Unreasonable delays.** Filing unfounded "citizen petitions" and patents to delay the marketing of a generic drug.

There are times when delay may be justified: Market exclusivity is sometimes granted to encourage research in neglected areas. Since 1998, the Department of Health and Human Services has given makers of more than 12 dozen brand-name drugs an extra six months of market exclusivity as an incentive to conduct clinical trials to determine how well their medicines work in children. Supporters of the program say it rewards drug manufacturers for performing time-consuming and crucial research. Critics charge that this is a government subsidy program that pays manufacturers for research they should be obligated to undertake.

**LEGISLATIVE STEALTH**
Most market monopolies benefit only drug companies and their stockholders. That's why drug manufacturers have lobbied congressional representatives to insert special patent-extending clauses for a particular drug into must-pass appropriation legislation. In 1996 a clause extending for two years the G.D. Searle patent on its non-steroidal anti-inflammatory drug Daypro (oxaprozin) passed as part of the omnibus budget bill, the legislation that prevented a federal government shutdown.

Since then, however, Congress seems to be more alert. It cut out the rider for a patent extension on Hoffmann-La Roche's pain reliever Toradol (ketorolac) that was inserted in the 1997 emergency legislation for flood victims and military missions. And last year Sen. Edward M. Kennedy, D-Mass., and other senators held a press conference to expose an attempt to extend Schering-Plough's patent for the allergy drug Claritin (loratadine) in the 2001 Military Construction Appropriations bill.

**DISABLING OTHER MANUFACTURERS**
It's not only brand-name companies that try to dodge competition. A major generic company has been charged with going to great lengths to remain the only player in its category. Mylan Laboratories, the nation's second largest generic-drug manufacturer, has settled FTC charges that it conspired with three chemical suppliers to deprive other generic-drug makers of the ingredients necessary to manufacture two generic antianxiety drugs, clorazepate and lorazepam. With the competition disabled, Mylan raised the wholesale price of clorazepate from $11.36 to $377 for a 500-count bottle of 7.5-milligram (mg) tablets in January 1998, says the FTC. Two months later Mylan raised the wholesale price of lorazepam from $7.30 to $190 for a 500-count bottle of 1-mg tablets. The arrangement cost consumers more than $120 million, the commission says.

In the largest monetary settlement in FTC history, Mylan Laboratories, denying wrongdoing, has agreed to pay $147 million to compensate patients, insurers, managed-care organizations, and state agencies and to pay attorneys' fees. Affected consumers can call 800 899-5806 or find information at www.assettlement.com.

**SWEETHEART DEALS**
In March 1998 generic manufacturer Geneva Pharmaceuticals received FDA approval to be the first to market generic capsules of Hytrin, used for benign prostate enlargement and high blood pressure. Then Geneva told Abbott Laboratories, which developed the drug, it would launch a generic version of Hytrin unless Abbott paid to keep

---

**Growing confidence in generic drugs**

To win FDA approval, a generic-drug maker must show that its product contains the identical active ingredients as its brand-name counterpart. And it must prove that the generic is bioequivalent, usually by showing that the active ingredient enters and leaves the bloodstream as rapidly and completely as its branded twin. Drugs that do not have the same therapeutic effect.

A recent FDA review of the bioequivalence of the 273 generic drugs approved in 1997 found just a 3.5 percent difference, on average, between generic and branded drugs. That's no greater than the difference between one batch of a brand-name drug and another batch off the same assembly line.

"Based on these results, practitioners and the public may be assured that if the FDA declares a generic drug to be therapeutically equivalent to an innovator drug, the two products will provide the same intended clinical effect," Jane Henney, M.D., then FDA commissioner, wrote in the December 1999 issue of the Journal of the American Medical Association.

That assurance even applies to 25 medications—primarily for epilepsy, heart-rhythm disturbances, and pulmonary disease—that are effective only within a very narrow range of blood levels and so have been dubbed "Narrow Therapeutic Index," or NTI drugs, says Gary Buehler, acting director of FDA's Office of Generic Drugs. He says a growing body of research supports the FDA's view that patients on NTI drugs can switch to generics without special monitoring. The exception is the thyroid hormone levothyroxine (Euthyroid, Levoxyl, Levothroid, Synthroid); bioequivalency data are still lacking, so Consumers Union's medical consultants advise patients not to switch products without being monitored.

The FDA has grown so confident of the generics it approves that it has stopped its longtime practice of designating them and their branded counterparts "B" drugs if they're not interchangeable because of actual or potential bioequivalence problems. "That was an artifact of the past," Buehler says. "We no longer approve drugs that are not equivalent."

Nevertheless, about 65 drugs approved in the past are still "B-rated," including particular dosage forms of common medications such as albuterol for asthma, estradiol for hormone-replacement therapy, and prednisone for inflammatory disease. Patients on "B" drugs who switch from brand to generic (or between generics) should be monitored. For more information on "B-rated" medications, refer to the "orange" book, the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations," which can be found at www.fda.gov/cder/orange/default.htm.

---

**JULY 2001 @ CONSUMER REPORTS 37**
it off the market, according to the FTC. The price: $4.5 million per month—more than Geneva might have received from actually marketing the drug, the FTC says. The two firms outlined how long the generic launch would be delayed and the terms of the payments, which were tied to the resolution of pending patent-infringement litigation.

Geneva’s inaction kept other generic competitors on the sidelines. As the first to receive FDA approval for a generic Hytrin, Geneva was granted a 180-day competition-free head start in the marketplace under the Hatch-Waxman Act. Until it used this head start, other generic companies could not enter the market. In settling the FTC charges, both companies denied any wrongdoing.

Pending are FTC charges that Schering-Plough, maker of K-Dur 20, a top-selling prescription potassium chloride supplement, illegally paid Upsher-Smith Laboratories and American Home Products—with which it was embroiled in a patent-infringement dispute—millions of dollars to delay launching their generic versions of the drug. The firms deny the charges. In a prepared statement issued in April, Schering-Plough said the payments were “patent litigation settlements” that were “lawful and benefited consumers.”

But the FTC contends that those two cases, and another involving Hoechst Marion Roussel (now Aventis), maker of Cardizem CD, and Andrx Corporation, have cost consumers more than $300 million. Aventis and Andrx denied the charges. The firms have entered an FTC-brokered agreement barring them from contractual arrangements that would delay generic-drug launches. Class-action lawsuits on behalf of consumers, insurers, and other payers have begun to appear.

**UNREASONABLE DELAYS**

Some drug makers register new patents of questionable significance for their product, then sue companies that want to produce a generic for patent infringement. These lawsuits can effectively give innovator companies up to another 30 months of market exclusivity under the Hatch-Waxman Act.

Just hours before the antianxiety drug Buspar (buspirone) was to go off patent in November 2000, Bristol-Myers Squibb submitted a new patent to the FDA—not for the drug, but for a metabolite, a substance produced in the body of patients taking the drug. The action forced Mylan to halt shipments of 46 million pills of generic buspirone. It took a victory in federal court (which Bristol says it is appealing) for Mylan to be able to market the generic. But in the meantime, Bristol earned an estimated $253 million. Mylan says it lost out on $200 million in sales. And consumers continued to pay top dollar for the antianxiety medicine.

Another delay tactic involves the FDA’s “citizen petition,” a rule meant to give everyone—from health professionals to patients—a voice on agency actions, including pointing out possible deficiencies in generic products. When a citizen petition is filed, the FDA places a hold on approval of the generic while it investigates the complaint.

The problem: Brand-name drug companies are the source of many of these petitions. The vast majority of citizen petitions are rejected because they’re baseless, says Dale Conner, director of the Division of Bioequivalence at the FDA Office of Generic Drugs. “Most of the time their motivation is simply to make it harder for the competition to come to market.”

The FTC is focusing on whether provisions of the Hatch-Waxman Act have encouraged competition as intended or, instead, facilitated the use of anticompetitive strategies to delay the marketing of generics. “We’re trying to figure out where the line should be drawn and then police that line,” says Richard Feinstein, an assistant director of the FTC’s bureau of competition.

---

**Why are there no generic biotech drugs?**

Although he has a rare and severe form of the bleeding disorder hemophilia, Larry Madeiros of Northville, N.Y., considers himself a lucky man. That’s because he can now take a biotech drug (a synthetic version of a natural biologic substance) to replace the clotting factor missing from his blood. The drug, Benefix (Recombinant Coagulation Factor IX), is synthesized in a laboratory, using nonhuman cells, so it is “inherently free” from the risk of major human blood-borne pathogens, according to its manufacturer, the Genetics Institute of Cambridge, Mass. Before the drug was available—and prior to the development of screening tests for HIV, the virus that causes AIDS—Madeiros used a blood-factor replacement derived from the plasma of thousands of donors—from which, he says, he contracted hepatitis and HIV. The biotech drug has “allowed me to lead a life that’s close to normal,” says Madeiros.

The catch: At the dosage he requires, it costs more than $5,000 every other day. The annual cost: $915,000 a year. A spokeswoman for the manufacturer says the drug is competitively priced.

At 38, Madeiros has already surpassed at least two lifetime caps on health-insurance drug benefits and changed jobs at least once to get a fresh start on a new “lifetime” drug-benefit cap. Biotech drugs are among the most expensive medications, yet there are no generic versions on the horizon.

That’s mainly because the Hatch-Waxman Act of 1984, which made it cheaper and easier for conventional generic drugs to win FDA approval, did not include similar provisions for all biologics. “Biotechnology was just a blip on the radar screen in 1984,”

Sen. Orrin Hatch, R-Utah, said in a March 2001 speech in which he promised a good deal of debate over the issue this year.

The FDA isn’t pushing for regulatory changes that would open the door to generic biologics. “There are significant unresolved scientific issues about how to show ‘sameness’ between complex biological macromolecules so that FDA can be assured that any generic biologic is safe, pure, and potent as well as ‘equivalent’ to an innovator product,” said Margaret Dotzel, FDA’s associate commission for policy, in a written statement released in December 2000.

“These are tough scientific issues but they’re not unsolvable,” says Roger Williams, M.D., chief executive officer of the United States Pharmacopeia, the organization that sets standards for drug manufacturing. A former director of the FDA’s Office of Generic Drugs, Williams says a USP committee is exploring the possibility of developing quality standards for biologics that may help both innovator and generic manufacturers.

Until cheaper generic biologics become available, Madeiros is trying to help people find ways to cover high-priced therapies through his work as executive director of Positudes, a nonprofit patient advocacy organization that he cofounded. (For more information, call toll free 866 767-4883.) Right now “there’s no quick fix, just a combination of Band-Aids,” Madeiros says. “To cover everyone, you need a whole lot of Band-Aids.”

Paying the bills: The costs of Larry Madeiros’ hemophilia treatments approach $1 million a year.
PATENT EXTENSIONS AS CARROTS
An above-board way for innovator drug companies to stave off competition is through a law that grants six months of market exclusivity to companies that agree to conduct pediatric clinical trials. Makers of 12 of the top 100 best-selling drugs and 16 other medications have been granted market exclusivity through the program, according to a January 2001 report to Congress.

It’s a lucrative business. Pediatric clinical trials typically cost several million dollars, but winning additional market-monopoly time can be worth much more. Without generic competition, the ulcer drug Prilosec (omeprazole), for example, earns revenues of $11 million a day for its manufacturer, AstraZeneca. The FDA says that so far 29 drugs, including Prilosec, Prozac (fluoxetine), and Claritin (loratadine), have conducted the required studies on children and have been granted additional exclusivity.

Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania, says that offering patent extensions to brand-name drug makers in return for needed pediatric clinical data is a good trade-off for society. “I can imagine similar programs aimed at trying to redress market imbalances in treatments for diseases of the poor and others who have no political lobby,” Caplan says. The pharmaceutical industry supports the pediatric research program and will lobby for its reauthorization.

But critics, such as Abbey Meyers, president of the nonprofit National Organization for Rare Disorders, say the program “bribes drug companies into doing research they should have been doing anyway so that pediatricians would know how to prescribe their drugs.”

Critics note that the patent extensions won’t help spur drug companies to do pediatric testing needed to fill knowledge gaps for key medications that are off patent. These include rescue inhalers for asthma, Proventil and Ventolin (albuterol), and Ritalin (methylphenidate), for attention deficit disorder.

THE BIG PAY-OFF
If “protect the monopoly” has become the innovators’ mantra, it’s because generic competition can have such a profound effect on the marketplace. Pharmacist are permitted, and sometimes required, to substitute lower-priced generic drugs for their brand-name counterparts, unless the prescribing physician directs otherwise. Many private health plans and state Medicaid programs encourage or insist on the use of generic drugs when available. It’s easy to see why. Generic drugs provide consumers with a significant price break (see table below), mostly because their manufacturers do not have to duplicate the expensive clinical trials that won their branded predecessors FDA approval.

The competition doesn’t seem to be harming the pharmaceutical industry. In fiscal year 2000, it was still the most profitable of any American industry, according to a study by Public Citizen. The 11 firms in the Fortune 500 drug-industry category enjoyed an 18.6 percent return on revenues, compared with the 4.9 percent median for all Fortune 500 industries, the study found. Despite industry claims that it needs extraordinary profits to finance risky, expensive research and development, the 11 drug companies in the Fortune 500 spent just 12 percent of revenues on R&D and 30 percent on marketing and administration; they took 17 percent as profits.

Though generic-drug makers are considerably less profitable than brand-name drug companies, two of the largest generic makers, Barr Laboratories and Teva Pharmaceutical Industries, had a return on revenues of 10 percent and 8.5 percent, respectively. A recent study conducted for Blue Cross and Blue Shield Association forecasts increased prices on some generics, the result, in part, of industry consolidation.

In May, a coalition of 17 consumer groups filed lawsuits charging that an “illegal agreement” between Barr Laboratories and AstraZeneca has “artificially inflated” the cost of tamoxifen, the generic name for Nolvadex, a widely prescribed breast-cancer drug. A spokeswoman for AstraZeneca said the agreement is lawful. In a statement, Barr said the suit “is without merit” and that it distributes its generic to drugstores, distributors, and wholesalers at approximately 15 percent less than the brand price. However, a recent price check for this report found that consumers were paying identical prices for Nolvadex and generic tamoxifen.

“I think that the pharmaceutical industry’s perspective is that their ultimate obligation is to their stockholders,” says Jane Henney, M.D., former FDA commissioner. “However, they are producing therapies that are important to patients across this country and so they do need to look at the ability of people to afford them. That’s really where the rubber meets the road: If you can’t afford it, then you can’t use it.”

Historically, competition in the market has pushed generic-drug prices lower over time. But prices for brand-name drugs tend to rise after generic competition is introduced. The reason may be that companies expect to retain brand-loyal customers through direct-to-consumer advertising and by encouraging “you get what you pay for” notions that cause some customers to doubt the quality of cheaper generic drugs.

To counter that, some generic-drug makers are marketing “branded generics” that sell at a somewhat higher price than no-brand generics, though they offer no added benefit beyond fancy packaging.

No-brand savings
Just how much money will a generic drug save you? The amounts shown below are the average retail prices a consumer might expect to pay at the pharmacy for a year’s worth of brand-name and generic medicines at the most widely prescribed dosages.

<table>
<thead>
<tr>
<th>PROBLEM</th>
<th>BRAND-NAME DRUG</th>
<th>GENERIC DRUG</th>
<th>ANNUAL SAVINGS</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(COST PER YEAR)</td>
<td>(COST PER YEAR)</td>
<td>(DOLLARS/PERCENT)</td>
<td></td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>Lanoxin ($85.44)</td>
<td>Digoxin ($67.64)</td>
<td>$17.80 / 21%</td>
<td>250 micrograms, once daily</td>
</tr>
<tr>
<td>Benign prostate enlargement</td>
<td>Cardura ($594.20)</td>
<td>Doxazosin ($302.95)</td>
<td>91.25 / 23</td>
<td>4 milligrams, once daily</td>
</tr>
<tr>
<td>Hytrin ($664.30)</td>
<td>Terezosin ($481.80)</td>
<td>182.50 / 21</td>
<td>5 milligrams, once daily</td>
<td></td>
</tr>
<tr>
<td>High blood pressure and congestive heart failure</td>
<td>Vasotec ($413.45)</td>
<td>Enalipril ($299.90)</td>
<td>113.15 / 27</td>
<td>10 milligrams, once daily</td>
</tr>
<tr>
<td>Pain, inflammation</td>
<td>Motrin ($481.80)</td>
<td>Ibuprofen ($240.90)</td>
<td>240.90 / 50</td>
<td>800 milligrams, three times a day</td>
</tr>
<tr>
<td>Thyroid insufficiency</td>
<td>Synthroid ($423.35)</td>
<td>Levothyroxine ($69.35)*</td>
<td>73.00 / 51</td>
<td>100 micrograms, once daily</td>
</tr>
</tbody>
</table>

* Before switching to a different product individuals may need to have blood tests to recaleibrate the dosage.

Doctors and consumers should resist marketing strategies that may end up boosting prices for generic drugs. Sale of low-cost, plain-vanilla generics is a way to let a little air out of ballooning prescription-drug costs. Indeed, a recent statistical analysis by researchers at the Managed Care Institute at Samford University in Birmingham, Ala., shows that an increase in the generic substitution rate of only 1 percent equals an additional saving of $1 billion a year. That could go a long way toward covering the cost of a prescription-drug benefit for people on Medicare or expanding government programs to help cover the uninsured.

RECOMMENDATIONS

Today most health and medical experts agree that generic medicines can be expected to have the same therapeutic effect as brand-name drugs. Therefore, it makes sense to choose cheaper generics and save money on out-of-pocket costs or substantially lower insurance co-pays.

However, pharmacists who initiate a switch from a brand-name drug to a generic, or from one generic to another, should be required to inform the consumer. If ever in doubt about why a medicine has a different color, shape, or taste, consumers should check with the pharmacist to make sure the prescription was correctly filled.

In developing Medicare prescription-drug benefit legislation, Congress should tap the benefit of low-cost generic drugs and use other means to curb excessive drug costs to taxpayers.

 Ensuring the availability of new generic drugs will require stepped-up regulatory enforcement from the FTC and perhaps the Justice Department.


A careful cost/benefit analysis is needed to determine whether the public interest is economically served by granting companies six months of market exclusivity for conducting clinical trials on children. Certainly these companies should be required to publicize the results of the trials.