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A CRITIC AT LARGE

HIGH PRICES

How to think about prescription drugs.

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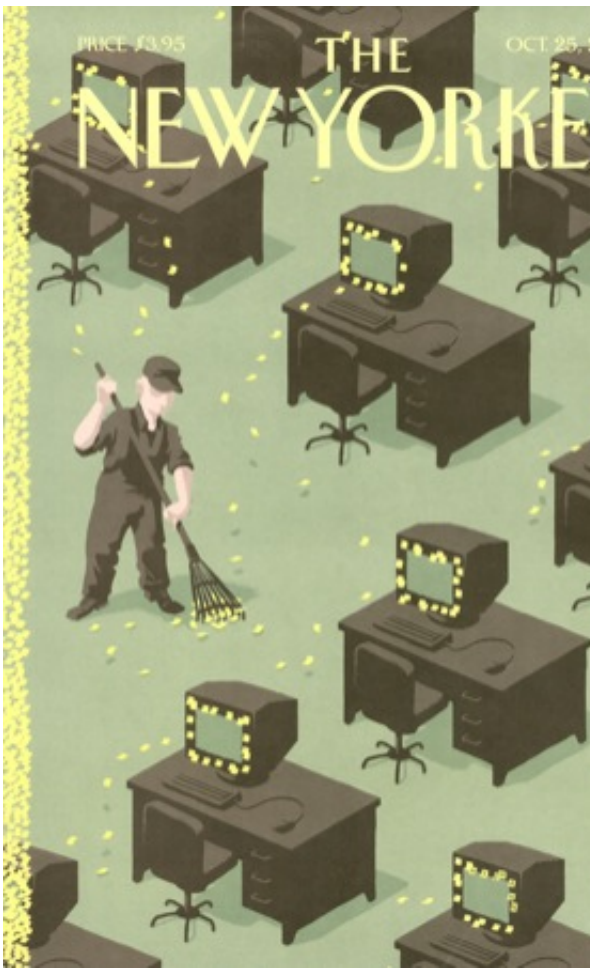

Ten years ago, the multinational pharmaceutical company AstraZeneca launched what was known inside the company as the Shark Fin Project. The team for the project was composed of lawyers, marketers, and scientists, and its focus was a prescription drug known as Prilosec, a heartburn medication that, in one five-year stretch of its extraordinary history, earned AstraZeneca twenty-six billion dollars. The patent on the drug was due to expire in April of 2001. The name Shark Fin was a reference to what Prilosec sales—and AstraZeneca's profits—would look like if nothing was done to fend off the ensuing low-priced generic competition.

The Shark Fin team drew up a list of fifty options. One idea was to devise a Prilosec 2.0—a version that worked faster or longer, or was more effective. Another idea was to combine it with a different heartburn remedy, or to change the formulation, so that it came in a liquid gel or in an extended-release form. In the end, AstraZeneca decided on a subtle piece of chemical reëngineering. Prilosec, like many drugs, is composed of two "isomers"—a left-hand and a right-hand version of the molecule. In some cases, removing one of the isomers can reduce side effects or make a drug work a little bit better, and in all cases the Patent Office recognizes something with one isomer as a separate invention from something with two. So AstraZeneca cut Prilosec in half.

AstraZeneca then had to prove that the single-isomer version of the drug was better than regular Prilosec. It chose as its target something called erosive esophagitis, a condition in which

patients took Prilosec, and half took Son of Prilosec. After one month, the two drugs were dead even. But after two months, to the delight of the Shark Fin team, the single-isomer version edged ahead—with a ninety-per-cent healing rate versus Prilosec's eighty-seven per cent. The new drug was called Nexium. A patent was filed, the F.D.A. gave its blessing, and, in March of 2001, Nexium hit the pharmacy shelves priced at a hundred and twenty dollars for a month's worth of pills. To keep cheaper generics at bay, and persuade patients and doctors to think of Nexium as state of the art, AstraZeneca spent half a billion dollars in marketing and advertising in the year following the launch. It is now one of the half-dozen top-selling drugs in America.

In the political uproar over prescription-drug costs, Nexium has become a symbol of everything that is wrong with the pharmaceutical industry. The big drug companies justify the high prices they charge—and the extraordinary profits they enjoy—by arguing that the search for innovative, life-saving medicines is risky and expensive. But Nexium is little more than a repackaged version of an old medicine. And the hundred and twenty dollars a month that AstraZeneca charges isn't to recoup the costs of risky research and development; the costs were for a series of clinical trials that told us nothing we needed to know, and a half-billion-dollar marketing campaign selling the solution to a problem we'd already solved. "The Prilosec pattern, repeated across the pharmaceutical industry, goes a long way to explain why the nation's prescription drug bill is rising an estimated 17 % a year even as general inflation is quiescent," the *Wall Street Journal* concluded, in a front-page article that first revealed the Shark Fin Project.

In "The Truth About the Drug Companies: How They Deceive Us and What to Do About It" (Random House; $24.95), Marcia Angell offers an even harsher assessment. Angell used to be the editor-in-chief of *The New England Journal of Medicine*, which is among the most powerful positions in American medicine, and in her view drug companies are troubled and corrupt. She thinks that they charge too much, engage in deceptive research, produce inferior products, borrow their best ideas from government-funded scientists, and buy the affections of physicians with trips and gifts. To her, the story of Nexium and drugs like it is proof that the pharmaceutical industry is "now primarily a marketing machine to sell drugs of dubious benefit."

Of course, it is also the case that Nexium is a prescription drug: every person who takes Nexium was given the drug with the approval of a doctor—and doctors are professionals who ought to know that there are many cheaper ways to treat heartburn. If the patient was coming in for the first time, the doctor could have prescribed what's known as an H2 antagonist, such as a generic version of Tagamet (cimetidine), which works perfectly well for many people and costs only about twenty-eight dollars a month. If the patient wasn't responding to Tagamet, the

The patient's insurance company could easily have stepped in as well. It could have picked up the tab for Nexium only if the patient had first tried generic Tagamet. Or it could have discouraged Nexium use, by requiring anyone who wanted the drug to pay the difference between it and generic omeprazole. Both the physician and the insurance company, meanwhile, could have sent the patient to any drugstore in America, where he or she would have found, next to the Maalox and the Pepcid, a package of over-the-counter Prilosec. O.T.C. Prilosec is identical to prescription Prilosec and effectively equivalent to prescription Nexium, and it costs only twenty dollars a month.

Throughout the current debate over prescription-drug costs—as seniors have gone on drug-buying bus trips to Canada, as state Medicaid programs and employers have become increasingly angry over rising health-care costs, and as John Kerry has made reining in the pharmaceutical industry a central theme of his Presidential campaign—the common assumption has been that the rise of drugs like Nexium is entirely the fault of the pharmaceutical industry. Is it? If doctors routinely prescribe drugs like Nexium and insurers routinely pay for them, after all, there is surely more than one culprit in the prescription-drug mess.

The problem with the way we think about prescription drugs begins with a basic misunderstanding about drug prices. The editorial board of the *Times* has pronounced them much too high; Marcia Angell calls them "intolerable." The perception that the drug industry is profiteering at the expense of the American consumer has given pharmaceutical firms a reputation on a par with that of cigarette manufacturers.

In fact, the complaint is only half true. The "intolerable" prices that Angell writes about are confined to the brand-name sector of the American drug marketplace. As the economists Patricia Danzon and Michael Furukawa recently pointed out in the journal *Health Affairs,* drugs still under patent protection are anywhere from twenty-five to forty per cent more expensive in the United States than in places like England, France, and Canada. Generic drugs are another story. Because there are so many companies in the United States that step in to make drugs once their patents expire, and because the price competition among those firms is so fierce, generic drugs here are among the cheapest in the world. And, according to Danzon and Furukawa's analysis, when prescription drugs are converted to over-the-counter status no other country even comes close to having prices as low as the United States.

It is not accurate to say, then, that the United States has higher prescription-drug prices than other countries. It is accurate to say only that the United States has a different pricing system from that of other countries. Americans pay more for drugs when they first come out and less as the drugs get older, while the rest of the world pays less in the beginning and more later. Whose pricing system is cheaper? It depends. If you are taking Mevacor for your cholesterol, the 20-

generic Mevacor (lovastatin) is about a dollar a pill in Canada and as low as sixty-five cents a pill in the United States. Of course, not every drug comes in a generic version. But so many important drugs have gone off-patent recently that the rate of increase in drug spending in the United States has fallen sharply for the past four years. And so many other drugs are going to go off-patent in the next few years—including the top-selling drug in this country, the anti-cholesterol medication Lipitor—that many Americans who now pay more for their drugs than their counterparts in other Western countries could soon be paying less.

The second misconception about prices has to do with their importance in driving up over-all drug costs. In one three-year period in the mid-nineteen-nineties, for example, the amount of money spent in the United States on asthma medication increased by almost a hundred per cent. But none of that was due to an increase in the price of asthma drugs. It was largely the result of an increase in the *prevalence* of usage—that is, in the number of people who were given a diagnosis of the disease and who then bought drugs to treat it. Part of that hundred-per-cent increase was also the result of a change in what's known as the *intensity* of drug use: in the mid-nineties, doctors were becoming far more aggressive in their attempts to prevent asthma attacks, and in those three years people with asthma went from filling about nine prescriptions a year to filling fourteen prescriptions a year. Last year, asthma costs jumped again, by twenty-six per cent, and price inflation played a role. But, once again, the big factor was prevalence. And this time around there was also a change in what's called the therapeutic mix; in an attempt to fight the disease more effectively, physicians are switching many of their patients to newer, better, and more expensive drugs, like Merck's Singulair.

Asthma is not an isolated case. In 2003, the amount that Americans spent on cholesterol-lowering drugs rose 23.8 per cent, and similar increases are forecast for the next few years. Why the increase? Well, the baby boomers are aging, and so are at greater risk for heart attacks. The incidence of obesity is increasing. In 2002, the National Institutes of Health lowered the thresholds for when people with high cholesterol ought to start taking drugs like Lipitor and Mevacor. In combination, those factors are having an enormous impact on both the prevalence and the intensity of cholesterol treatment. All told, prescription-drug spending in the United States rose 9.1 per cent last year. Only three of those percentage points were due to price increases, however, which means that inflation was about the same in the drug sector as it was in the over-all economy. Angell's book and almost every other account of the prescription-drug crisis take it for granted that cost increases are evidence of how we've been cheated by the industry. In fact, drug expenditures are rising rapidly in the United States not so much because we're being charged more for prescription drugs but because more people are taking more medications in more expensive combinations. It's not price that matters; it's volume.

This is a critical fact, and it ought to fundamentally change the way we think about the problem of drug costs. Last year, hospital expenditures rose by the same amount as drug expenditures—nine per cent. Yet almost all of that (eight percentage points) was due to inflation. That's something to be upset about: when it comes to hospital services, we're spending more and getting less. When it comes to drugs, though, we're spending more and we're getting more, and that makes the question of how we ought to respond to rising drug costs a little more ambiguous.

Take CareSource, a nonprofit group that administers Medicaid for close to four hundred thousand patients in Ohio and Michigan. CareSource runs a tightly managed pharmacy program and substitutes generics for brand-name drugs whenever possible. Nonetheless, the group's pharmacy managers are forecasting at least ten-per-cent increases in their prescription-drug spending in the upcoming year. The voters of Ohio and Michigan can hardly be happy with that news. Then again, it's not as if that money were being wasted.

The drug that CareSource spends more money on than any other is Singulair, Merck's new asthma pill. That's because Medicaid covers a lot of young, lowerincome families, where asthma is epidemic and Singulair is a highly effective drug. Isn't the point of having a Medicaid program to give the poor and the ailing a chance to live a healthy life? This year, too, the number of patients covered by CareSource who are either blind or disabled or have received a diagnosis of aids grew from fifteen to eighteen per cent. The treatment of aids is one of the pharmaceutical industry's great success stories: drugs are now available that can turn what was once a death sentence into a manageable chronic disease. The evidence suggests, furthermore, that aggressively treating diseases like aids and asthma saves money in the long term by preventing far more expensive hospital visits. But there is no way to treat these diseases in the short term—and make sick people healthy—without spending more on drugs.

The economist J. D. Klienke points out that if all physicians followed the treatment guidelines laid down by the National Institutes of Health the number of Americans being treated for hypertension would rise from twenty million to forty-three million, the use of asthma medication would increase somewhere between twofold and tenfold, and the number of Americans on one of the so-called "statin" class of cholesterol-lowering medications would increase by at least a factor of ten. By these measures, it doesn't seem that we are spending too much on prescription drugs. If the federal government's own medical researchers are to be believed, we're spending too little.

The fact that volume matters more than price also means that the emphasis of the prescription-drug debate is all wrong. We've been focussed on the drug manufacturers. But decisions about prevalence, therapeutic mix, and intensity aren't made by the producers of

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