Bargain No More

The maddening costs of generic medications.

BY JIM INCOLLINGO, CORRESPONDING EDITOR

Just as US citizens recognize death, taxes, and presbyopia as inevitable, they are largely resigned to the fact that prices will rise for most of the goods and services on which modern lives depend. The technical rationale may be lost in the haze of a long-ago economics class, but they nevertheless accept a measure of price inflation as a staple of a capitalist economic reality. As long as prices do not rise too often or too high, most people manage with minor grumbling, and the system grinds onward.

When that expectation of relative reasonableness is dashed, however, high anxiety can ensue. If a trip to the pharmacy reveals that the bargain price of a long-used, effective medication has suddenly spiked by 500%, 600%—even 1,000%—a patient may be forgiven for reeling.

Such tremors have been resonating through the health care system for more than 2 years, and the complaints are building. Anxious patients who cannot afford their medications sometimes go without, and frustrated doctors wonder why these patients are not healing as expected. Time spent negotiating with pharmacists by phone has multiplied, yet this is time most physicians cannot spare. Pharmacists themselves are struggling to cope with insurance reimbursement rates that lag well behind rising prices.

Left unchecked, this out-of-balance market could have dire consequences: lower compliance, increased treatment times and costs, and poor outcomes, to name a few. Duty bound to head off such adverse events, physicians are resorting to stopgap workarounds to ensure that their patients are properly medicated, even if the practice incurs an extra cost.

Why have prices gone haywire? Most observers point to one or more of the following: increased demand, decreased supply, evolving insurance plans and governmental regulation, and corporate greed or business savvy.

UP, UP, AND AWAY

Prices for a range of drugs have jumped recently, but certain generic medications—traditionally the "bargain brands" of the drug industry and 86% of all prescriptions filled[1]—are among the worst offenders. For example, the price of generic digoxin, an anti-arrhythmic drug made by Lannett, rose nearly 800% in 2013.[2] The company's stock price rose 500% during the same period.[3] (This year has been less rosy for the company, having received a subpoena from the Attorney General of Connecticut as part of an investigation of possible antitrust law violations over the marketing of digoxin.[3])

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Rising along with the price of nearly 30 other medications highlighted in a December 2013 survey by the National Community Pharmacists Association, the price of Pfizer's antibiotic doxycycline jumped almost 1,000% last year. The survey results were sufficiently alarming to prompt a letter from the organization's CEO B. Douglas Hoey to the Senate Health Education Labor & Pensions Committee and the US House Energy and Commerce Committee in which Mr. Hoey requested congressional hearings on the matter. To date, none has transpired.

For ophthalmologists specifically, the problem has come largely from price increases for perioperative medications. Steven Dell, MD, is chief medical editor of *Cataract & Refractive Surgery Today*. In his practice in Austin, Dr. Dell has been dealing with this problem directly. "The thing that has most captured the attention of ophthalmologists in particular has been the increase in the price of our generic topical steroids," he observes. "Right now, the price of generic prednisolone acetate is not that different than the price of branded Pred Forte [Allergan]." He adds, "That's a bizarre turn, considering

the generic [prednisolone] acetate was selling for much, much less a year or 2 ago."

Price is just one factor in doctors' prescribing decisions. Another is that not all drugs are equal. Despite insurance carriers' position that generic medications are equivalent to the branded drugs on which they are based, eye surgeons know, perhaps better than other specialists, that is not always the case. Unlike oral medications that are buffered by the digestive system or injectables that are buffered by the liver, eye drops are applied directly to the target organ. As such, the eye is particularly sensitive to variations in carrier media and formulation consistency not normally considered significant with medicines administered by other routes.

"One of the problems is that there are quite a few different companies that make certain drugs," explains New York-based surgeon Marguerite McDonald. "There are patients who are well controlled on one of those generic equivalents, but their condition goes out of control if they get it from a different generic company."

Across the country in Orange County, California, refractive surgeon John Hovanesian boils it down: "The conflict between cost and product consistency is the problem we face. Patients nowadays are increasingly getting a less-consistent product but paying close to the same premium price for a generic."

Paying more for less is never pleasant, but being priced out of the drug market altogether can amount to a personal crisis. Repeated over many thousands of patients, it begins to look like a crisis of public health. Doctors and patients are galled by the feeling that the carpet of reliably accessible quality medications on which the body of modern medicine stands has been abruptly yanked away.

Says Dr. Dell, "It's clear we've made great strides in reducing things like postoperative corneal edema and certainly retinal cystoid macular edema, but those things have been reduced through the use of effective topical medications. There's a huge debate about whether the efficacy of generics is the same as branded drugs, but what we're talking about here are people who are failing to even get the generic drug."

IT IS NOT JUST THE MONEY

For patients, the price spikes are made sharper still by the trend toward high-deductible, low-premium health insurance plans that began after the passage of the Patient Protection and Affordable Care Act (ACA) in 2010. With reforms such as the opening of local health insurance exchanges to foster price competition as well as a mandated base level of coverage that includes prescription medications, the ACA has resulted in millions of newly insured health care consumers.

However, the competition among insurers to snap up these new customers has been fought largely over the size of monthly premium payments—a knowable, certain expense for the purchaser. To compensate for revenue lost due to slashed premiums, insurers raised deductibles and restructured their plans accordingly. Customers with these high-deductible policies must pay all drug costs out of pocket until they meet the deductible limit, which typically only happens if they fall ill or suffer an injury and need medication. Plans with a low monthly payment may seem preferable, but if policyholders' good luck runs dry, they find themselves in a pharmacy staring at sky-high price tags for prescription medicine. What happens next is sadly predictable.

Carlos Buznego, MD, has been studying pharmaceutical price spikes at the socioeconomic level, but he encounters them firsthand in his Miami practice. "Just today, a patient called to say she showed up at the pharmacy and was told that her prescriptions would cost $500," he relates. "This is not uncommon, and these patients might have a significant deductible on top of that, so with doctors' and facility fees for the surgery, that large bill for the pharmacy amounts to sticker shock for the patients."

If an unmet deductible is not the problem, some permutation of the insurance plan's formulary may cause headaches (sometimes literally). A formulary may mandate certain branded or generic drugs to the exclusion of others. Physicians tend to learn of these stipulations after the fact, often from a distraught phone call from the patient or pharmacist. Dr. Buznego explained, "If we normally prescribe brand X antibiotic, brand X steroid, and brand X NSAID [nonsteroidal antiinflammatory drug], it turns out that, on that plan, they may not be covered for brand X but for brand Y, or they may be covered for a generic," he says. "Using that example, there really could be nine different options or permutations of what the patient might be on."

For physicians and their staff, keeping track of and knowing the differences have been getting increasingly difficult. According to Dr. Buznego, resolving the aforementioned problems "involves additional phone calls to the physician and the physician's staff, and they're busy in clinic, then have a whole bunch of call back messages. This raises issues for the staff, pharmacy, physician, and patients."

"My staff [members] are spending a lot of time on this," William Trattler, MD, at the Center for Excellence in Eye Care in Miami, concurs. "They get callbacks saying, 'These medications cost too much. What are the alterna-

tives? What can we do?' There's not always a solution."

Too frequently, according to Dr. Buznego, "It becomes a really mixed-up situation when what we prescribed is not what the patient is taking. There's a big mishmash of what the patients are on versus what we prescribed for them, and there's a whole lot of confusion from the patient's point of view."

Dr. McDonald worries that "the next phase may be a situation where the patient comes back a week after surgery with a bag full of stuff you've never seen, you never approved, [and] you never even knew they were on."

Vexing as this confusion can be, skyrocketing prices force physicians to contend with a more worrisome eventuality: patients "re- or deprescribing" their medications, that is, reducing the dosages or simply not filling prescriptions. Worse still, Dr. Buznego has found that patients are rarely forthcoming about such behavior, because they are embarrassed about not being able to afford medication or worried about disappointing their physicians.

Dr. Dell acknowledges the weak link in the system. "We can do really phenomenal surgery, we can put in these really advanced-technology IOLs, we can use magnificent intraoperative technology and techniques, and a lot of that can be undone by patients' simply not filling their prescriptions."

Ultimately, the opacity built into the pharmaceutical pricing and reimbursement systems leads to widespread uncertainty, inefficiency, and real costs for patients, physicians, and pharmacists. Finding out the actual out-of-pocket price of a medication is difficult until the point of sale. Prescription coverage plans seem to have institutionalized cost ignorance for doctors, pharmacists, and patients alike.

Dr. Trattler expresses frustration at not being able to "write a prescription to any patient with any context—any acknowledgement—as to how they're going to pay for their prescription. So, whatever drug I prescribe, I don't know what their insurance coverage will be, and I don't know how much the markup may be at one pharmacy versus another. There could be major differences in the patient's out-of-pocket cost for the same product. If you don't know if the cost is going to be $10 or $100, it's very difficult to prepare the patient."

WHY IS THIS HAPPENING NOW?

Analysis

It is axiomatic that corporate spokespeople have little interest in speaking unvarnished truths about their corporation's decision-making process. When asked by journalists about rising prices, generic drug manufacturers have pointed to the "value" of their medicines, the need to provide incentives for ongoing investment in research and development, and factors such as development risk, the ever-increasing cost of doing business, and "market forces." To get at the truth requires research and sober analysis.

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Dr. Buznego has been thinking about fluctuating prices in the pharmaceutical market for months. Before an audience of colleagues at the American-European Congress of Ophthalmic Surgery Summer Symposium in July 2014, he presented the results of his analysis of the underlying reasons for rising generic drug prices.[4] Ultimately, he says, it amounts to demand's outstripping supply via proliferating pathways: industry consolidation's reducing the number of manufacturers, the ACA's increasing the number of prescription drug buyers, laws mandating the use of generics for health care entitlements, and insurance and pharmacy company policies favoring generics for profitability.

Fewer Manufacturers

The wave of pharmaceutical industry mergers and acquisitions continues to wash over health care consumers and providers alike, and its net effect is stark: fewer drug manufacturers making fewer drugs. As Dr. Trattler notes, "This is the United States, and companies are built for profit." Apart from taxes and regulation, competition is the chief limit on profits for desirable commodities such as health care services. When competition thins out, companies are free to pursue profits without fear that their sales prices will be undercut. Fewer manufacturers can also mean less available product and occasional bona fide drug shortages. Likewise, according to Dr. Buznego, "many generic makers have narrowed their range of production and oftentimes are discontinuing certain medications with small profit margins to concentrate their efforts on products with larger profit margins. That's left many products with fewer producers and pushed-up prices."

In the case of generic prednisolone acetate ophthalmic suspension, there are currently only two producers in the

United States. One is Sandoz, a subsidiary of Novartis, which also owns Alcon, and Pacific Pharma, owned by Allergan. When Sandoz increased its price for prednisolone acetate, Allergan followed suit. In a May 7 earnings teleconference with industry analysts, CEO David E. I. Pyott reported that Allergan "increased our prices of the generic to parity with Sandoz as well as increasing the price for branded Pred Forte by 80%."

More Prescription Drug Consumers

The ACA has brought millions of new consumers into the prescription drug market, resulting in surging demand for these medicines. Dr. Buznego comments, "More people have insurance, and so more people are seeking care and more getting prescription [medications]."

Generics: the Law

Many states (and even the federal government) now have mandatory substitution laws. Enacted during the past 2 decades during the golden age of cheap generics, these laws apply to prescription drug coverage for public employees and pensioners and those on public assistance. They require a generic substitution for a branded drug every time such a generic is available. Even when a physician writes a prescription specifically for the branded drug, Dr. Buznego explains, "If there's a generic substitute, that's the drug that will be filled." Needless to say, those who profit from the sale of generic drugs do not oppose these laws.

Policy

The tiered pricing in many managed care plans offers pharmacies higher profits for using generics, so pharmacists are often eager to suggest generics to cost-conscious patients. In Dr. Hovanesian's view, this has "given [an] unfair advantage to generics." He continues, "We can prescribe a drug, do everything in our power to say that we feel it is medically in the best interest of the patient and have no vested interest in that product, and still have it substituted. … It's a broken system that allows that."

The profit motive can also wear directly on pharmacists' professional integrity. If it wears thin enough, a reasonable suggestion to save money with a generic substitute can morph into bad-mouthing the branded drug that was prescribed or the doctor who prescribed it. In such cases, patients are left worried and confused.

While encouraging the sale of generics by pharmacies, insurance plans mandate that their policyholders use generics and often will not include branded medications in their formularies. According to Dr. McDonald, "The generic companies have a bit of a captive audience now. They know that their drug is the one that'll be dispensed, so they've got a lock on the market, and I think they feel the freedom to increase their prices."

FOREIGN ENTANGLEMENTS

Also influencing the pharmaceutical market are regulatory actions taken against substandard drug manufacturers around the globe. Ironically, when they first came on the scene in the early part of this century, Indian, Chinese, and other foreign pharmaceutical manufacturers drove competition up and prices down to a base of affordability that led to today's great demand for generics.

Unfortunately, along with the much-reduced costs of production available overseas came the possibility of much-reduced regulation and oversight. As a result, unscrupulous, incapable, or simply noncompliant manufacturers have been caught allowing impurities and other intolerable problems into the distribution chain. When found to be in violation of FDA standards, several facilities shut down. The resultant reduction in overall supply has implications for price. Higher prices should attract new manufacturers to rush in to fill the void, but they will face a long wait before their applications are approved, because the FDA is currently processing a backlog of Abbreviated New Drug Applications for generic medications.

A straightforward analysis of the supply-and-demand factors yields a plausible result, as laid out clearly by Dr. Buznego and others. However, a macroeconomic analysis based on publicly available information may miss factors invisible to public scrutiny. Despite accepting the macroanalysis, some observers maintain that prices do not rise by hundreds of percentage points overnight without extraordinary activity, legal or otherwise, hatched in the boardrooms of pharmaceutical empires across the globe. Such opinions may be based more on intuition and experience than on empirical evidence. Cary Silverman, MD, of East Hanover, New Jersey, says bluntly, "I think there's price gouging. I really do. There's no reason why prednisolone acetate should be $80 a bottle. It's crazy."

AN INDUSTRY INSIDER, THE ACA, AND UNINTENDED CONSEQUENCES

Getting a pharmaceutical industry insider to go on the record with an honest appraisal of the reasons for wildly rising prices is unlikely. For something other than the public relations bluster, an off-the-record source was essential for this article.

The industry insider who spoke with *CRST* on condition of anonymity has been working in the ophthalmo-

logical pharmaceutical and device industry for many years. He blames the recent price surges largely on a business calculation as a result of the ACA's implementation costs and the looming prescription drug price controls created by the law. While not denying any of the other broad factors at play, he thinks the main problem is that drug makers jacked up prices in advance of coming restrictions. At the same time, patients began moving away from high-premium plans and toward high-deductible plans.

The response of some manufacturers of generic drugs to the ACA's limitations on costs and profit has been nakedly capitalistic. Says the industry insider, "The reality is that they still have to answer to shareholders, and they still have to show profits. Where you're seeing skyrocketing generic prices this year is probably a result of their analyses of upcoming parts of the bill." He believes that "knowing that price controls were coming, generic manufacturers chose what would have been a long-term price increase over 5 to 10 years, and they took it all in 1 year, not knowing if they were going to be able to do so the following year and be stuck. So, that's where you see for a number of manufacturers across the board, not just ophthalmology, but every specialty in the United States, generic prices have skyrocketed year after year, and it's an unintended consequence of the ACA."

The other unintended consequence, he says, is that "insurance providers are having to shift costs at an even more accelerated rate than before onto employers and patients. The way they've done it is that they figure that people can't afford the higher premiums per se, so they keep premiums the same but put people in a high-deductible plan. Now, instead of not having a deductible, you now have to pay through $3,000 or more depending on the plan, and you have to pay everything 100% cash until you reach that out-of-pocket limit. Only then does your insurance do anything for you. The average single patient is now at around an annual $3,000 deductible." That brings the story back to a patient in a pharmacy who is holding a prescription he or she cannot afford to fill. As the industry insider puts it, at that point, "your insurance doesn't mean [anything]. You gotta pay 100% cash for the drug."

USE THE BRAND!

Eschewing generics in favor of branded drugs has helped in some cases, especially with the proliferation of discount programs and coupons from manufacturers. In addition to rough price parity with generics due to the markdowns, the branded drugs are also free of the

potential efficacy and tolerability problems of generics. "Why do I use branded medications?" Dr. Buznego asks rhetorically. "Because they're comfortable, they're used once or twice daily, and they don't leave the patient feeling uncomfortable with their eye all gooped up."

The industry insider is even more bullish. "I think branded drugs are going to come back into vogue," he says. "In a lot of cases now, branded drugs are cheaper than generics this year, and manufacturers offer coupon cards, discounts, and rebates that make branded drugs very affordable. If you're lucky enough to have your generic drugs covered, they can cost a $10 or $20 [copayment], and as a result of the ACA, people are not reimbursed for generic [copayments] anymore. They're having to pay cash for their drugs."

"On the nonsteroidal side," Dr. Dell advises, "the importance of branded drugs is pretty significant, but even a generic is better than nothing."

Better still for patients is a branded drug given away. Free samples given to physicians have made a real difference to patients on the margins or those caught somewhere without adequate coverage. Even so, Dr. Buznego finds that "giving free samples is often a stopgap measure to get the patient over a hump, but it is probably not a long-term or widespread solution to the problem."

"If people really can't afford it, we tell them to come in and pick up some samples, but that really doesn't cut it as a true solution," Dr. Silverman agrees.

WHAT IS REALLY NECESSARY?

Are perisurgical drops necessary? Maybe not, says Dr. Buznego. "All of these issues surrounding the difficulty of medications, confusion and cost, is getting a whole lot of doctors more interested in the possibilities of surgery without drops," he explains. "There's some movement by a few companies to go into that space, but they're facing typical FDA new-drug issues. Some doctors are trying to solve the problem through compounded medications, which may not be FDA approved for these indications, but the move toward compounding is being pushed back by state and federal regulation that's come about due to recent headline disasters with compounded medications."

Dr. Trattler is in the vanguard of dropless advocates, and he is looking forward to clinical use of the fixed combination of an antibiotic and anti-inflammatory drug, TriMoxi (Imprimis Pharmaceuticals). "TriMoxi is a medication that we instill inside the eye during cataract surgery," he says. "The goal of it is to reduce or eliminate the need for pre- and postoperative medications in and around cataract surgery." If it works, a lot of prednisolone acetate prescriptions may be moot.

Dr. Dell agrees that, if the price "problem becomes more and more acute, it will drive more and more surgeons to look at nontraditional methods of delivering pharmaceuticals [postoperatively], and that might be ultimately detrimental to the market share of the manufacturers who create these drugs."

EDUCATION AND HOPE

Of all the responses to the generics price crisis, "the most effective tool we have for coping with this," Dr. Hovanesian advises, "is physicians' educating patients."

Of course, education requires a free flow of information, and that would mean adding some much-needed transparency to the prescription pharmaceutical pricing and insurance coverage systems. "I'd like complete visibility of the costs of the medication," Dr. Trattler says, "so that I knew how much the patient was paying. I wish there was a little app or website that could provide immediate details of the patient's out-of-pocket costs at any of the local pharmacies for a particular medication, because currently, I have no idea."

In lieu of that "little app" that would lay bare the hidden truth, there remains some hope.

"The outrageous prices for generics are not a new normal, because these price rises are unsustainable over the long term," says the industry insider. "I don't think you're going to see big price increases for generics annualized. I think the big jumps in prices this year were because, in following years, they will likely have ceilings on the prices, so they took the profits ahead of the uncertainty."

Relief may also come from a tidal change in the same market forces responsible for some of the original price upswing. Dr. Hovanesian says, "Market forces are going to intervene at some point as more generic makers come into the market. Competition will drive prices down." He warns, however, that "when things go up in price, whether it's wine or cars or generic drugs, they rarely come back down to the same level they once were. I fear that, even if there is more competition that comes into the market, it's going to mean that all of us are paying more for generic drugs." ■

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