The Struggle to Contain Drug Price Increases

JOHN MORRISSEY

Medical price inflation is a fact of life, and price hikes for medications, vaccines and other pharmaceutical therapies that cure or lessen ill health are all part of it. But prices of many drugs that trudged along the inflation curve for decades now are shooting skyward. New breakthroughs that thwart serious illnesses are going to market at prices that also break the bank. Generic versions that should be a brake on prices are delayed or don't get made at all — and if they do, sometimes they aren't much cheaper than the brand-name drugs they copy.

"We have seen price increases that have far outpaced inflation, and certainly existing drugs today, not just the new ones entering the market," said Craig Frost, system vice president of pharmacy operations at Catholic Health Initiatives, Englewood, Colorado.

Insulin that has treated diabetes for 90 years shot up during the past decade from $88 a vial to $307, with no change in product or use to explain that jump, said Richard Bankowitz, MD, chief medical officer of America's Health Insurance Plans (AHIP), Washington, D.C. For new drugs, the price at the outset runs six figures or more for a course of treatment.

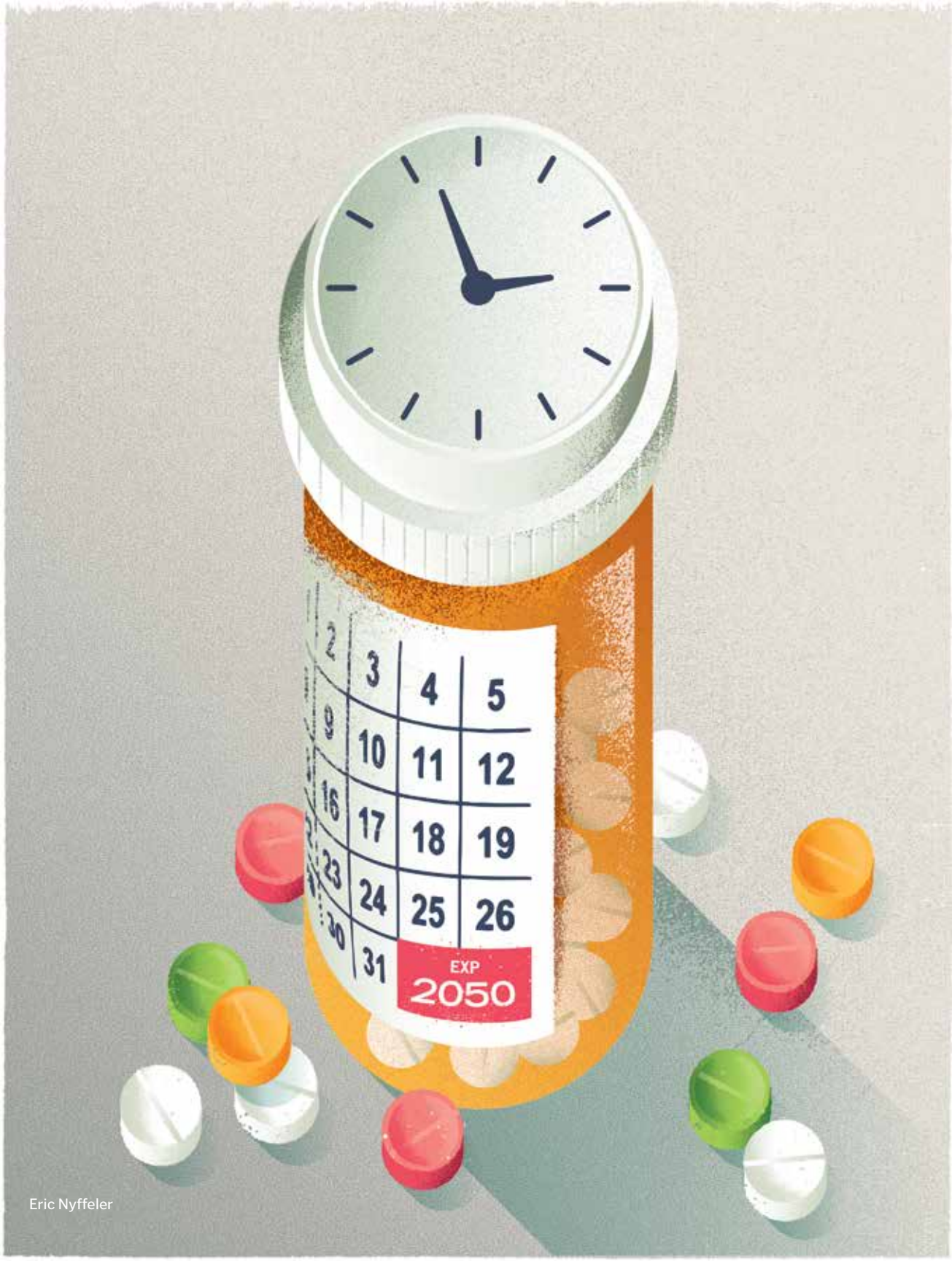
"What we're facing now are launch prices of $750,000 to $1 million, in some cases, and there's no clear reason for why they're priced that way," Bankowitz said. "We're told that we need these extremely high launch prices to justify the investment in R&D, yet no one really knows what that investment is."

The United States has it worse than the rest of the world, observers say, for a market basket of reasons including patent and regulatory issues, insurance coverage and congressional decisions going back more than a decade. Prices are a function of what manufacturers think they can get, said John Rother, executive director of the Campaign for Sustainable Rx Pricing, Washington, D.C. And with health insurance, "manufacturers think they can keep raising prices and people won't object. I think maybe that's starting to change now."

The federal government and prominent health systems have begun to push back against some of the reasons why pharmaceuticals have been able to operate unchecked during the past decade, but any impact on prices will be years away. Meanwhile, the cost of drugs relative to other health care services continues its rise.

AHIP periodically breaks out the expenses that each insurance premium dollar supports, and 2017 was the first time the prescription drugs category was reported to be the highest category of expense. At 22.1 cents of the insurance premium dollar, it edged out physician services (22 cents), outpatient services (19.8 cents) and inpatient services (15.8 cents). Compare that to 2008, when drug prices accounted for 14 cents and physician services took 33 cents.

A long-standing driver of propped-up prices



Eric Nyffeler

— the 20-year patent for new pharmaceuticals approved by the Food and Drug Administration — along with the rise of additional patenting tactics and the full flex of market power have combined to spur high initial prices of drugs, extended and often indefinite protection of those high prices and steadily or sharply rising prices for drugs years or decades after their patent period ends.

PATENTS AND MARKET EXCLUSIVITY

Manufacturers of branded products take advantage of market exclusivity to "often price the drug at whatever they want," said Bankowitz. "So they use the monopoly power to introduce drugs with extremely high launch prices. And they also introduce year-after-year price increases to existing drugs. This has resulted in an enormous strain on the health care system."

The 20-year run of a pharmaceutical patent starts when the unique product is presented to the FDA for approval via a new-drug application. That triggers a process of clinical trials to test the compound on animals and then humans to determine that it's safe and does what is claimed. The application can take five to 10 years to reach approval, which shortens the patent period by that amount of time.

Drugmakers argue that inventing drugs and developing the processes to make and deliver them is a lengthy, risky and expensive proposition and that the approval process adds significant extra time and expense. An oft-quoted study done at Tufts University tallied the costs and set the typical expense for one new drug at $2.6 billion.[1]

Pharmaceutical companies contend that the ticking clock on the patent means they have to recover those costs by charging what they do for the branded drugs while they can. That's the standard argument to justify the prices, but to health care opinion-makers, it's a hypothetical math problem that doesn't show the work.

The specific costs sunk into the development of any particular brand-name drug are not disclosed to check the basis of setting a price that reflects the research, development and application process, said Rother. This lack of transparency keeps the health care industry and advocates for patients in the dark.

The length of time during which a drug enjoys its monopoly is no longer predictably as long as the original patent. A tool chest of legal, regulatory and marketing devices is helping pharmaceutical makers tinker with and extend their drugs' exclusive status on the market and keep competition away. They include techniques such as "evergreening," "product-hopping," withholding product samples to forestall generic competition, paying competitors to delay getting into the market and creating patent "estates," that is, portfolios of patents.

TACTICAL TOOLS

Tweaks to older drugs can make them "new" under FDA provisions. "Drug manufacturers will make small changes to their approved drugs and then attempt to patent those changes, or gain additional market exclusivity in order to keep competition at bay for as long as possible," said Amy Kelbick, senior legislative representative on the federal health and family team of AARP, the group representing people 50 years and older. That's the basis of "evergreening."

A related tactic, "product hopping," is when a manufacturer withdraws the original product and replaces it with a slightly modified version — usually delivered differently, such as a longer-release preparation — which picks up an additional period of exclusivity.

Exclusivity is the term for exclusive marketing rights granted by the FDA. They can run concurrently with a patent, but also they can be granted additionally as an incentive to produce certain innovations, such as drugs that help a small population with a rare disease, or certain pediatric uses. Exclusivity can last from three months up to seven years, depending on the type.

The Orphan Drug Act of 1983 is an example of abusing a well-intended law, said Bankowitz. Meant to spur development of drugs for diseases affecting 200,000 or fewer people, which would not otherwise attract commercial interest, it instead has been used to carve out a small population for special treatment within a much larger market opportunity for a drug.

"The way the law has been written, once that exclusivity has been granted, it extends to all of the indications," Bankowitz said.

For example, the rheumatoid arthritis drug Humira has been "repurposed" as an orphan drug twice since its launch in 2002. In 2008, it gained seven-year orphan status for juvenile arthritis in patients over 4 years old. In 2014, it received another orphan designation, this time for patients 2 years to 4 years old.

"In a case like Humira, there's a very small amount of patients between the ages of 2 and 4," Bankowitz said. "But that doesn't stop them from extending exclusivity and raising the price for everybody who receives Humira. And that's not the way the law was intended."

Seven of the 10 top-selling drugs have at least one orphan drug indication, according to AHIP.

BRAND PROTECTIONS

The end of patent protection or exclusivity marks the beginning of potential generic competition — but only if generic drug manufacturers can get access to the branded drug, launch it on the market and get it onto drug formularies. They face obstacles at every phase.

A crucial first step is to get samples from the patent owner to do bio-equivalence testing and other measures to show the FDA that the generic product meets required standards. Drugs often are unsafe if not reliably administered by trained professionals, or if they are given to people who aren't candidates for the drug. Since 2007, the FDA has required some drugs to undergo risk and evaluation mitigation strategies (REMS).

"In some cases, this includes restrictions on how these drugs can be distributed," Bankowitz explained. "The brand manufacturers have taken advantage of this. They claim that these restrictions justify withholding the drug from generic manufacturers."

An FDA official testified before Congress in 2017 that the agency had 150 inquiries on file from generic developers whose requests for samples were refused on REMS grounds.

Another tactic is for manufacturers holding expiring patents to "pay for delay," which AHIP describes as "anti-competitive settlements with generic manufacturers that prevent generics from entering the market in a timely manner." By settling with a generic drug maker for a sum of money, "brand-name pharmaceuticals stay high, and the brand and generic share the benefits of the brand's monopoly benefits," AHIP testimony contended in a Dec. 8, 2017, statement to the Federal Trade Commission.[2]

In cases where the drugs are complicated formulations produced by living cells, called biologics, the brand is protected by what's called a patent estate, gaining a patent for nearly every aspect of that formulation and its production. A competitor might be able to reproduce the product itself, known as a biosimilar drug, but can't manufacture it because the competitor can't penetrate that patent estate, the extensive group of patents that surrounds it, said Bankowitz. A lot of those patents are introduced in the years just before exclusivity would expire, involving some production aspect, which further extends the exclusive rights.

"This goes on and on and on, and so the patent estate really creates a barrier to production of a biosimilar," Bankowitz said.

When generics do gain FDA approval, manufacturers may offer to rebate part of the cost that an insurer would otherwise pay to carry a brand-name drug in its formulary, on the condition that the payer not carry a newly introduced, less expensive generic or comparable-drug competitor, said Frost of CHI. Pharmacy benefit management companies with tremendous negotiating leverage can extract a sizable rebate that is not transparent to its customers, "so prices remain artificially high," he said.

EFFECT OF GENERICS

The FDA says nearly 80 percent of prescriptions are filled by generics, at price levels that have moderated drug expenditures nationally. But the impact of generic competition might not start with introduction of an alternative to the brand-name drug but, rather, the accumulation of generics that compete with one another. A recent study calculated that over a five-year span, prescriptions for monopoly generics increased by an average of 47 percent and as much as 73 percent, while generics with at least four competitors decreased by 29 percent to 42 percent.[3]

A lone generic or off-patent drug has a market advantage and green light to raise prices, similar to a patented brand, said Rother. That problem came into focus when Turing Pharmaceuticals, a start-up firm incorporated in Switzerland with offices in New York City, acquired the rights in 2015 to a then-62-year-old drug called Daraprim and raised the price from $13.50 to $750 per pill. The drug is prescribed to treat toxoplasmosis, a disease caused by infection from a parasite, and it can be serious for immunosuppressed people, pregnant women and their newborns. Daraprim has no competitor, and there is little chance that any would take on the FDA application burden to serve a small market, Rother said.

As diseases get more attention amid initia-

tives to prevent or closely manage the illnesses of populations, prices of associated drugs have shot up. "The three manufacturers of insulin have all raised prices in unison, step by step over the last few years," Rother noted. "That seems to be a pretty clear abuse of the system."

Large price increases in vaccines are driven in part by their inclusion as an essential health benefit, a preventive service provided with no copayment, said Bankowitz. An example is pneumonia vaccine. "Everyone should have access to it, it's a public health concern. And to use effective prevention and exploit it as a marketing tactic to raise the price is really unconscionable, " he said.

A drug named Sovaldi that treats and sometimes cures hepatitis C went on the market about five years ago at $1,000 per pill, to be taken in a treatment course that lasts three months.

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"That was what really triggered this explosion" of price increases, said Rother. "Once the rest of the industry saw that they could get away with it for this drug, then a lot of other drugs came along that were priced equally aggressively."

EXTRA VARIABLES

For physicians and their patients, the high and rising prices for drug therapies and their impact on prescribing decisions "turns the value equation upside down," said Frost. What used to be a fairly certain expected outcome for expected cost now is complicated by the extra variable of price and reimbursement.

Along with the usual consideration of side effects and toxic consequences for a particular patient, the "financial toxicity" of the medication becomes part of the decision process, because "if you can't sustain payment for a certain medication therapy, then you're not going to achieve the outcome you desire," Frost explained. "The most effective therapy is not always the most *cost*-effective therapy."

At CHI Franciscan Health based in Tacoma, Washington, pharmacists have been added to physician clinics to guide prescribers to the most cost-effective therapy choices. Drugs that pharmaceutical marketers and sales reps promote often "become front of mind" for physicians, but cost more than other options, said Timothy Lynch, division senior director of pharmacy services. "If you cannot get these patients on a therapy regimen that is sustainable, then you're at risk for readmissions, and then nonpayment for those encounters."

Passing out name-brand samples from drug reps would seem a logical response to a patient's inability to afford the drug — until the samples run out and the patient must shoulder the drug cost or stop the regimen because it is unaffordable.

CHI Franciscan is working with physicians to eliminate drug samples. That dispensing practice "starts them on higher-cost therapies when there might be a generic alternative that provides the same efficacy but at a much lower cost," said Lynch. The alternative drug may cost money up front, but increases the chance of success over time when the patient can sustain the expense. So a drug therapy that is affordable becomes a higher priority than the drug that would perform best and be the most appropriate.

"It doesn't make a lot of sense to prescribe a 'Cadillac' medication that a patient can't afford and would end them right back in the hospital," said Frost. "This patient would probably be managed better on the newer therapy, but we'll use something a little bit older rather than nothing at all. That kind of choice happens all the time."

QUICKLY TO MARKET

Advocacy groups such as AARP and the Campaign for Sustainable Rx Pricing say pharmaceutical companies should not only transparently justify prices according to research and development costs, but also be subject to rules that would make competition more effective — that is, eliminating the gaming of FDA loopholes and making sure that generic drugs are able to get to market quickly.

Those pleas bore some fruit in early January 2018, when the FDA announced steps to streamline generic drug review, reduce the gaming that can delay generic drug entry and resolve scientific and regulatory obstacles that can make it difficult to win approval of generic versions of certain complex drugs.[4]

Two weeks after the FDA announcement,

three Catholic health systems along with Utah-based Intermountain Healthcare and the U.S. Department of Veterans Affairs launched plans to develop a not-for-profit generic drug company aimed at making essential generic medications more available and affordable.[5]

The new company intends to be an FDA-approved manufacturer and jump in to produce essential generics administered in hospitals and dispensed at pharmacies, increasing the supply "rather than waiting and hoping for generic drug companies to address this need," said Anthony Tersigni, president and CEO of Ascension, the St. Louis-based Catholic system, in the statement announcing the initiative.

Richard Gilfillan, MD, CEO of Trinity Health, Livonia, Michigan, added, "There is a dangerous gap today between the demand and supply of affordable prescription drugs. If the only way to provide our communities with affordable drugs is to produce them ourselves, then that is what we will do."

SSM Health, St. Louis, also is a founding participant of the initiative. The five founding members represent more than 450 hospitals, and additional health systems are expected to join.

A spokesman for Ascension said there is no timeline for initiating a drug-making process or an estimate of when the first product will enter the market. Any such product would be years away, subject to the internal development process and FDA approval. And when it takes its position in line, there's quite a wait.

GENERIC APPLICATION BACKLOG

At the start of 2017, according to the FDA, its backlog of generic drug applications stood at 2,400, an improvement from 4,000 in 2016, but still aggravating a situation in which brand-name manufacturers are free to up their prices long past the original patent date. The FDA needs more resources, said Rother.

Rother also advocated that drug pricing be based, in part, on relative impact on health status. Even though some drugs are proven safe and effective, they don't have the effect on people that other lifesaving drugs have.

AARP's Kelbick asserted that extra market exclusivity or patent protection should be granted only "in extremely limited circumstances and only for innovations that meet an unmet medical need and substantially improve upon existing therapies."

The high cost of prescription drugs continues to be a top concern among AARP members, Kelbick said. "On average, older Americans take 4.5 medications every month, and many of them struggle to afford those costs. In addition, many of those medications are for chronic conditions, like multiple sclerosis, diabetes and heart disease, so patients must find a way to afford these medications every month. And missing or skipping doses, which many older Americans are forced to do because of the cost, only worsens their health outcomes."

The upward climb of drug prices won't level off as long as "there is no competition, there's no accountability and there's no transparency," Bankowitz said. "We want to cover innovative therapies at a price that makes sense, that gives a fair return for the R&D and the risks that the pharmaceutical manufacturer takes."

"But we don't want to see an abuse of the system," he said. "It doesn't do anyone any good if we have an innovative treatment, but nobody can afford it."

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NOTES

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