As Drug Costs Rise, Don't Count on a One-Size-Fits-All Solution

By AUSTIN FRAKT

A majority of Americans prefer greater regulation of prescription drug prices, meaning government intervention to lower them.

But don't count on a single policy to address a nuanced problem.

"All low-priced drugs are alike; all high-priced drugs are high priced in their own way," Craig Garthwaite, a health economist from Northwestern University's Kellogg School of Management, wrote with a colleague.

Outside of a few government programs — like Medicaid and the Veterans Health Administration — low-priced drugs are alike in that competition is the sole source of downward pressure on prices. When many generic versions of a brand-name drug enter the market, competition can push their prices 80 percent below the brand price, or sometimes even more.

In contrast, high-priced drugs lack competition for various reasons, "not all of which imply our goal should be to reduce prices," Mr. Garthwaite said.

Consider two drugs, Humira and Daraprim

Humira, an injectable drug from AbbVie, is a good example. It's used to treat severe rheumatoid and other forms of arthritis, plaque psoriasis and Crohn's disease. It's also the best-selling prescription drug in the world, with a nearly $40,000 annual price tag per person (even accounting for rebates).

Since its approval by the Food and Drug Administration in 2002, Humira has been protected from direct competition by patents and F.D.A.-provided market exclusivity. This government protection from competition is a source of profit intended as an incentive for innovation.

"One-size-fits-all incentives like patents and exclusivity periods may not provide the right incentive for Humira or any other drug," said Rachel Sachs, associate professor of law at Washington University in St. Louis. "We probably are under-rewarding drug innovation for some types of diseases, such as early-stage cancers requiring long clinical trials, and over-rewarding it for others."

Daraprim, currently manufactured by Vyera Pharmaceuticals (formerly Turing), treats a life-threatening parasitic infection. It was discovered in 1952. In 2015, Martin Shkreli, then Turing's chief executive, increased Daraprim's price by more than 5,000 percent, to $750 from $13.50 per pill.

Mr. Shkreli was able to do this because Daraprim lacked competition, but the reason was different than for Humira. Daraprim's chemical structure and means of manufacture may be used by other drug manufacturers to make and market a generic equivalent. The obstacles to doing so aren't governmental. They're found in the market.

If a competitor entered the market, it's likely that Vyera would drop Daraprim's price — exactly what we'd expect and want from competition. But the cost of starting production of the drug, relative to the return on that cost, may prove a deterrent.

"At a lower price level, a competitor may not be able to recoup its investment," said Dr. Aaron Kesselheim, a professor of medicine at Brigham and Women's Hospital and Harvard Medical School. "That, coupled with the small market for this drug, makes it relatively unappealing to a for-profit company."

Daraprim isn't alone. Other drugs that have lost their patents have had rapid price increases for similar reasons. The price for captopril, a drug for hypertension and heart failure, rose 2,800 percent in 2013.

The same year, the price for clomipramine, which treats depression and obsessive-compulsive disorder, increased 3,700 percent. And the antibiotic doxycycline hyclate's price jumped 2,000 to 5,000 percent (depending on formulation) in six months, from October 2013 to April 2014.

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Prescription drugs differ in how competition, or lack of it, affects their cost.

Some ideas to push down prices

The F.D.A. has already taken action to increase generic competition. A 2012 law authorized the F.D.A. to charge generic drug manufacturers user fees, and those funds enabled it to speed up generic approvals. But this doesn't address barriers in the market that keep some prices high for drugs whose patents have expired.

"We could do more through importation to respond to sudden price increases of off-patent drugs," Dr. Kesselheim said. "Manufacturers serving markets overseas might be willing to sell in the U.S. if we were to acknowledge regulatory approvals in other developed countries with high standards."

Not requiring those manufacturers to undergo approvals in the United States would reduce barriers to market entry, potentially increasing competition.

The duration of market exclusivity varies by type of drug. Until recently, the vast majority of new drugs were so-called small-molecule drugs produced through chemical processes. A manufacturer can expect to be granted about five years of market exclusivity from the F.D.A. for these kinds of drugs, though some — like those that treat rare conditions — can obtain longer exclusivity.

Some companies find elaborate ways to effectively achieve much longer periods of exclusivity. "One way is to build up a so-called thicket of patents, claiming ownership of often minor characteristics of a drug or its manufacture," Dr. Kesselheim said. "Many are trivial, but collectively they slow down competition." For example, some pertain to small changes in packaging or formulations.

When the F.D.A. treats these as "new" drugs, it can buy a company additional years of protection from competition and high prices. "More could be done to scrutinize drug patent applications and throw them out if the modifications are trivial," Dr. Kesselheim said.

Competition doesn't work well with biologic drugs

An increasing share of new drugs are biologics, which are much more complex and are regulated differently. They're made up of proteins produced by living organisms and can cost 20 times more to manufacture than small-molecule drugs.

Some of today's most expensive drugs are biologics, including Humira. The first biologic, a human formulation of insulin, was marketed in 1982. By 2016, they accounted for half of F.D.A. approvals.

Humira owes its popularity to its effectiveness. The same could be said of many other expensive biologic drugs, like Herceptin for certain kinds of breast cancer.

To encourage investment in them, biologics get longer market exclusivity — 12 years — than small-molecule drugs. As with the small-molecule drugs, the exclusivity can be extended in various ways.

But even after that, biologics are protected from competition to an extent because they are harder to duplicate than small-molecule drugs. A biosimilar — a drug intended to mimic the therapeutic effect of a specific biologic — is not like a small-molecule generic drug. A generic drug can exactly duplicate the chemical structure of the brand drug it is intended to mimic, but that's not easily achieved for biosimilars. Because they rely on living organisms, their structure and clinical performance depend on many subtleties of manufacturing.

This means biosimilars may not behave exactly like original biologics, giving those original drugs a leg up in the market.

Reflecting this, some of today's drug pricing proposals focus on biologics. A recently proposed change to Medicare would link the prices of many biologics to those in other countries, which are lower. Another proposal has been to automatically reduce prices once their market exclusivity period has expired.

Lower drug prices could lead to shortages

A final complication in addressing prices is that, for some drugs, it may not be a good way to achieve the pace of innovation we may want. Here, antibiotics offer a good example. Although we desperately need new antibiotics to combat resistant superbugs, few pharmaceutical companies are willing to invest in their development. The problem is that they would serve a market we would want to be as small as possible. Ideally, nobody would need a powerful antibiotic, and there is no price at which a manufacturer would make a product that is never purchased.

"We should not pay for antibiotics by the dose, like other drugs," said Kevin Outterson of Boston University School of Law. "Instead, buying access to new antibiotics — a Netflix model — could encourage innovation even if they're rarely used."

Policy ideas to push drug prices downward are summarized by the Drug Policy Lab at the Memorial Sloan Kettering Cancer Center, at which Peter Bach is director of the Center for Health Policy and Outcomes.

In some cases, lowering drug prices could invite shortages. "Though Daraprim's price could be lower and Vyera would still make a profit, if it was pushed too low, there could be a shortage," Dr. Bach said. "For drugs prone to shortage, it might make sense to subsidize the price."

Although there appears to be a mandate to lower drug prices, it's an issue that defies a simple solution.