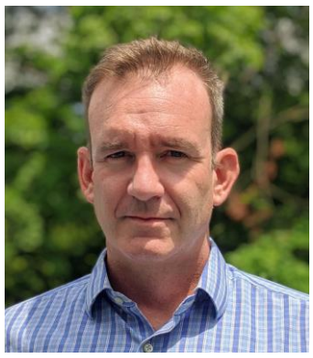
Timmerman Report

When Raising Drug Prices Helps Patients

By Chris Morrison and Peter Kolchinsky, July 23, 2020



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Sometimes there are good, patient-friendly reasons to raise drug prices. Proposed legislation that aims to eliminate price hikes on prescription drugs will have unintended consequences.

San Francisco-based Jaguar Health, for two years in a row, lost more than $30 million a year. Revenue from its only product, a diarrhea treatment for HIV patients, was only $5.8 million in 2019.

The drug works, and it addresses a real need. Market research suggests about one out of every five HIV patients suffers from diarrhea related to their antiretroviral treatment regimens, and there are more than a million HIV patients in the US.

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But the drug, crofelemer (Mytesi), wasn't being prescribed anywhere near that widely. Worse, when the drug was prescribed, insurance companies often refused to pay for it, wearing down doctors and patients with onerous paperwork and phone calls.

Jaguar couldn't go on like this forever, and had to make a decision earlier this year. It could take the drug off the market, cutting its losses. Or, it could raise the drug's price to try to get the company to profitability.

So, Jaguar raised the price, roughly three-fold from $668 for a 60-pill supply to $2,206.

Predictably, Jaguar took heat in the press, in part because the hike came after a failed attempt to gain Emergency Use Authorization from the FDA to treat COVID-19-related diarrhea (expanded use into COVID-19 patients might have allowed the company to break-even without raising the price). And Jaguar briefly caught the attention of lawmakers who might soon be considering legislation that would impose mandatory rebates from drugmakers that increase their products' prices more than inflation. Legislation under consideration by the Senate Finance Committee, the Prescription Drug Pricing Reduction Act, would penalize big price increases, like Mytesi's, especially for drugs covered under Medicare Part D.

Price hikes are routinely pilloried as attempts to wring every dollar from a vulnerable patient's wallet. But are all large price increases a form of gouging?

Jaguar's new price puts it on a path to sustainability. It lets it continue treating HIV patients who were benefitting from Mytesi and provides extra revenue that it can use to expand its patient assistance programs that provide free drug to low-income patients falling through various holes in the US safety net. With higher revenues from the few prescriptions that are covered, Jaguar now helps cover patients' out-of-pocket costs. It also funds a service that helps physicians navigate prior authorization roadblocks insurers ostensibly rely on to prevent inappropriate utilization; these end up also interfering with appropriate treatment with Mytesi.

An experienced drug marketer might have done all this from Day One, knowing just how hard insurers would push back on paying for a drug like Mytesi. But Jaguar, which sells Mytesi through its subsidiary Napo Pharmaceuticals, wasn't an experienced drug marketer. In fact, it never expected to be selling Mytesi itself, having counted on a larger partner, Salix Pharmaceuticals. But after a legal dispute in which Jaguar accused Salix of failing to adequately

commercialize Mytesi (then known as Fulyzaq), Jaguar regained its rights in 2016, inheriting a drug for a relatively small group of patients, yet being sold at a mass-market low price.

To Jaguar, the common US practice of setting artificially high prices and offering hefty rebates to insurers to remove access barriers was foreign territory. Jaguar eventually learned it needed to inflate Mytesi's list price just to allow the middlemen to extract a rebate, a sliver of which they would keep to pad their own profits.

It's not unusual for a drug to be mispriced. Nor is it rare for companies to raise prices for drugs that reach a smaller patient population than originally expected. These tweaks typically go unnoticed when price increases are in the single-digit percentage range, and the companies implementing them are larger. Any corresponding price reductions are typically hidden in negotiated rebates.

For already profitable, large companies, net price increases can preserve or boost profits. For small companies like Jaguar with only one marketable product, the ability to re-price a mispriced drug can mean the difference between surviving and going out of business.

Pricing and shortages

The Prescription Drug Pricing Reduction Act ignores other reasons to raise prices. Sometimes a higher price is necessary for a company simply to manufacture enough of it to meet demand.

Take Bacillus Calmette-Guerin (BCG), an inexpensive, hundred-year-old, live-attenuated tuberculosis vaccine made from bacteria that infect cattle. In the US where TB is rare, the vaccine is used as an immune-stimulating bladder cancer treatment.

When manufacturing problems drove Sanofi from the BCG market a few years ago, the pharmaceutical giant Merck remained as the sole manufacturer. Despite being left with a monopoly, Merck did not do what economists might expect in such a situation – it didn't raise the price, and it didn't boost its production capacity enough to serve all the US patients who had previously been getting supplied by Sanofi.

This meant that a lot of bladder cancer patients were being left in the lurch, without access to an effective drug.

Ken Frazier, CEO, Merck

During remarks at the annual BIO convention in June 2019, Merck CEO Ken Frazier acknowledged the problem, noting that Merck only supplied 28% of the US market for BCG when the other manufacturers dropped out. Merck doubled its output fairly quickly, he said, but it is now capacity constrained.

BCG isn't patented, so anyone is free to jump into the market. There isn't a strong market incentive to invest in new manufacturing capacity, in part because manufacturing of a live-attenuated virus is non-trivial.

This means Merck is all alone, the sole supplier of an old, tricky-to-make drug, and not making enough of it. If the company wanted to, it could cash in on its monopoly by doubling, tripling, quadrupling, quintupling the price. "But that's not the right thing to do," Frazier said. And yet, Merck has not sufficiently invested the necessary millions of dollars it would require to expand production to ensure that patients don't go without.

This failure is confusing and frustrating to many observers, given Merck's size and skill in the treatment of cancer.

Merck charges a high price for its newer oncology drugs, like the PD-1 inhibitor pembrolizumab (Keytruda). That monoclonal antibody drug is approved to treat several cancers, including bladder cancer in patients who do not benefit from treatment with BCG. Merck has invested in substantial manufacturing capacity for Keytruda. There is a market incentive to do so, with a

patented drug that generates $11 billion-per-year in revenue. Merck has invested to ensure that there will not be any supply shortages of this drug.

Why is Keytruda worth keeping in stock but BCG not worth it? Probably because Merck charges such different amounts for these two drugs. To patients who need BCG, it would be well worth it for Merck to charge whatever it needed to justify keeping BCG as well stocked as Keytruda.

If Merck is trying to be charitable, then it should invest in expanding BCG production. Keeping the price static while not investing in production is robbing patients of a drug that only Merck can currently provide.

But Merck is a business. It shouldn't be expected to give away its products for free, or charge less than it costs to make them. So then what if raising the price of BCG is the right thing to do?

An unlikely solution

At some price point, at some level of revenue, it would be worth Merck's time and capital to expand BCG manufacturing to make enough for every patient who needs it.

Merck should do that, starting today.

Here are two ways this could play out.

Were Merck to raise the price of BCG so steeply that it became a blockbuster on par with its newer cancer drugs, it would certainly attract unwanted attention. Elected officials, and the media, would accuse the company of price-gouging. Raising the price would also invite competitors, who could enter the market, expand the supply and eventually help drive down profit margins.

Or, Merck could raise BCG's price modestly, making it profitable enough to merit investment in high-quality, reliable production. In this scenario, Merck is unlikely to attract competitors. And while it might attract some attention for increasing its price at all, any negative publicity would be undeserved. Rather, Merck would be striking a balance between charity and gouging, protecting its brand and profitability for the long run.

Hopefully the public, media, and Congress would see this as an act of responsible stewardship of an important medical resource.

In fact, all off-patent, generic drugs should be priced in this zone: high enough to be worth making reliably and low enough that they can still be considered commodities.

Patients who can't get BCG today because of supply constraints would take either scenario. Any means of increasing production would be an improvement over the status quo. BCG is clearly priced too low. Repricing it would enable Merck and others to treat more patients with a drug that saves lives and spares patients from invasive (and expensive) surgery that often results in permanent impairment. And yet, if Merck raised BCG's price it could run afoul of proposals like the Prescription Drug Pricing Reduction Act.

For Merck, a huge company generating billions of dollars per year in profit, there is a third scenario. Pressured from all sides, Merck can afford to spend the few tens of millions necessary to expand its manufacturing supply without increasing BCG's price at all. It would probably lose money doing so. But it would be a true hero to patients while avoiding the PR headache of explaining a perfectly reasonable price hike. Were Merck to do this, it would only be because Keytruda and other branded drugs Merck sells are profitable enough to subsidize investment in BCG supply expansion.

But few companies are as large and diversified as Merck.

Jaguar, for example, couldn't afford to continue funding production of Mytesi without raising its price. It's too early to know whether Mytesi's new price and access programs that this new price

supports will save Jaguar. But the price hike gives it a chance to ensure that it can keep supplying patients who rely on the drug.

Any legislation that caps drug price increases should carve out exceptions for the Jaguars of the world facing do-or-die situations that would leave patients in the lurch if they go out of business. New legislation should account for companies that misprice their drugs because they didn't anticipate the US insurance system's ability to keep drugs from patients who need them. Commercializing a prescription drug cannot fall under the adage of "measure twice, cut once." It can take years for a company to undertake "price discovery" and for a drug to find its footing and niche in any therapeutic marketplace.

A more reasonable version of the Prescription Drug Pricing Reduction Act would delay imposition of price increase caps for several years after a drug's launch to enable companies to determine how payers will handle access. How many patients a drug might reach is a key element of price discovery. This Act would also allow manufacturers to make price adjustments that would support funding of adequate, high-quality supply as a market evolves.

Rethinking reforms

Beyond putting Jaguar out of business and keeping BCG in short supply, passing the Prescription Drug Pricing Reduction Act would have another unintended consequence. It would logically lead companies to launch new drugs at even higher prices than they otherwise might have, to make sure that they don't risk underpricing them.

If a company knows it cannot tweak its drug's price, it will err on the side of caution from the start. That means pricing high on the assumption that few patients will be allowed to get the drug (a self-fulfilling prophecy – the higher the price, the more payers push back). That would leave room to negotiate bigger rebates with payers if more patients get treated than expected. But if pricing that drug with the needed safety margin also means setting a price so high that it would trigger outrage, the safest thing might be to not develop that drug in the first place.

That would be the worst unintended consequence of all.

The Prescription Drug Pricing Reduction Act, like other bills circulating around Congress, contains an important reform that is worth preserving. It calls for lowering out-of-pocket costs for patients. Caps on price increases are merely the concession Congress wants in trade. The trade-off between increasing affordability for patients (which also makes it easier for drug companies to sell their products) and seeking value for society goes back to the Hatch-Waxman Act of 1984.

Hatch-Waxman traded an extension of the patent-protected period for branded drugs for the abbreviated generic drug approval pathway and generic interchangeability that brought about the modern era of generic drugs and patent cliffs. Later, the Affordable Care Act expanded insurance coverage to more Americans (which also made it easier for drug companies to sell their products) and established biosimilars as a new path toward affordable, off-patent biologics.

Drugs going generic is the price control we have long had and is the one we need to shore up. As the only aspect of healthcare that can go generic and drop in price, drugs are unique. When factoring in all the money losing biotech companies, the drug industry's overall profit margins are only around 10-12% – a clear sign that drugs are not systematically overpriced. That patients can't afford them is purely a function of out-of-pocket costs that insurance reforms can fix.

And so, there is indeed a grand bargain to be struck today that continues in the tradition of Hatch-Waxman and the ACA. Let's lower out-of-pocket costs for patients (all patients, not just those on Medicare). And let's make sure that once a drug's patents expire, society has a reliable, inexpensive supply, protected against both profiteering and shortages. These products should be treated as a National Strategic Resource, the way we treat medical countermeasures to combat pandemics or biological attacks.

For those situations, the US agency BARDA contracts with companies to make medicines at pre-negotiated prices. Those prices are high enough to ensure a quality supply but far lower than

what a theoretical monopolist might charge during a pandemic or attack. A similar contract with Merck to produce BCG at some reasonable margin over its cost of reliable production would provide all the BCG doses that US patients need.

Mytesi, by the way, is also complex to manufacture. Jaguar's drug is purified from the sap of a tree found in the Amazon rain forest. It reached the market in 2012 and remains the only oral medicine approved under the FDA's botanical drug product pathway. When Mytesi's patents expire, competing manufacturers would probably struggle to replicate that complex supply chain and might not bother to try, leaving Jaguar with a perpetual monopoly.

Jaguar should harvest a substantial reward for having invented the drug. But when its patents expire, a BARDA-like supply contract would allow society to get long-term value from Jaguar's invention, simulating genericization.

During the patent-protected years of a new drug's life, Congress should avoid price controls and their unintended consequences. While there will always be those who assume every price-hike is an act of gouging, it is essential that Congress not fall for that facile conclusion and certainly not adopt harmful legislation in response to it.

America needs Congress to be more sophisticated about pursuing the right reforms to bring about affordable biomedical innovation.

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