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**WHY ARE SOME GENERIC DRUGS SKYROCKETING IN PRICE?**

**Testimony of:**

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## Summary of major points

- Generic drugs are one of the central components of the health care system. The generic drug industry has a long history of producing high quality drugs at very reasonable prices, which saves patients money, promotes adherence, and improves clinical outcomes.
- Generic drugs are inexpensive because they can be reliably synthesized and packaged for pennies per pill and they are made by manufacturers that can make a profit charging closer to the unit cost of production because their development costs were low. Competition among these manufacturers leads prices to approach the unit cost of production.
- Competition among generic or multisource drug manufacturers can vanish for a number of reasons, including manufacturers' business decisions, fluctuations in market supply and demand, anticompetitive behavior from sellers or purchasers, and re-assertion of patent or market exclusivity rights.
- The first solution is greater transparency: all increases in multisource drug prices of greater than 100% should be reported to the Department of Health and Human Services, which can investigate the rationale for the increase in price and determine whether some sort of public intervention is necessary.
- The FDA Office of Generic Drugs can responsibly fast-track potential generic drug entrants into markets where high prices result from manufacturers exploiting natural monopolies, waiving the user fees to further reduce barriers to entry for potential competitors.
- The Federal Trade Commission requires increased funding to be able to intervene in the generic drug market to ensure that price changes do not stem from anticompetitive behavior.
- Interventions can also come at the government payor level. If the Medicare Part D non-interference provision was waived for multisource drugs, then the Centers for Medicare and Medicaid would be in a better position to combat exorbitant increases in drug prices.
- Over the long-term, reforms to the patent and drug market exclusivity system may be warranted to help prevent more older drugs from soaring in price.

**Chairman Sanders, Ranking Member Burr, and Members of the Subcommittee:**

My name is Aaron Kesselheim. I am an internal medicine physician, lawyer, and health policy researcher in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital in Boston and an Associate Professor of Medicine at Harvard Medical School. I lead the Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research team studies the intersections between laws and regulations and the development, utilization, and affordability of drugs. It is an honor to have the opportunity to share my thoughts with you about the rising prices of some generic drugs.

Generic drugs are one of the central components of the health care system. Generic drugs become available after the expiration of the market exclusivity period for brand-name drugs, and are the main way that many patients are able to afford the medications their doctors prescribe for them. The FDA reviews them carefully for purity and bioequivalence with the brand-name, standards which are almost always met before the drug is marketed.<sup>1</sup> Meta-analyses I have led, including one published in the Journal of the American Medical Association in 2008,<sup>2</sup> found no evidence of any clinical differences in studies comparing brand-name and generic drugs, even among the small number of special "critical dose" drugs that have their effective and toxic ranges separated by relatively small differences.

Having the same effectiveness and safety as their brand-name counterparts, generic drugs can provide reliable clinical outcomes for patients. What sets them apart from brand-name drugs is their low cost. When generic manufacturers market their versions after the end of the brand-name drug's market exclusivity period, prices can over time be reduced by as much as 80-90%. With low-cost generic drugs currently making up about 84% of all prescriptions, the cost savings related to generic drug prescribing has saved US patients over a trillion dollars in the last decade alone.<sup>3</sup> Inexpensive generic drugs translate to improved patient adherence and better patient outcomes. A recent study led by Josh Gagne in my Division showed that patients initiating a low-cost cholesterol-lowering drug had better

medication adherence and, as a result, an 8% reduction in hospitalization for acute heart disease, stroke, and death compared to patients initiating a high-cost cholesterol-lowering drug.<sup>4</sup>

Why are generic drugs inexpensive? They are inexpensive because most small molecule prescription drugs can be reliably synthesized and packaged for pennies per pill. Brand-name drugs sell for much more—recently, the \$1,000 per pill cost of sofosbuvir (Sovaldi) for hepatitis C virus has been widely debated—because they are protected by government-issued patents and various FDA rules that prevent competitors from making their own versions of the drug. The government provides limited periods of market exclusivity for brand-name drugs because innovative drug development is expensive. These monopoly periods permit the brand-name manufacturers to charge far above the unit cost of producing the pill to help compensate for the millions of dollars in research costs involved in clinical trials and other tests leading to the development of a new drug. After the market exclusivity period ends, competition is initiated by other manufacturers that do not have as high of development costs and can therefore still make a profit charging closer to the unit cost of production. Competition leads prices to decrease for these multisource drugs and approach the unit cost of production.

We take for granted that older drugs are inexpensive, but competition is the reason why they are reliably inexpensive. This competition can vanish for a number of reasons, including business decisions by manufacturers, fluctuations in the supply and demand of the market, anticompetitive behavior, and re-assertion of patent or market exclusivity rights. When any of these things happen, prices skyrocket.

First, generic drug prices can rise because of a confluence of business decisions and profit-seeking from manufacturers. Take the case of albendazole, a broad-spectrum anti-parasitic medication first marketed by corporate predecessors to GlaxoSmithKline (GSK) outside the US in 1982 and approved by the FDA in 1996. Albendazole is rarely used in the US, and the parasitic infections it treats usually only occur in poorer populations such as immigrants and refugees. Though its patents have expired, GSK remained the sole producer of the drug until the company sold its US marketing

rights to Amedra Pharmaceuticals, a small private firm, in October 2010. In 2011, Teva, the producer of the only potential therapeutically interchangeable competitor mebendazole (Vermox), discontinued production of its product for non-safety related reasons. In last week's New England Journal of Medicine, my co-authors and I reported that between late 2010 and 2013, the listed Average Wholesale Price for US patients rose from about \$6 to over \$119 per typical daily dose. For a routine 6-month course of therapy, an uninsured patient therefore faces tens of thousands of dollars in costs. Insurance payors were also strongly affected, particularly Medicaid, the federal- and state-funded health insurance program for the poor. Medicaid spending on albendazole rose from less than \$100,000 in 2008 (\$36.10/prescription) to over \$7.5 million in 2013 (\$241.30/prescription).<sup>5</sup> In this case, Amedra exploited an existing monopoly on a niche drug, a tactic that was successful in part because of the exit of another manufacturer from the market. It is worth pointing out that companies in these circumstances can earn high revenues without having made much, if any, investments in research and development.

Second, competition can languish because of changes in the drug industry and manufacturing challenges. For example, the number of manufacturers producing oral digoxin tablets, used for atrial fibrillation and heart failure, fell from 8 to 3 companies from 2002 to 2013; during that time, the price of digoxin reportedly rose by 637%.<sup>5</sup> The market contraction was thought to be related in part to safety-related drug recalls and manufacturers deciding to leave the market. The cost of a generic product is closely related to the number of generic manufacturers producing it, with the first generic manufacturer pricing its drug only slightly below the brand-name manufacturer's price, and the second pricing it at only about half the price. By the FDA's estimation, it is not until the number of generic manufacturers reaches more than 5 that the price falls to under 25% of the brand-name price.<sup>6</sup> Shortages from reduced supply or increased demand can play a role in these circumstances. For example, hospitals like Brigham and Women's Hospital, where I see patients, have been struggling with intermittent shortages of normal saline (that's salt water) and other vital unpatented, multisource basic healthcare products due to

unexpected demand and variations in supply from manufacturers with production irregularities at their plants. These changes can sometimes lead to spikes in the price of the products.

Third, competition can be interrupted due to horizontal or vertical mergers, or inappropriate anticompetitive behavior. These sorts of activities fall under the oversight of the Federal Trade Commission (FTC). When the FTC has reviewed mergers of generic drug manufacturers, it has sometimes ordered the new entity to relinquish control of certain drug products if the transaction would lead to anticompetitive effects from a decrease in the number of independent competitors in the markets at issue.<sup>7</sup> A more recent case of a potentially anti-competitive business arrangement supporting high prices for a very old drug occurred in the case of the 60 year-old drug ACTH, now marketed as H.P. Acthar Gel, a treatment for hard-to-manage seizures in young children, as well as severe cases of multiple sclerosis. The medication used to sell for as little as \$40 per vial until a small company called Questcor bought it in 2001. According to reports in the New York Times, the manufacturer raised the price immediately to \$700 per vial, and then increased it to \$23,000 per vial in 2007.<sup>8</sup> When another company sought to bring a lower-cost competing drug named Synacthen into the market in 2013, Questcor bought the rights to Synacthen.<sup>9</sup> Synacthen remains unapproved, while H.P. Acthar Gel cost Medicare more than \$141 million in 2012 alone<sup>10</sup> for a drug first FDA-approved in 1952.

Finally, competition among multisource drug manufacturers can be squeezed out by companies winning patents or new market exclusivities issued by the FDA. Thalidomide, for example, is famous for its tragic role in helping modernize the FDA in the 1960s, and was later discovered to be effective in treating a rare type of cancer, multiple myeloma. However, despite the fact that there are no remaining patents on the underlying active ingredient in thalidomide, competing generic versions have remained blocked because of patents that the current manufacturer of the drug received on its distribution pathway.<sup>11</sup> In the case of the anti-gout drug colchicine, the FDA sought to bring production of generic colchicine under its regulatory umbrella. Versions of colchicine had been available in the US since the

19th century and thus it was never formally approved by the FDA as an individual pill. It was sold by multiple manufacturers at about 9 cents per pill until the FDA formally approved one version of it in 2009 and gave that manufacturer a period of market exclusivity. After the FDA's action, this manufacturer raised the price to \$4.85 per pill.<sup>12</sup> Another price jump happened under similar circumstances in 2011 when the FDA approved a synthetic progestin drug called 17 alpha-hydroxyprogesterone caproate (17OHP), which is used to reduce the risk of preterm birth in pregnant women, and was available through many different compounding pharmacies at about \$300 per dose.<sup>13</sup> In 2011, the FDA approved one manufacturer's version of it. When the manufacturer raised the price to \$30,000 per dose, the FDA—under pressure from legislators—announced that it would continue to permit production of the drug from compounded sources.<sup>14</sup> With competition in the market re-established, the company could not sustain its intended exorbitant price.

So what can be done? I do not support wholesale changes to the current system of manufacturing or regulating generic drugs. The generic drug industry serves an extremely valuable function in the health care marketplace, and has a long history of producing high quality drugs at very reasonable prices, which saves patients money, promotes adherence, and improves clinical outcomes. But when generic drugs skyrocket in price, there is something wrong with those markets, and the root causes of the problems need to be identified and fixed. Failures in the generic drug market are events that legislators and policymakers need to take seriously, because they can lead to disruptions in supplies of lifesaving drugs to patients. Thus, I first suggest investment into research surveying the extent of high generic drug prices, as well as a comprehensive examination of their causes. We need a systematic approach to understanding the problem so that focused solutions can be developed. If the markups are related to other points along the drug distribution chain, such as wholesalers or pharmacies, this should be clarified.

However, because high prices for some generic drugs are already reaching critical levels, more immediate actions are necessary. It is critical for the government to be aware of spikes in drug prices so that it can adequately respond. Therefore, all increases in multisource drug prices of greater than 100% should be reported to the Secretary of the Department of Health and Human Services so that she can investigate the rationale for the increase in price and determine whether some sort of public intervention is necessary. Publication of these price hikes should immediately follow so that physicians and patients can be warned about the impending changes. Too often, patients are not aware of these fluctuations in price until they try to fill a drug at their pharmacy, which can lead to patients having to choose between filling their medication and other basic necessities and then to gaps in medication adherence. Physicians may be able to determine alternative inexpensive medication regimens for patients, a process that will be aided by advanced notice of these changes.

In addition to greater price transparency, there are some potential short-term options to help mitigate high prices. One option would be for the FDA Office of Generic Drugs to take a more proactive posture and fast-track potential generic drug entrants into markets where high prices result from manufacturers exploiting natural monopolies. While albenazole may not be of interest to many manufacturers at a low price, its current high price and growing number of prescriptions may now attract additional entrants, which would help bring the price back down. The FDA should do everything in its current power to facilitate these new market entrants as quickly and as safely as possible. According to the FDA, the standard processing time for a generic manufacturer's application is about 10 months, which does not include the time it takes to the generic manufacturer address any deficiencies in its proposal. Legislation in 2012 created new generic drug user fees that promise to reduce such wait times by providing greater funding for FDA staff. In addition, under its current legal authority, the FDA can create special pathways that permit the private market to function more efficiently. Substantial increases in an unpatented drug's prices should trigger the FDA to issue public announcements seeking other



generic manufacturers of the product and that those responding to such a request should receive expedited reviews of their manufacturing processes and bioequivalence data.<sup>5</sup> Generic drug user fees could be waived in these circumstances to further reduce barriers to entry for potential competitors.<sup>5</sup>

Ultimately, policymakers might be forced to apply a lesson from the childhood vaccine field, in which production of needed vaccines occasionally became threatened in part because manufacturers were not assured of enough profit to continue. The federal government intervened with guaranteed volume purchases,<sup>15</sup> which made companies' investments in producing these vital products more economically attractive. Since the government is currently the largest single payor of drug bills in the country, we may need to consider a system that would come into play if a vital generic drug comes to be produced by only 2 or 3 manufacturers, or its price begins to rise uncontrollably. At that point, the government, perhaps through the Veterans Administration, Medicare, or Department of Defense, could issue a commitment to purchase a fixed amount of this drug at a more reasonable cost over a certain period of time, to encourage restoration of a more competitive marketplace for that product.

The Federal Trade Commission also should play an important role in intervening in the generic drug market to ensure that price changes do not stem from anticompetitive behavior. The FTC clearly has interest in this area, but needs greater resources to help it enforce the maintenance of competitive markets in the generic drug industry on behalf of both suppliers and purchasers of multisource drugs. The FTC's work would be aided by greater transparency that might alert it to the possibility of inappropriate behavior.

Interventions can also come at the government payor level. It is worth noting that Medicare currently negotiates or sets prices for basically every health care service it pays for—physician time, radiology services, laboratory services, hospital stays—but it is forbidden from negotiating the prices of prescription drugs. A clause in the statute creating the government's \$80 billion per year Medicare Part D program, for example, explicitly states that the Secretary of HHS cannot interfere with the

negotiations of drug prices or institute a price structure. If this non-interference provision was waived for multisource drugs, then the Centers for Medicare and Medicaid would be in a better position to combat exorbitant increases in drug prices. Such a change would require Congressional action.

Finally, over the long-term, reforms to the patent and drug market exclusivity system may be warranted to help prevent older drugs from soaring in price. Under current interpretation of basic patentability requirements, such as novelty and non-obviousness, there is a relatively low bar to obtaining new patents on peripheral aspects of old, unpatented drug products, such as the business method patent at issue in the thalidomide case. While true research or business innovations deserve patents, it may be worth clarifying the legal standards for issuing patents in the pharmaceutical market so that minor changes in an older drug's formulation or other limited alterations do not lead to new market exclusivity protections. Similarly, in the future, the FDA should be wary when its actions lead to new market exclusivity protection for old and inexpensive products, knowing that extremely high prices will inevitably result, so that the colchicine case is not repeated.

In conclusion, I want to thank this subcommittee for its attention to the very important issue of high generic drug prices, which are affecting more patients with each passing year. Without timely intervention from legislators and other government policymakers, this issue threatens to grow worse, impacting countless lives. As I was preparing for this hearing, I was chatting with a physician colleague of mine who told me about a call he received from a market research firm asking questions on behalf of a manufacturer of a decades-old drug that currently sells for \$70 for an entire course of therapy but faces little competition in the market at present. After the standard questions about his perceptions of the drug's clinical utility and side effects, the final question posed to my colleague was: "Would you still prescribe this drug if the price was \$10,000?" As a health care system and as a nation, we need to keep that question off the table for generic drugs.

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