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High U.S. Prescription Drug Prices:

Anatomy of the Problem and Prospects for Reform

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Chairman Doggett, Ranking Member Nunes, and Members of the Committee:

My name is Ameet Sarpatwari. I am an epidemiologist and lawyer in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital in Boston and an Instructor in Medicine at Harvard Medical School. At these institutions, I help lead the Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research team that studies the intersection between laws and regulations and the development, utilization, and affordability of prescription drugs. Thank you for the opportunity to talk with you today about high US drug prices. I will focus my remarks on the scope and origins of the problem and the merits of several proposed solutions to bring relief to millions of Americans struggling to afford their medications.

The Problem of High Prescription Drug Prices

US prescription drug spending has grown substantially in recent years, totaling over $450 billion dollars in 2016.[1] Between 2011 and 2015, net spending on prescription drugs in Medicare Part B, Medicare Part D, and Medicaid increased 156%, 59%, and 55% respectively[2,3,4]—well in excess of medical inflation. Among some private payers, prescription drugs now account for one-fourth of total health care expenditures.[5] Without intervention, the Centers for Medicare and Medicaid Services (CMS) has estimated that spending on prescription drugs will increase faster than on any other major medical good or service over the next decade.[6]

Such growth has been driven by higher launch prices and routine markups on existing brand-name drugs. In 2017, the first 3 Food and Drug Administration (FDA)-approved gene therapies—tisagenlecleucel (Kymriah), axicabtagene ciloleucel (Yescarta), and voritigene neparvovec-rzyl (Luxturna)—entered the market, with launch prices of $475,000, $373,000, and $850,000, respectively, setting a possible floor for the dozens of new gene therapies under development. That same year, the average annual list price of a cancer medication was over $150,000, almost double that in 2013.[7]

Meanwhile, list prices of many of existing brand-name drugs have risen dramatically. Such markups accounted for 60% of increased US drug revenues between 2014 and 2017.[8] Following a partial pause in the latter half of 2018, manufacturers have resumed the practice, increasing the prices of 400 drugs an average of 6.5% in January 2019.[9] Among these products were the decades-old blockbusters adalimumab (Humira) and recombinant insulin (Lantus), which have more than doubled in list price since their launch.[10,11]

These high and rising prices have harmed patients. In an October 2018 national survey, one-third of 1,006 respondents stated that they skipped a prescription fill in the

past year due to cost.[12] Stories of patients rationing their insulin have featured prominently on the nightly news.[13] Seniors have been especially impacted. Even with Medicare Part D coverage, annual out-of-pocket costs for some drugs exceed $10,000.[14]

The Claimed and Real Reasons for High Prescription Drug Prices

The pharmaceutical industry has attempted to deflect responsibility for the current pricing landscape. It has cast blame for high list prices on pharmacy benefit managers (PBMs), alleging that they have not passed on negotiated rebates to payers or patients. However, drug manufacturers have vigorously fought attempts to shed light on net prices,[15,16] while reaping record profits. Between 2006 and 2015, the annual average profit margins of the largest 25 pharmaceutical companies ranged from 15% to 20%, more than double the 4% to 9% of largest 500 non-pharmaceutical companies.[17] Large rebates, moreover, are not issued for many drugs. Using data provided by health plans, the consulting group Milliman found that drugs with rebates greater than 12% of gross costs accounted for just 10% of fills and 50% of gross spending in Medicare Part D in 2016.[18]

At the same time, the pharmaceutical industry has argued that high prices are necessary for innovation. Yet among the largest drug manufacturers, the average proportion of revenues that goes to research and is less than 20%, about half the percentage that goes to marketing.[19] Additionally, clinically meaningful innovation often occurs outside of industry. Although drug manufacturers perform a critical task in steering investigational drugs through pre-approval testing, more than half of the most transformative drugs over the past 3 decades originated from US-government sponsored settings.[20]

The real reason we are seeing surging drug prices is because we allow pharmaceutical companies to charge whatever the market will bear, while also hindering payers' negotiating ability and permitting strategies that undercut competition. Public payers, in particular, have been tightly handcuffed. CMS is statutorily prohibited from negotiating drug prices in Medicare Part D. Under federal regulations, Medicare Part D plans must cover all drugs within 6 drug classes, including cancer therapies, many of which have not been shown to extend or improve life.[21] Formulary management and price negotiation do not exist within Medicare Part B, which reimburses drug manufactures on the basis of average sales price, encouraging utilization of high-cost drugs. Finally, Medicaid must generally cover all FDA-approved drugs regardless of value.

The one known market-based mechanism that consistently lowers drug prices is robust generic or biosimilar competition.[22,23] However, brand-name manufacturers have employed a variety of tactics to delay or limit such competition.[24] Some brand-name

manufacturers have used restricted distribution networks to prevent generic or biosimilar manufacturers from accessing brand-name drug samples necessary to perform bioequivalence testing. These schemes are sometimes tied to risk evaluation and mitigation strategies (REMS)—safety programs that the FDA requires for drugs posing special risks.[25] In May 2018, the FDA Commissioner reported that the agency had received more than 150 reports from generic manufacturers unable to access sufficient samples of brand-name drugs and posted a list of brand-name companies that were the subject of these complaints.[26]

In other cases, brand-name manufacturers have filed "citizen petitions" with the FDA near the end of their market exclusivity period, arguing that the agency should deny approval of generic versions of their drug for pretextual safety or effectiveness reasons. For example, in 2012, after ceasing production of the tablet formulation of the opioid reversal drug buprenorphine/naloxone (Suboxone), Reckitt filed a citizen petition with the FDA requesting that the agency not approve generic versions of it, claiming that they would pose an unacceptably high safety risk. Of course, this purported risk did not stop Reckitt from aggressively marketing the drug for over a decade. The citizen petition took the FDA 5 months for the FDA to reject, at which time 2 safe, effective, and lower-cost generic versions of the drug were able to enter market.[27]

Another prominent strategy brand-name manufacturers have used to delay generic or biosimilar competition is by obtaining additional patents on peripheral components of a drug, such as its method of use or delivery system. For example, AbbVie has received over 100 patents on adalimumab. Such secondary patents are also secured for reformulations of existing products. Sometimes these new formulations offer clinically meaningful benefits. However, in other cases, they offer little-to-no discernable advantages, as with Abbott's introduction of 54mg, 160mg, and 200mg tablet formulations of fenofibrate (Tricor), for which 67mg, 134mg, and 200mg capsule formulations were already on the market.[28] In our recent study of all new small-molecule drugs approved in 2002, we found that in half of the cases in which a new formulation was introduced and generic entry was observed, manufacturers gained more than 2 years of additional market exclusivity relative to the original product.[29]

The dozens of patents on blockbuster drugs can lead to protracted litigation and settlements that benefit both the brand-name and generic or biosimilar manufacturer but not the public. This is particularly true of the stunted US biosimilar market. As of February 2019, the FDA had approved 17 biosimilars. Yet, only 7 biosimilars had been marketed. Patent litigation was ongoing in 2 cases and resulted in settlements delaying biosimilar entry in 7.[30] The most prominent example involved adalimumab; owing to patent

settlements, it is likely that biosimilars will not be available in the US market until 2023, 5 years after their introduction in the European Union.[31]

Proposed Solutions

Several solutions have been proposed to address the high and rising price of prescription drugs in the US. I will address the administration's proposed changes to the rebate safe harbor, value-based pricing, and ways to combat strategies to delay or limit generic and biosimilar competition.

Changing the Rebate Safe Harbor

In February, the Department of Health and Human Services (HHS) issued a proposed rule to remove the safe harbor for prescription drug rebates provided to Medicaid Part D plan sponsors, Medicaid managed care organizations, and the PBMs they contract, leaving such arrangements subject to liability under the federal anti-kickback statute. In its place, the proposed rule would provide a safe harbor for point-of-sale discounts. The pharmaceutical industry has strongly championed the proposal,[32] and the administration argues that it would likely result in net savings for about 30% of Part D beneficiaries.[33]

However, the impact of the proposed rule is dependent on questionable assumptions. While PBMs have been caught engaging in troubling business practices,[34] which have been shielded by an opaque marketplace, they have also used rebates to negotiate lower drug prices in many cases. For this reason, Medicare Part D gets better prices than Medicare Part B on some very expensive drugs.[35] It is doubtful that, absent other reforms, plans will be able to have the same leverage to extract similar savings as PBMs. The fact that no CEO in last week's Senate Finance Committee hearing would commit to lowering list prices were Congress to prohibit rebates should give policymakers serious pause. Rather than seeking to eliminate PBMs, a better solution would be to set reasonable rules for their practices so that they can continue to contribute positive inputs into the system, such as promoting adherence and use of generics.

Enhancing the Negotiating Ability of Public Payers

Another promising avenue for reform would be to enhance the negotiating ability of public payers. Importantly, it is the ability of the Veterans Administration to set its own formulary and not cover drugs that do not offer patients added benefit that gives it greater leverage than Medicare in securing reasonable prices. Within Medicaid, states have already proposed greater flexibility to determine drug coverage. For example, in September 2017,

Massachusetts requested a waiver to operate a closed formulary, with coverage determinations based on efficacy and cost, and robust safeguards to ensure patient access to necessary treatments.[36] However, CMS rejected the request. Given the current state and expected trajectory of drug prices, as well as increasing concerns over the quality of new drugs coming to market, Congress should reexamine the need and scope current prescription drug coverage requirements in Medicaid and Medicare.

Value-Based Pricing

Were these requirements to remain in place, greater use of value-based pricing—arriving at drugs' prices based on rigorous, transparent, and replicable analysis of their benefits—would be helpful. The Medicare Negotiation and Competitive Licensing Act would instruct the Secretary of the Department of Health and Human Services to negotiate prices with drug manufacturers for Medicare Part D plans based in part on such analysis. Such authorization would provide substantial cost-savings to patients and the federal government, while also incentivizing the industry to pursue transformative innovation.

In pursuing value-based pricing, however, it is critical to distinguish approaches that claim its mantle but do not actually tie prices to clinical benefits. For example, the pharmaceutical industry has championed outcomes-based contracting, in which a refund is given to a payer when a patient does not achieve a specified response, claiming that the increase in such contracts is evidence that drug manufacturers "are willing to put their money where their mouth is when it comes to better value in health care."[37] Yet, such contracts offer illusory savings. For example, a pharmaceutical company can promise a full-refund in the event a patient does not respond to a drug but price it such that the refund would be largely symbolic.

Consider the case of the PCSK9 inhibitor evolucumab (Repatha). The Institute for Clinical and Economic Review (ICER) reported that a value-based price of the drug would be $1,725-$2,242 per-person, per-year based on new clinical trial data. The drug's maker, Amgen, entered into an outcomes-based contract with a payer in which a full-refund will be given to patients who suffer a heart attack or stroke. However, if the same proportion of patients suffer these adverse events as in the clinical trial, the per-person price of the drug—post-refund—would be $13,620.[38]

Combatting Strategies to Delay or Limit Generic and Biosimilar Entry

A multi-pronged approach can help combat strategies to delay or limit generic and biosimilar competition. Legislation is needed to tackle persisting problems with restricted distribution. The bipartisan Creates and Restoring Equal Access to Equivalent Samples

(CREATES) Act would allow generic and biosimilar manufacturers to petition courts for injunctive relief when brand-name manufacturers refuse to provide samples of their drugs for bioequivalence testing on "commercially reasonable, market-based" terms. To ensure patient safety, generic and biosimilar manufacturers seeking samples of REMS-covered drugs would have to subject their testing protocol to FDA review. Passage of this bill would be an important step in facilitating the timely approval of generic and biosimilar drugs, resulting in a more competitive marketplace.[39]

Regarding citizen petition abuse, the FDA announced last October that it would forward petitions judged "to have been submitted with the primary purpose of delaying an approval" to the Federal Trade Commission for possible antitrust enforcement.[40] This policy is commendable, but as Professor Michael Carrier has written,[41] additional measures would be helpful. For example, to better ascertain the full extent of the problem, the FDA should report the resources expended to review each citizen petition and, in instances of simultaneous rejection of the petition and approval of a generic drug, when the agency would have likely approved the generic absent the petition. Similarly, Congress can replace the difficult-to-determine standards the FDA must currently meet to summarily reject a citizen petition—that it is "submitted with the primary purpose of delaying" generic approval and does not "on its face raise valid scientific or regulatory issues"—with a filing requirement that a citizen petition be filed within a year that the information on which it is based was known.

To address patent thickets and product hopping, the United States Patent and Trademark Office can more strictly interpret the standards of novelty and non-obviousness, decreasing the likelihood of inappropriately granted patents delaying generic or biosimilar availability. Meanwhile, Congress should resist calls to carve-out pharmaceutical patents from the Patent Trial and Appeals Board, which was established in 2011 to administratively review granted patents, enabling faster decisions than litigation. Congress should, however, consider removing the automatic provision of a 30-month stay in cases when a brand-name manufacturer sues a generic manufacturer in response to a so-called "Paragraph IV" notice letter, permitting the generic manufacturer to launch at risk. Finally, in response to patent settlements stunting the growth of the biosimilar market, Congress can pass the Preserve Access to Affordable Generics Act, which would require parties to such settlements to disclose all other agreements they have entered into within the same timeframe as the settlement, facilitating regulatory review of potentially anticompetive business practices.

Conclusion

Americans have identified "taking action to lower drug prices" as one of the most important priorities for the new Congress.[42] Their concern is understandable. We pay the highest drug prices in the world, which often are not connected to the value the drugs provide. Implementation of sensible reforms to increase the negotiating ability of payers and to promote greater competition in the marketplace—a number of which I have identified in my testimony—would help make drugs more affordable without jeopardizing the development of tomorrow's cures. Chairman Doggett, Ranking Member Nunes, and Members of the Committee, thank you for your focus on the important issue of high drug prices and for the opportunity to testify before you today. I look forward to answering your questions.

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