

HARVARD MEDICAL SCHOOL  
BRIGHAM AND WOMEN'S HOSPITAL  
*Department of Medicine  
Division of Pharmacoepidemiology  
and Pharmacoeconomics*



**Aaron S. Kesselheim, M.D., J.D., M.P.H.**  
*Associate Professor of Medicine  
Director of the Program on Regulation,  
Therapeutics, and Law (PORTAL)*

## ORIGINS OF AND SOLUTIONS TO HIGH DRUG PRICES IN THE US

**Testimony of:**

**Aaron S. Kesselheim, M.D., J.D., M.P.H.**

**Associate Professor of Medicine, Harvard Medical School**

**Director, Program On Regulation, Therapeutics, And Law (PORTAL)**

**Division of Pharmacoepidemiology and Pharmacoeconomics**

**Department of Medicine, Brigham and Women's Hospital**

**Boston, MA**

**[www.PORTALresearch.org](http://www.PORTALresearch.org)**

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Committee on Oversight and Reform  
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## Summary of Major Points

- The main driver of prescription drug spending is patent-protected brand-name drugs, which make up only about 10% of prescriptions but three-quarters of drug spending.
- Many patients cannot afford to fill their prescriptions for costly drugs; as a result, high drug prices can lead to poor clinical consequences which cause human suffering and avoidable medical expenditures. This has become a major driver in US health care spending
- The underlying reason for high drug prices is that the government gives patents and other market exclusivities to brand-name drug manufacturers as a spur to innovation. While in effect, these patents allow manufacturers to charge any price they want, or whatever the market will bear. At the same time, the pharmaceutical purchasing market that is expected to provide a counter-weight to these government-granted monopolies is inefficient, since various laws and other factors prevent payors from being able to effectively negotiate low prices in many circumstances. For example, Medicaid requires state programs to cover essentially all drugs the FDA has approved, and Medicare maintains several “protected classes” such as drugs for cancer and mental illness, which all Medicare programs are required to cover at whatever price the manufacturer sets.
- No other advanced economy allows drug manufacturers to set whatever price they want for their products, and this is not the case for most other goods and services the government purchases.
- These periods of government-granted monopoly are often extended well beyond anything the founding fathers planned, by add-on patents, other exclusivities, and settlements between large manufacturers and generic/biosimilar manufacturers, in which the latter are provided valuable consideration for not marketing competing versions of their drugs.
- To address these problems, during drugs’ market exclusivity periods, which can last on average 14-15 years for first-in-class drugs, government payors should have more flexibility to create evidence-based program-wide formularies and negotiate prices for drugs.
- It would also help to change patent policy to make biosimilars and generics more accessible and to help cut through “patent thickets” that block timely or efficient entry.
- Changes made to rationalize US drug prices will **not** substantially reduce drug innovation because (1) much of the most important drug innovation arises from publicly-funded research occurring in government or academic laboratories, or start-up companies spun out of these institutions, and (2) rational solutions that bring payments for drugs in line with their value to patients will encourage the best type of innovation—that leading to the most clinically necessary products.

## **Chairman Cummings, Ranking Member Jordan, and Members of the Committee:**

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, where I am an Associate Professor of Medicine at Harvard Medical School. I lead the Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research team that studies the intersections between laws and regulations and the development, utilization, and affordability of drugs. We are here today to talk about the high prices of many prescription drugs in the US and solutions that Congress can consider right now.<sup>1</sup>

## **Prescription Drug Spending in the US and Comparable Countries**

Prescription drugs make up about a \$450 billion market in the US, and are one of the fastest rising health care costs. Some payors are reporting now that as much as one in every four health care dollars is going to prescription drugs. Medications are awesome tools for physicians and patients, but their costs have gotten out of control, putting them beyond the reach of many people. List prices for brand-name drugs have increased from about 8% to 16% per year over the last decade, well beyond the consumer products index general inflation rate of 1-3% per year.<sup>2</sup> US drug prices and spending far exceed those of other similar industrialized countries around the world. For example, in countries like Canada, Germany, France, and Australia, all of which have excellent health care systems, the per-capita expenditures for prescription drugs is about \$400 per year compared to the \$850 Americans spend per capita on prescription drugs.<sup>3</sup> The main driver of this is brand-name drugs, which make up only about 10% of prescriptions but three-quarters of drug spending.<sup>4</sup>

High prescription drug prices are becoming an increasing burden for patients and our health care system. The essential policy dilemma is that while drugs are among the most cost-effective interventions in medicine and the drug industry plays an important role in bringing these products forward—a process that can require substantial resources—increasing drug prices in the US can make important breakthroughs unaffordable to many of our patients. Since high drug prices can lead to poor clinical consequences and have become a major driver in US health care spending, my goal is to provide an overall landscape of US prescription drug spending, widely discussed explanations for high drug prices, and policy solutions.

The underlying reason for high drug prices is that the federal government gives patents and other market exclusivities to brand-name drug manufacturers and allows them to charge whatever the market will bear.<sup>5</sup> At the same time, the pharmaceutical purchasing market that is expected to provide a counter-weight to monopolist manufacturers is extremely inefficient, since various laws and other factors prevent payors from being able to effectively negotiate low prices in many circumstances. To make things worse, manufacturers often extend their patent and market exclusivity rights as long as possible through various strategies and use their substantial lobbying power to block sensible political reforms. Many of these issues are less pressing in other comparable countries that seek to negotiate drug prices based on estimates of the clinical value that the drugs provide and that use buying power to provide for a fairer negotiation in the free market. The difference can be stark. For example, currently the government pays for drugs administered in hospitals or physician offices to older patients through Medicare Part B based on the ‘average sales price’ alone—that is, what the market can bear—with no consideration as to the value or cost-effectiveness of the drug. Among the 75 drugs with the highest annual Part B expenditures in 2016 (accounting for about \$20 billion, or 77% of Part B drug spending), prices

for 65 of the 67 with evaluable data (97%) were considerably higher than the median prices in other high-income countries (Japan, Germany, Switzerland and UK), generally made and sold by the same manufacturers as in the US. In May 2018, drug prices were a median of 46% to 60% lower in those countries than in the US's Medicare drug benefit program.<sup>6</sup>

### **Setting and Maintaining High Prices During Brand-Name Market Exclusivity**

Manufacturers' ability to set their own prices starts at the time a drug is first approved by the Food and Drug Administration (FDA). At that point, the law guarantees at least about six to seven years of market exclusivity, during which time the FDA will not approve any direct competitors. That is reasonable, to reward and encourage innovation. Certain antibiotics get an additional 5 years, and biologics get 12 years. In addition to this guaranteed minimum period of market exclusivity, brand-name drugs are also protected by patents that last 20 years. On average, new drugs get about 12 to 14 years of competition-free exclusivity, while first-in-class drugs—often the most innovative products—get on average about 14 to 15 years.<sup>7</sup>

During the market exclusivity period, there are important limits placed on public and private payors that prevent them from negotiating effectively with manufacturers. For example, Medicaid cannot exclude most FDA-approved drugs from its formulary, while Medicare does not use a national formulary or negotiate drug prices for Part B drugs or on behalf of the individual Medicare Part D plans.<sup>8</sup> There are also six “protected drug classes” for which Medicare Part D plans have to cover all approved drugs, such as drugs for cancer and mental illness. This undermines effective price negotiation, since it is hard to negotiate an effective price if a Part D insurer is forced by the federal government to cover the drug, even if it is no better than 1 or 2 or 3 similar products. Among federal government payors, the Department of Veterans Affairs has the

most flexibility in terms of setting its formulary and in negotiating on behalf of all its enrollees around the country. As a result, the VA often pays less for many drugs.<sup>9</sup>

The system – doctors, patients, payors, and the government – also suffers badly from the absence of comparative effectiveness research that documents the effectiveness and safety of drugs against one another. Many drugs are approved and then used for years without any information on how well they work compared to other drug or non-drug treatments on the market.<sup>10</sup> Comparative effectiveness information does not reliably emerge after approval either, since there is no entity responsible for systematically generating such evidence.

### **Strategies that Delay Generic and Biosimilar Competition**

The best kind of competition that consistently and substantially lowers prescription drug prices comes from interchangeable generic drugs that emerge after a drug's market exclusivity period ends. State drug product selection laws then facilitate the process of circulating generic drugs to patients by mandating or authorizing pharmacists to fill a prescription with the corresponding generic drug. Automatic substitution helps generic manufacturers compete based on price and ensures that prices reach closer to the cost of production.

However, this brand-to-generic transition period can be delayed or prolonged for a number of problematic reasons. Nearly all manufacturers seek, and the federal government grants, dozens of additional patents on their drugs during the course of development and the brand-name exclusivity period.<sup>11</sup> Such secondary patents cover peripheral components of the drug as well as different compositions, formulations, polymorphs, and prodrugs; this often extends the market exclusivity of these drugs by years.<sup>12</sup> For example, an older active pharmaceutical product can suddenly become expensive if packaged in a new delivery device, as has been observed with

EpiPen, for which the manufacturer raised the price from \$50 to over \$600 for a two-pack over the course of a decade starting in 2007, even though the only active component, epinephrine, was isolated over 100 years ago.<sup>13</sup> In one study, we found that the number of drug-device combinations with patents listed by the FDA increased from 42 (with 85 associated patents) in 2000 to 127 (with 844 associated patents) in 2016. In 2000, only 4 drug-device combination products (out of 42, 10%) cited 3 delivery-device patents. By 2016, 53 (out of 127, 41%) listed 3 or more such patents, and 17 (13%) listed 10 or more. As we all know, the nation is facing a major opioid crisis. For years, we have had an antidote, naloxone that can save a person's life in the case of overdose. But the manufacturer of the naloxone autoinjector Evzio increased the price from \$575 per dose to \$4,100 per dose from 2014 to 2017.<sup>14</sup>

Generic manufacturers often sue to invalidate these patents in order to bring their drugs to market. But such litigation can lead to settlements in which the generic manufacturer agrees to drop the lawsuit in exchange for some valuable consideration from the brand-name manufacturer – one variation of which is called a “Pay for Delay” arrangement. While settlements can be efficient ways to end litigation, these settlements also prop up weak patents and delay generic entry. The most recent notable example of this occurred with adalimumab (Humira), a treatment for rheumatoid arthritis and other conditions that was originally approved by the FDA two decades ago and is one of the best-selling drugs in the world, generating \$89 billion in revenue from 2011 to 2017. Since its initial approval, the manufacturer has accumulated over 100 unexpired patents, creating a thicket that has delayed efforts to introduce biosimilar versions of the drug that might competitively lower prices. In settlements of cases arising from these patents, adalimumab biosimilar manufacturers agreed to delay introducing their versions into the US until 2023, even though these biosimilar drugs are currently helping reduce spending on rheumatoid arthritis in

countries across Europe. Meanwhile, the average wholesale price of adalimumab has increased 25 times in the last 15 years—a total of nearly 450%—including a 9.7% increase in January 2018.<sup>15</sup>

Other strategies intended to delay generic entry do not directly involve patents. For example, to win FDA approval of its a generic drug, a manufacturer needs to conduct bioequivalent studies showing that its product is bioequivalent to the brand-name version. Yet there have reportedly been over 150 cases in which brand-name manufacturers have refused to provide the necessary samples to generic manufacturers for such bioequivalence testing.<sup>16</sup> Another delaying strategy includes filing so-called ‘citizen petitions’ with the FDA.<sup>17</sup> Most citizen petitions related to generic drugs are actually filed by brand-name manufacturers claiming that their product has a special characteristic, and thus, the generic should not be approved; this can have the effect of substantially delaying entry of a more affordable generic product.<sup>18</sup> The manufacturer for the brand-name oral antibiotic Vancocin filed 24 different ‘citizen petitions’ over a period of 6 years.<sup>19</sup>

### **Policy and Legislative Solutions**

Congress can take action on these problems. High prescription drug prices in the US arise from two sources: a fundamentally inefficient market in which brand-name manufacturers have a disproportionate ability to set high prices (due to patents and legal limitations on payors that were passed by Congress in past years) and various strategies that permit brand-name manufacturers to extend their market dominance far beyond the expiration of the original patent on the key discovery: the underlying drug active ingredient. Fortunately, these issues are addressable with rational legislative and regulatory policymaking that can help get us back to a more optimally competitive marketplace, while still allowing drug manufacturers to earn a



healthy profit on true innovation rather than legal manipulation. In addition, we need to return to the basic principle—dating back to the Patent Act of 1790—that to encourage new innovation, patent-protected market exclusivity periods should only exist for limited periods of time.

Several solutions also exist for improving competitive price negotiation during the market exclusivity period. For example, authorizing Medicare to create a program-wide formulary and negotiate prices for drugs could be accomplished by statute. Medicare currently sets or negotiates prices for all medical interventions except prescription drugs. The formulary and negotiation process could be designed in a way to maximize the chance that the final negotiated price falls within a particular widely accepted range of value for money, or cost-effectiveness, depending on the clinical scenario. In this way, drugs could be included on the Medicare formulary and sold at a price that more closely approximates the benefit that they provide to patients, rather than whatever the manufacturer wants to charge, irrespective of a drug's actual value.

Other, more incremental steps that may not require legislative change could also lead to price savings. Such steps could include: shifting drugs from Medicare Part B to Part D (we recently estimated savings of 7-18%—\$1-\$4 billion—per year<sup>6</sup>); instituting inflation-based rebates for Part B drugs to insulate the government and patients from drug price increases that exceed inflation (CBO estimated \$1.5 billion in savings from 2019-2028); shifting dual-eligible Medicaid plus Medicare beneficiaries back to Medicaid, where they had received prescription drug coverage prior to 2006 (CBO estimated \$154 billion in savings from 2019-2028); reducing Medicare's reinsurance subsidy from 80% to 20%, as suggested by the MedPAC; removing the cap on Medicaid drug rebates, which could reduce the incentive for manufacturers to increase drug prices faster than inflation; allowing plans to remove protected class status if prices rise too much (we at PORTAL have examined this and found that nearly all drugs covered by Medicare Part D plans in a

protected class would have lost their protected status based on price increases in the past few years); and allowing state Medicaid programs to implement formularies that exclude drugs with minimal clinical or economic value.

In addition, producing and actively disseminating information about the clinical and economic value of drugs would be helpful for supporting negotiations between with private manufacturers and payors. The Patient-Centered Outcomes Research Institute, which was created in 2010, was originally conceived to conduct this value-based research on drugs. However, the political process diverted it away from funding the kind of comparative effectiveness research that would help doctors, patients, and payors make decisions about which drugs to prescribe, take, and pay for. There may be an opportunity to re-direct its priorities as it comes up for its ten-year renewal in the very near future.

Another range of possible solutions could help cut through patent thickets that block timely or efficient generic entry. For example, many secondary patents may not have been appropriately granted by the Patent Office. Re-examining these decisions by the Patent Trial and Appeals Board (PTAB), which was created in 2011 to administratively review patents that had been approved by the Patent and Trademark Office, could help overturn them more expeditiously than costly litigation.<sup>20</sup> Whenever a new patent is listed with the FDA, it could be subject to automatic review in front of the PTAB to determine whether it meets the basic criteria for patentability. Congress could also re-examine whether certain kinds of secondary patents—such as patents covering drug delivery devices, as for insulin or epinephrine—should be able to be listed by FDA as patented products at all. Others ideas include providing specific rules to the Federal Trade Commission to exclude problematic brand/generic (or biosimilar) legal settlements and passage of CREATES Act, which would make it illegal for brand-name manufacturers to withhold samples for their products

when generic manufacturers request them.<sup>21</sup> With each of these measures, the goal should be to ensure that manufacturers are not able to indefinitely extend their exclusivity periods beyond what the original patent laws intended. This will also incentivize them more effectively to invest in the next generation of cures.

### **Impact on Innovation**

Changes made to rationalize US drug prices along the lines of what I have discussed will not substantially reduce drug innovation for two main reasons. First, studies show that much of the most important drug innovation arises from publicly-funded research paid for by the National Institutes of Health and occurring in government or academic laboratories, or start-up companies spun out of these institutions.<sup>22</sup> Often, this National Institutes of Health-funded work goes beyond basic and translational science and into drug product discovery,<sup>23</sup> at which point it attracts later-stage investment from private manufacturers interested in bringing the drugs to market. Thus, as long as the US government continues its decades-long commitment to investing strongly drug development through the NIH, there will be a consistent supply of potentially transformative approaches, targets, or even compounds that could be brought forward into clinical development.

Second, the recommendations listed above are all intended to bring US drug prices more in line with the actual clinical value that the drug provides—that is, to rationalize payment for drugs in the US so that US patients stop paying exorbitant prices for drugs that offer minimal clinical impact or lack cost-effectiveness. Currently, substantial drug spending in the US goes to such cost-ineffective products; for example, we found that Medicare spent nearly a billion dollars in 2016 alone on brand-name drugs made up of two or more generic constituents when effective formularies could have guided many more patients to lower-cost and equally effective

alternatives.<sup>24</sup> Paying for drugs closer in line with their value may mean that there are some circumstances in which prices will be very high for drugs that offer substantial gains in clinical outcomes (or value) over existing treatments, and that is appropriate. But Medicare, Medicaid and other US payors will be able to better afford to cover such products for the patients who need them if these payors are not wasting vast sums of money on drugs that do not offer such advantages, as they currently do. By contrast, in the existing marketplace, incentives for innovation are misaligned with patient or public health goals because even marginally effective drugs or incremental improvements can lead to substantial revenues. Thus, reforms along the lines that I have proposed will not stifle innovation, but will rather encourage the best type of innovation, leading to the most truly new and clinically necessary products.

## **Conclusion**

Over the past few decades, the US pharmaceutical industry has become among the most consistently profitable industry sectors in the world, in part because we give drug manufacturers wide latitude to set the prices for their products. But the prices set at a level to maximize manufacturer revenues and are often well beyond the clinical value that the drugs provide, because the marketplace is fractured and inefficient. Recently, there has been growing recognition that patients can no longer afford their medications at these prices, and the system is increasingly paying extremely high prices for drugs, far beyond costs in other comparable countries. The solution to this problem involves intelligent legislation and regulation to ensure that US patients and payors pay prices commensurate with the clinical value that the drugs provide, and to ensure that even expensive drugs face generic or biosimilar competition after a reasonable and fair time frame, as originally envisioned by the Patent Act. This hearing is a great sign that Congress is

moving in this direction, and I am honored to be here to share my thoughts and happy to continue working with the legislators here to craft sensible solutions.

## References

- <sup>1</sup> Some of this testimony was originally delivered at the 2018 Stuart Rome lecture at the University of Maryland Francis Carey King School of Law in Baltimore, MD (forthcoming *Journal of Health Care Law and Policy*, 2019).
- <sup>2</sup> Schondelmeyer SW, Purvis L. Trends in Retail Prices of Brand Name Prescription Drugs Widely Used by Older Americans: 2017 Year-End Update. Sept 2018.
- <sup>3</sup> Kesselheim AS, Avorn J, Sarpatwari A. The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform, 316 *JAMA* 858 (2016).
- <sup>4</sup> *Id.* at 860.
- <sup>5</sup> Aimee Picchi, The Cost of Biogen's New Drug: \$750,000 Per Patient, CBS News Moneywatch (Dec. 29, 2009, 2:00 PM), <https://www.cbsnews.com/news/the-cost-of-biogens-new-drug-spinraza-750000-per-patient/> (noting that a pharmaceutical company claimed that a \$750,000 price tag on a rare disease drug is consistent with other therapies for rare diseases); Courtney Hutchison, Provenge Cancer Vaccine: Can You Put a Price on Delaying Death?, ABC News (July 29, 2010), <https://abcnews.go.com/Health/ProstateCancerNews/provenge-cancer-vaccine-months-life-worth-100k/story?id=11269159>; Judy Silber, Onyx Gets OK for Kidney Cancer Drug, *Contra Costa Times*, Dec. 21, 2005, at F4; Amy Dockser Marcus, Price Becomes Factor in Cancer Treatment, *Wall St. J.*, Sept. 7, 2004, at D.1.
- <sup>6</sup> Hwang TJ, Jain N, Lauffenburger JC, Vokinger KN, Kesselheim AS. Analysis of proposed Medicare Part B to Part D shift with associated changes in total spending and patient cost-sharing for prescription drugs. *JAMA Intern Med.* 2019 Jan 14. doi: 10.1001/jamainternmed.2018.6417.
- <sup>7</sup> Wang B, Liu J, Kesselheim AS. Variation in Time of Market Exclusivity among Top-Selling Prescription Drugs in the United States, 175 *JAMA* 635 (2015).
- <sup>8</sup> Kesselheim AS, Avorn J, Sarpatwari A. The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform, 316 *JAMA* 858 (2016).
- <sup>9</sup> Venker B, Stephenson KB, Gellad WF. Assessment of Spending in Medicare Part D If Medication Prices from the Department of Veterans Affairs Were Used. *JAMA Intern Med.* 2019 Jan 14. doi: 10.1001/jamainternmed.2018.5874.
- <sup>10</sup> Goldberg NH et al. Availability of Comparative Efficacy Data at the Time of Drug Approval in the United States, 305 *JAMA* 1786, 1787 (2011).
- <sup>11</sup> Vokinger KN et al. Strategies That Delay Market Entry of Generic Drugs, 177 *JAMA Internal Med.* 1665, 1665–66 (2017).
- <sup>12</sup> Amin T, Kesselheim AS, Secondary Patenting of Branded Pharmaceuticals: A Case Study of How Patents on Two HIV Drugs Could Be Extended for Decades, 31 *Health Affairs* 2286 (2012).
- <sup>13</sup> Sneader W. The discovery and synthesis of epinephrine. *Drug News Perspectives* 2001;14(8):491-494.
- <sup>14</sup> [https://www.portman.senate.gov/public/index.cfm?a=files.serve&File\\_id=B8E40E60-FE5C-4123-A97E-868A201C10EC](https://www.portman.senate.gov/public/index.cfm?a=files.serve&File_id=B8E40E60-FE5C-4123-A97E-868A201C10EC)
- <sup>15</sup> Humira. Red Book AWP Price History. Accessed April 30, 2018
- <sup>16</sup> Kerstin N. Vokinger, et al., Strategies That Delay Market Entry of Generic Drugs, 177 *JAMA Internal Med.* 1665 (2017).
- <sup>17</sup> Carrier MA, Minniti C. Citizen Petitions: Long, Late-Filed, and At-Last Denied, 66 *Am. Univ. L. Rev.* 305 (2016) (concluding that 92% of citizen petitions are filed by brand-name pharmaceutical companies with indicia of their purpose being to delay generic approval).
- <sup>18</sup> Kerstin N. Vokinger et al., Strategies that Delay Market Entry of Generic Drugs, 177 *JAMA Internal Med.* 1665 (2017).
- <sup>19</sup> FTC Charges that Shire ViroPharma Inc. Abused Government Processes through Serial, Sham Petitioning to Delay Generics and Maintain its Monopoly over Vancocin HCL Capsules, FTC (Feb. 7, 2017), <https://www.ftc.gov/news-events/press-releases/2017/02/ftc-charges-shire-viropharma-inc-abused-government-processes> (announcing the filing of a complaint against the manufacturer, alleging antitrust violations including abusing the citizen petition process in order to delay generic Vancocin entry to the market).
- <sup>20</sup> Darrow JJ, Beall RF, Kesselheim AS. The Generic Drug Industry Embraces a Faster, Cheaper Pathway for Challenging Patents, *Applied Health Econ. & Health Pol'y*, Aug. 2018, at 1–2.
- <sup>21</sup> S. 974, 115th Cong. (2017).
- <sup>22</sup> Kesselheim AS, Tan YT, Avorn J. The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. *Health Affairs* 2015;34:286-294
- <sup>23</sup> Stevens AJ, Jensen JJ, Wyller K, Kilgore PC, Chatterjee S, Rohrbaugh ML. The role of public-sector research in the discovery of drugs and vaccines. *New England Journal of Medicine* 2011;364(6):535-541.
- <sup>24</sup> Sacks CA, Lee CC, Kesselheim AS, Avorn J. Medicare spending on brand-name combination medications vs their generic constituents. *JAMA* 2018;320(7):650-656.