Transparency in Drug Pricing:

Issues to Consider from the Research Lab to the Consumer

An ML Strategies White Paper

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Since 2014, drug pricing has grown in importance in health care policy conversations. From Gilead Sciences's Hepatitis C treatment costing $84,000 per course of treatment to Turing Pharmaceutical's 5,000 percent price hike of Daraprim, lawmakers, consumers, and insurance companies alike are raising concerns about the cost of pharmaceuticals. President Obama, as well as presidential candidates Hillary Clinton, Senator Bernie Sanders, and Donald Trump have all called for government intervention. One clear challenge to understanding drug pricing is the difficulty in ascertaining how the prices are developed. As complaints grow about exorbitant pharmaceutical prices, manufacturers are coming under pressure to increase transparency by disclosing research and development (R&D) costs and profits of medicines in order to justify the current prices.

Pricing Before The Drug Leaves The Manufacturer

Innovator Drugs

The costs involved in creating a drug are complex. As is the case with all goods, the price must reflect the cost of production. Obviously, there is the cost of R&D for the drug itself. Less well known but equally important is the cost of failed R&D on other drugs and R&D for future drug development. Once the pharmaceutical product has completed the approval process, it goes on to production and will have marketing costs associated with its entry into the market. Finally, as is the case with all for-profit entities, there will be a return on investment for the investors. Arguably, the costs that go into determining the price of a drug can be reduced to those specific factors: actual production costs, current R&D, failed R&D, future R&D, marketing, and return on investment. While this may seem like a logical approach to drug pricing, recent investigations have found even more complex factors influencing pricing. According to documents provided by Gilead to the Senate Committee on Finance, the pricing process can be based on clinical attributes, value determination, market research with payers, and the cost of current product regimens.[1]

The Price of an Innovator Drug

X = Production, R&D, Failed R&D, Future R&D, Marketing, and ROI of Investors

Production

Production costs are relatively low once the drug has been developed and approved, but the price floor for these drugs is unknown. Data on the costs of active ingredients for drugs are generally privileged information. According to researchers, the costs of raw materials for a drug are extremely low and are hiked along the way.[2] Manufacturers often purchase active pharmaceutical ingredients (API) in bulk, the cost of which is inconsequential compared to the revenue generated from the wholesale sale of the tablets. There is minimal interest in reforming manufacturing technologies as savings would be inconsequential compared to savings from improving marketing, clinical trials, and drug development methods.[3] These limited costs of production are demonstrated when generics enter the market who have not incurred R&D costs. Arguably, the price of a drug in a competitive generic market will drive towards cost of production as much as possible.

Research and Development

The driving cost factor behind innovator drugs is R&D. R&D costs are estimated to be as high as $5.5 billion per successful pharmaceutical[4] and $2.6 billion on average[5], a figure that is in part due to the inclusion of research projects that fail. The R&D phase for a drug runs from laboratory work on the development of specific molecules through FDA-required human testing clinical trials. A company can expect to spend $350 million on the clinical trial phase before the drug even goes to market.[6] The data involved in arriving at these research and development costs in clinical trials is incredibly obscure, with the majority coming from out-of-pocket clinical phase costs.[7] A 2014 study by Tufts gathered that clinical success, attrition rates, and length of clinical trial phases were also contributing factors to cost.[8]

Larger pharmaceutical companies must recoup lost capital, including sunk costs regarding failed research. The Pharmaceutical Research Manufacturers Association (PhRMA) estimates that a drug could take 10-15 years to develop, which includes the developmental process as well as complying with FDA's standards and regulations for safety and effectiveness. It is estimated that 95 percent of experimental medicines that are studied in humans fail to be deemed both effective and safe.[9] Companies that launch only one drug have an average cost of $351 million compared to an average cost of $5.5 billion for companies that have 8-13 drugs approved.[10] According to PhRMA, only 12 percent of drugs that make it to clinical trials ever get approved for human usage.[11] Those that make it to market pay for future R&D, including research that fails to produce an approved drug.

1 United States Senate Committee on Finance, The Price of Sovaldi and its Impact on the U.S. Health Care System, (Dec., 2015), http://www.finance.senate.gov/imo/media/doc/1%20The%20Price%20of%20Sovaldi%20and%20Its%20Impact%20on%20the%20U.S.%20Health%20Care%20System%20(Full%20Report).pdf
2 United States Senate Committee on Finance, The Price of Sovaldi and its Impact on the U.S. Health Care System, (Dec., 2015), http://www.finance.senate.gov/imo/media/doc/1%20The%20Price%20of%20Sovaldi%20and%20Its%20Impact%20on%20the%20U.S.%20Health%20Care%20System%20(Full%20Report).pdf
3 Girish Malhotra, Pharmaceutical Costs, Technology Innovation, Opportunities, and Reality, PharmPro (Mar. 10, 2010), http://www.pharmpro.com/article/2010/03/pharmaceutical-costs-technology-innovation-opportunities-reality
4 Ibid.
5 Matthew Herper, The Cost of Creating a New Drug Now $5 billion, Pushing Big Pharma to Change, Forbes (Aug. 11, 2013), http://www.forbes.com/sites/matthewherper/2013/08/11/how-the-staggering-cost-of-inventing-new-drugs-is-shaping-the-future-of-medicine/#176093836bfc.
6 Avalere Health, Follow the Pill, prepared for the Henry J. Kaiser Family Foundation (Mar., 2005), http://avalere.com/research/docs/Follow_the_Pill.pdf.
7 Tufts Center for the Study of Drug Development, How the Tufts Center for the Study of Drug Development Pegged the Cost of a New Drug at $2.6 billion, (Nov. 18, 2014), http://csdd.tufts.edu/files/uploads/cost_study_backgrounder.pdf
8 Ibid.
9 Avalere Health, op. cit.
10 Herper, op. cit.
11 PhRMA, Policy Solutions: Delivering Innovative Treatment to Patients, (Mar., 2016), http://phrma.org/sites/default/files/policy-solutions.pdf

Research into pharmaceutical responses for complex conditions can be costly and require pricing reflective of the costs. This research will only continue, though, if an innovating company has the opportunity to recoup its costs for the development outlined above. The industry has used these R&D costs as a justification for pricing, when it is debatable how much current return needs to retrospectively pay for current and failed R&D as those are arguably sunk costs—dollars already spent that cannot be recovered so they are irrelevant to current profit-maximizing pricing decisions.[12] The more important information, manufacturers have argued recently, is an analysis of value; the costs that are saved by the healthcare system in the future that can be enormous justifies some of these large prices.[13]

Marketing

Sales and marketing are often larger costs than R&D for pharmaceutical companies.[14] GlobalData research found that in 2013, Johnson & Johnson spent $9.3 billion more on sales and marketing than R&D, including direct-to-consumer marketing and marketing to physicians who prescribe.[15] The United States and New Zealand are the only countries in the world that allow direct-to-consumer advertising, which allows manufacturers to raise patients' awareness of different treatment options and the patient to be more involved in choosing drugs. It goes beyond that, though, as doctors are also enticed to prescribe certain drugs over others.[16] From August to December of 2013, pharmaceutical companies spent $3.5 billion on advertising to physicians and teaching hospitals.[17]

Generic Drugs

The Hatch-Waxman Act enables a generic pharmaceutical manufacturer to develop a copy of a patented innovator drug without risking liability for patent infringement damages. The generic manufacturer must only demonstrate bioequivalence, but it cannot be marketed until the period of market exclusivity has ended unless the generic manufacturer is able to win litigation and prove a brand patent invalid or not infringed by the generic. In this case, there is a 180 day market exclusivity period for generic manufacturers, a huge incentive and benefit for a company that is able to set their price without fear of additional competition.

The Price of the Drug after Entry of the First Generic

Y = X minus an unknown percent driven by the market

The current U.S. patent system grants branded products 11.5 years of market exclusivity. While this period allows the pharmaceutical manufacturer to recover the costs of capital, afterwards the market opens to generic competition. According to IMS Health data, the health care system saw a decrease in costs of $65.2 billion due to patent expirations between 2007 and 2011, or $13 billion a year.[18] The pressure of this potential competition also effects the decisions made by the innovator in initial pricing of a drug. The Senate Finance Committee report found that Gilead was extremely concerned about the advent of competition (in this case from a similar though not generic competitor) influencing the initial pricing decision regarding Sovaldi.[19]

As the period of market exclusivity ends, the pricing structure moves from one reflecting the cost of production and R&D to one reflecting this higher level of competition. When the first generic enters the market, the price of the original innovator drug begins to react to market forces. Competition between the innovator and the generic drug manufacturer allows purchasers to drive down prices. In 2011, the average price of a generic was $33 compared to the $265 average price of a branded drug.[20] With much more limited costs related to R&D and with the intense competition surrounding generic drugs, prices of generics begin to fall.

The Price of the Drug with a Competitive Generic Market

Z = Cost of Production plus a percentage necessary to maintain generic participation

In a fully competitive generic market with numerous manufacturers, the price of a drug begins to fall closer to actual productions costs.

Prices only begin to fall after at least four or five generics enter the market.[21] At some point the price is driven so close to the cost of production, some generic manufacturers will exit the market. As generic manufacturers exit the market and there is less competition, the price of the drug can begin to rise again. By 2013, the majority of generic manufacturers of Digoxin, a cheap medicine whose use had declined, had stopped production and distribution, leaving two companies to dominate the market.[22] One company began a price increase and the other soon followed.

In a few limited instances, a generic market never develops. In 2015, Turing Pharmaceuticals raised the price of Daraprim from $13.50 per tablet to $750 per tablet, something

12 Andrew Pollack, Drug Prices Soar, Prompting Calls for Justification, NY Times (Jul. 23, 2015), http://www.nytimes.com/2015/07/23/business/drug-companies-pushed-from-far-and-wide-to-explain-high-prices.html.
13 Ibid.
14 Richard Anderson, Pharmaceutical Industry Gets High On Fat Profits, BBC News (Nov. 6, 2014), http://www.bbc.com/news/business-28212223
15 Ibid.
16 World Health Organization, Direct-to-consumer advertising under fire, http://www.who.int/bulletin/volumes/87/8/09-040809/en/
17 Charles Ornstein, Our First Dive Into the New Open Payments System, Health Impact News, http://healthimpactnews.com/2014/doctors-earn-3-5-billion-in-kick-backs-from-pharmaceutical-companies/
18 Pollack, op. cit.
19 United States Senate Committee on Finance, op. cit.
20 Devon M. Herrick, What is Increasing the Cost of Generic Drugs? (Part I: The Supply Chain), National Center for Policy Analysis (Sep. 21, 2015), http://www.ncpa.org/pub/what-is-increasing-the-cost-of-generic-drugs-part-i-the-supply-chain.
21 Elisabeth Rosenthal, Rapid Price Increases for Some Generic Drugs Catch Users by Surprise, NY Times (July. 8, 2014), http://www.nytimes.com/2014/07/09/health/some-generic-drug-prices-are-soaring.html.
22 Ibid.

the company was able to do solely due to the fact that generic competition never developed for the drug. Several policy changes have been considered by Congress to address this particular instance.

Between The Manufacturer And The Consumer

Manufacturers of pharmaceuticals don't sell drugs directly to the ultimate consumer. Between the manufacturer and consumer exists a complex supply chain that adds additional costs to the final price the consumer sees. The relationships between the different entities of the drug supply chain are complex with substantial differences in what each player pays for varying amounts of drugs. Most drugs are dispensed by pharmacies who obtain the drugs from wholesalers, often utilizing the services of a Group Purchasing Organization (GPO).[23] The pharmacy is frequently reimbursed in whole or in part by a government program or private insurer who may have utilized the services of a pharmaceutical benefit manager (PBM) in negotiating prices.

Manufacturers

Many drugs are the result of mergers, acquisitions, and partnerships, making it difficult to make sense of all the costs involved in creating a drug.[24] Manufacturers develop algorithms to account for expected demand, future competition, and potential marketing costs. Using these algorithms, they establish the wholesale acquisition cost (WAC), which is the baseline price at which wholesale distributors purchase products. The retail list price is then established as the average wholesale price (AWP). The purpose of the AWP is two-fold: as the basis for reimbursement by third-party payers and as the base price for negotiations between manufacturers and private sector purchasers.[25] For brand manufacturers, this negotiation process is typically a discount based on a percentage of AWP or WAC.[26] Although pharmaceutical companies express a level of transparency generally about the process, it is not apparent how manufacturers create these algorithms or come to specific values placed on AWP or WAC. There have also been questions about the validity of AWP, often referred to as "Ain't What's Paid", and whether it truly represents the average price across the three major wholesalers.[27] This sticker price is easily manipulated and can often vary from the true acquisition cost by a large amount.

Wholesale Distributors

Three major distributors account for 90 percent of the market: McKesson Corporation, Amerisource Bergen Corp, and Cardinal Health, Inc.[28] These wholesale distributors are responsible for purchasing drugs from manufacturers to distribute to pharmacies. For branded products, the purchase price is fairly uniform with a discounted rate off of WAC, by volume or prompt pay.[29] For generic products, the purchase price is highly variable accounting for efforts to drive market share or the volume sold. The wholesale distributor then sells the product to pharmacies at WAC plus a negotiated percentage. Wholesalers oftentimes also facilitate discounts negotiated between manufacturers and pharmacies, distributing drugs to a pharmacy based on its negotiations with a different manufacture. In this case, they use chargeback as a pricing mechanism, which allows them to carry products for customers paying very different prices to manufacturers.[30] The distributor keeps track of sales under prices negotiated between manufacturer and pharmacy and charges back the manufacturer for the difference between negotiated price and WAC. The consumer, though, is completely unaware of these behind-the-scenes negotiations, particularly because there is no specific data released. Although wholesalers are clear that chargeback is a mechanism that can occur, the specific numbers behind it are obscure in the public eye.

Pharmacies

At the pharmacy level, negotiated contracts are created between wholesalers, pharmacies, and PBMs. In the past, retail pharmacies were able to sell drugs straight to the consumer. They now must enter into a relationship with PBMs and wholesalers. This creates constant tension between the three groups as each one is interested in profit-maximization. When a local pharmacy processes a prescription, they are given certain information, such as whether the drug is covered under a health plan and the reimbursement to which the pharmacy is entitled. This process can get thorny as pharmacies lack clear information regarding the determination of these reimbursements.[31] For example, there may be a significant difference between what a PBM pays the pharmacy for a prescription drug and what it bills to the health plan and consumer.[32]

Smaller retail pharmacies are able to join group-purchasing organizations (GPOs) where they can receive discounts by using this purchasing power to negotiate with wholesalers

23 Ellyn Sternfield, State Pharmaceutical Pricing Disclosure Laws: Old Story, New Refrain, Mintz Levin (Aug. 26, 2015), https://www.healthlawpolicymatters.com/2015/08/26/state-pharmaceutical-pricing-disclosure-laws-old-story-new-refrain/

24 Robert Langreth, Big Pharma's Favorite Prescription: Higher Prices, Bloomberg Business (Mar. 8, 2014), http://www.bloomberg.com/news/articles/2014-05-08/why-prescription-drug-prices-keep-rising-higher

25 Avalere, op. cit.

26 Department of Health and Human Services, Office of the Inspector General, Medicaid Drug Price Comparison: Average Sales Price to Average Wholesale Price, (Jun., 2005), http://oig.hhs.gov/oei/reports/oei-03-05-00200.pdf

27 Frederic R. Curtiss, Phillip Lettrich, & Kathleen A. Fairman, What is the Price Benchmark to Replace Average Wholesale Price (AWP)?, Academy of Managed Care Pharmacy (Sep., 2010), http://www.amcp.org/data/jmcp/492-501.pdf

28 Turner Investments, Why the Big Three Drug Distributors Could Get Bigger, (Jan. 28, 2011), http://www.turnerinvestments.com/why-the-big-three-drug-distributors-could-get-bigger/

29 Avalere, op. cit.

30 Ibid.

31 United States House Subcommittee on Regulatory Reform, Commercial and Antitrust Law, State of Competition in the Pharmacy Benefits Manager and Pharmacy Marketplaces, (Nov. 17, 2015), https://judiciary.house.gov/wp-content/uploads/2015/11/114-52-97631.pdf

32 Ibid.

or manufacturers. Some of these groups further reduce costs through direct rebate deals as well as mail-order and specialty services. Although pharmacies have a right to reimbursement, the actual amount that they are reimbursed is completely unknown to the public. Data regarding reimbursement to pharmacies available to the public is incredibly limited, and costs that pharmacies pass on, including dispensing fees and overhead costs, are also generally unknown.

Pharmaceutical Benefit Managers

As pharmaceutical benefit managers (PBMs) play a key role creating formularies by determining which pharmacies are used by their consumers as well as negotiating price, they have greatly increased their influence over drug pricing between different entities in the pharmaceutical supply chain. They initially contract with health plans to manage drug costs. According to research, PBMs will save consumers and payers almost $2 trillion in prescription drug costs—a 35 percent savings—over the next decade.[33] PBMs play an intermediary role between pharmacies, health plans, and manufacturers, receiving payment not only for services they provide health plans, including processing prescriptions and negotiating prices between pharmacies and wholesalers, but also based on performance metrics in contracts and rebates secured from manufacturers. This intermediary role could be harmed if transparency measures were put in place; it would challenge the value of a PBM's negotiating power.[34] PBMs have stated that their tactics as the middleman kept drug prices from rising more than five percent in one year.[35] However, there is significant controversy regarding savings and whether they are being passed on. In a recent lawsuit, Anthem, one of the nation's largest health plans, claimed that Express Scripts, one of the nation's largest PBMs, had not been transparent because an independent audit found that the insurer was overpaying by at least $3 billion annually.[36]

In past years, PBMs have come under scrutiny for undisclosed incentives from manufacturers, not passing manufacturer rebates on to plan sponsors, and driving beneficiaries to mail-order services, effectively inflating prescription drug costs for consumers. Health plans and pharmacies allege that PBMs typically achieve great discounts, but these discounts are not necessarily passed on to the consumer or the health plans that they contract with.[37] A recent letter from the National Community Pharmacists Association to Centers for Medicare and Medicaid Services expresses concerns about PBMs reimbursing pharmacies through an inaccurate "market price of acquiring a drug", a requirement of Maximum Allowable Cost (MAC).[38] The organization believes that pharmacies should be reimbursed based on the cost of a drug. When a prescription drug pricing standard is not published publicly, pharmacies are unable to discern if their reimbursements are consistent with contractual arrangements.[39] State legislatures are using transparency and fiduciary provisions to regulate PBM business practices. The provisions require PBMs to disclose all rebate, discount, and revenue arrangements made with drug manufacturers.[40] A PBM's potential fiduciary duty is what has created the most controversy. It requires PBMs to act in the best interest of health plans in a way that conflicts with their intermediary role, which is essentially the foundation of a PBM.[41] As the middleman, PBMs compile lists of preferred medicines for their health plans, based on negotiated prices with drug makers. But that does not necessarily mean that they are acting in the health plan's best interest when requiring a patient to follow step therapy on a preferred drug list which may be more costly to both the plan and patient.[42]

Legislation

Between 2006 and 2013, drug prices increased by 9.4 percent, and health care payers have been struggling to meet these rising costs.[43] In at least 11 states, measures are being taken on transparency due to the extreme costs of certain drugs as well as the steady increase of pharmaceutical prices over time. Legislation has been proposed in each of these states requiring manufacturers to justify their prices by disclosing costs of R&D, production, and marketing.[44] The goals of these measures are to educate policymakers and consumers on the rationale behind high drug prices, to shame manufacturers into creating more moderate prices, and to actually place a ceiling on prices in some states. The Pharmaceutical Research and Manufacturers of America (PhRMA) opposes these measures, stating that the information being sought by states is unrelated to pricing; pricing really involves the marketplace, competition, and how beneficial the drugs are.[45] By bringing about this discussion into pricing and transparency policymakers

33 Visante, Pharmacy Benefit Managers (PBMs): Generating Savings For Plan Sponsors and Consumers, prepared for Pharmaceutical Care Management Association (Sep., 2011), http://www.pcmanet.org/images/stories/uploads/2011/Sept2011/pbms%20savings%20study%202011%20final.pdf.

34 Ed Silverman, Anthem and Express Scripts War Could Change the Pharmacy Benefits Model, StatNews (Mar. 22, 2016), http://www.statnews.com/pharmalot/2016/03/22/express-scripts-anthem-drug-prices/

35 Ibid.

36 Ibid.

37 Steven Barlas, Employers and Drugstores Press for PBM Transparency, NCBI (Mar., 2015), http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357353/

38 Susan Pilch, Re: Non-Compliance of Part D Plans/PBMS With Federal Statutory Requirement Regarding Use of Drug Pricing Standards, NCPA (Apr. 1, 2016), http://www.ncpa.co/pdf/mac-letter-cms-2016.pdf

39 Ibid.

40 Prescription Policy Choices, PBM Fiduciary Duty and Transparency, AMCP, http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=12062

41 Ibid.

42 Silverman, op. cit

43 Michael Ollove, High Drug Prices Prompt Demand for Transparency, The Pew Charitable Trusts (Mar. 7, 2016), http://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2016/03/07/high-drug-prices-prompt-demands-for-transparency?utm_campaign=2016-03-07%20Stateline%20Daily&utm_medium=email&utm_source=Eloqua&utm_source=hs_email&utm_medium=email&utm_content=27035476&_hsenc=p2ANqtz-8WiuLA7SbOT8LASkjui7r77tivc0JM087Z3d3avI-Laq2xzLxWnnciS-X5l-quvMlDb-D3RyZFhRNNZEDhXNZ5hAJCrCG12VFHeLhjHXQgSHI_n9J0&_hsmi=27035476.

44 Pollack, op. cit.

45 Ibid.

have found a way to showcase the deliberate barriers that reduce the availability of affordable drugs to patients.

Conclusion

A drug manufacturer decides on the price of a drug. Between the manufacturer and the consumer, there are a number of stakeholders who play a role and may add additional costs that are felt by the consumer. There is a rationale that suggests transparency in the pharmaceutical supply chain increases the likelihood of lower prices. The reality behind that economic theory has yet to be proven. It is clear, however, that there is exceedingly little transparency in the current system. The complex relationships in the pharmaceutical supply chain are intertwined, and it is up to policymakers to determine what the appropriate amount of transparency in the supply chain is. While there is an argument to be made that transparency could lower prices, it is also possible that increased transparency could limit the ability of certain stakeholders to achieve deeper discounts. Policymakers must tread carefully because reversing course will be difficult once set.

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