

# Drug Money (Part 1): What Limits Competition in the Pharmaceutical Market?

## Introduction

In the last year, the public's outrage about high healthcare costs became more narrowly targeted on pharmaceutical companies. Two major stories about price increases on pharmaceutical products helped fuel the public's frustration. First in February, Turing Pharmaceuticals CEO Martin Shkreli testified before congress about his company's decision to raise the price of Daraprim, the drug used to treat parasitic diseases, particularly occurring in HIV and AIDS patients, from \$13.50 to \$750 per dose.[\[1\]](#) And then in November, Mylan CEO Heather Bresch testified before Congress about a nearly 500 percent price increase of the epinephrine delivery device used treat emergent allergic reactions, EpiPen.[\[2\]](#) These stories became symbolic of the growing financial burdens being put on consumers who rely on pharmaceutical drugs and devices. A poll conducted in September 2016 showed that four out of five Americans felt that drug prices are unreasonably high.[\[3\]](#) As election season rolled in, politicians tapped into public frustration about drug costs. Lowering drug prices became the only healthcare issue in the 2016 election that transcended party lines.[\[4\]](#) Some health policy commentators contend that pharmaceuticals have been unfairly targeted for criticism because other healthcare costs have more of a significant impact on overall spending.[\[5\]](#) However, in 2015, expenditures on prescription drugs rose faster than overall healthcare spending. [\[6\]](#) Despite the growing momentum in favor of addressing the ever-increasing cost of drugs, untangling all the factors that contribute to

pharmaceutical pricing will not be easy.

## **Factors Affecting Competition in Pharmaceutical Markets**

In order to explore the role of competition and the market in rising pharmaceutical drug costs, The Source is publishing this three-part issue brief series: *Drug Money*. This first brief in the series focuses on the key factors that contribute to the lack of competition in the pharmaceutical market, including (1) inherent characteristics of the market for pharmaceutical products|(2) laws and regulations inhibiting competition|and (3) generic delay tactics by pharmaceutical companies. Each of these factors is discussed in turn below. Much of the lack of competition in pharmaceuticals results not from any one factor, but from complex interactions between the economic forces, government regulations, and private actors.

### **1. Characteristics of Pharmaceutical Markets**

The market for pharmaceutical products exhibits several inherent characteristics that inhibit strong competition.<sup>[7]</sup> First, the pharmaceutical market is an innovation market.<sup>[8]</sup> Simply put, it is extremely risky and expensive to develop new pharmaceuticals. Pharmaceutical companies have very high fixed costs associated with researching and developing new drugs, and take large financial risks when innovating because new drugs may turn out to be ineffective or unsafe.<sup>[9]</sup> Economists estimate that the cost to successfully take a drug from the laboratory to market exceeds \$2.8 billion.<sup>[10]</sup> These high fixed costs create barriers to entry, making it challenging and time consuming for competitors to enter the market. Pharmaceutical companies have the ability to set and maintain high prices for their products

because so few competitors can enter the market and drive down prices.<sup>[11]</sup>

In theory, the high start-up costs for entering the market would be eliminated once a patent on a brand name drug expires, as generic competitors could formulate a competitor drug and flood the market with cheap alternatives. Brand name drugs are pioneer drugs that are the first of their kind in the market. These drugs typically cost more than generic drugs because pharmaceutical companies participate in years of research and development to invent their drugs.<sup>[12]</sup> Brand name drug companies are also burdened with costly investment in formal testing to prove the safety and effectiveness of the new drug in order to get FDA approval.<sup>[13]</sup> Generic drugs are nearly identical versions of their brand name drug counterparts.<sup>[14]</sup> While generics are much cheaper than brand name drugs, they are not lower in quality.<sup>[15]</sup> They contain the same active ingredients as the brand name drug, but they may include different inactive ingredients.<sup>[16]</sup> Generic drug companies sell their drugs at lower prices because they do not have to invest in research, development, and marketing, as do brand name drugs.<sup>[17]</sup>

Second, the pharmaceutical market is characterized by a low elasticity of demand, which means that changes in the price or quantity of pharmaceutical product in the market have little effect on the demand for that product.<sup>[18]</sup> Demand in this market is inelastic because consumers buy pharmaceuticals out of medical necessity, and alternative products (with the exception of generic alternatives) often make ineffective substitutes.<sup>[19]</sup> Thus, because of this low elasticity of demand, drug manufacturers have significant power when pricing their products.<sup>[20]</sup> As a result, many patients must accept higher prices because no viable alternative to their pharmaceuticals exist, and they must continue to buy their

pharmaceuticals in order to maintain good health.

High research and development costs and low elasticity of demand are inherent to the nature of pharmaceutical products. Producing safe and effective pharmaceuticals costs enormous amounts of money. Reduced supply or increased out-of-pocket costs of drugs does not substantially affect demand, because individuals rely on pharmaceutical products out of medical necessity. These factors are inherent challenges to promoting healthy competition in pharmaceutical markets. However, the United States has also adopted laws and regulations that purposefully inhibit competition in the pharmaceutical market in order to protect other interests. These constructed limitations make it easier for private actors to further limit competition in this market.

## **2. Laws Limiting Competition**

Strict regulatory programs, such as the patent system and Food and Drug Administration (FDA), can sometimes promote anticompetitive behavior. For the pharmaceutical industry, these two programs unfortunately facilitate a trade-off – restricting competition to promote other important interests. The FDA limits the pool of potential competitors in order to protect consumers through ensuring drug safety and efficacy, and also to promote new drug innovation and generic competition under the Hatch-Waxman Act. The patent system limits competition in order to promote innovation and public disclosure of new inventions. These regulations significantly restrict pharmaceutical company actions, but they also create potential opportunities for those companies to use these regulations to limit competition.

### **a) The Regulatory Basics**

A quick refresher on the basics of the FDA and the patent system

will help frame the later discussion about private actions taken to limit competition in the pharmaceutical market. The FDA primarily oversees the safety and efficacy of pharmaceutical products under the Federal Food, Drug, and Cosmetic Act.<sup>[21]</sup> In order to get a new brand name drug approved by the FDA, a drug maker must file a New Drug Application (NDA), which requires costly investment in formal testing to prove the safety and effectiveness of the new.<sup>[22]</sup> After approval of a drug, the FDA regulates the production and distribution of the pharmaceutical product.<sup>[23]</sup> This FDA approval process creates significant barriers to entry because pharmaceutical companies must front the expenses related to complying with the FDA regulatory scheme before selling pharmaceuticals.<sup>[24]</sup> Even after receiving FDA approval, if production and marketing is not up to FDA standards, the FDA has the power to slow down production, which also may contribute to high product prices.<sup>[25]</sup> Any new market entrants must have significant start-up capital and the ability to sustain a long runway on rollout. Each of these factors makes it more difficult for competitors to enter the pharmaceutical market.

Patents are particularly important to the pharmaceutical industry due to the high research and development costs required for creating new pharmaceuticals. The United States Patent and Trademark Office (PTO) awards patents, which give the owner of a patent 20 years of market exclusivity from the date of filing.<sup>[26]</sup> If another company puts a competing product on the market, the patent-holder can sue the infringing party for damages and an injunction to stop the infringement.<sup>[27]</sup> In defending against a patent infringement suit, the alleged patent infringer can raise a total defense to infringement by proving that the patent at issue is invalid.<sup>[28]</sup> This 20 year patent monopoly period allows the pharmaceutical company to raise revenue to recoup its investment in research and development,

and re-invest in developing new products.

Patents are not, however, always effective at protecting a pharmaceutical company's investment. Drug patents are often filed well before the drug enters the market. In some cases a drug patent expires before the drug actually comes to market.[\[29\]](#) On average, pharmaceutical drugs take about 12 years to move from discovery to market due to FDA approval requirements,[\[30\]](#) but some take longer than the twenty year patent term.[\[31\]](#) Congress sought to resolve this problem in the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act. [\[32\]](#)

### **b) The Hatch-Waxman Act**

The Hatch-Waxman Act strikes a balance between promoting the interests of brand name and generic drug companies. For brand name drug companies, the Act fixed the problem of a patent expiring before a new drug entered the market by creating FDA exclusivity grants for certain types of drugs that often have lower profit potential or longer approval processes.[\[33\]](#) To receive an FDA exclusivity grant, a brand name drug must either fall under (1) the Orphan Drug Act, for drugs intended to treat a disease or condition affecting fewer than 200,000 people in the United States| (2) New Chemical Exclusivity, for drugs containing a chemical that has not been previously approved by the FDA| (3) “Other” Exclusivity, for drugs used in new clinical investigations with results that have not been previously relied on by the FDA| or (4) Pediatric Exclusivity, for drugs used in new pediatric studies following a written request from the FDA.[\[34\]](#)

Like patents, exclusivity grants give pharmaceutical manufacturers a temporary monopoly to incentivize new drug development. If a drug qualifies for an exclusivity grant, the

FDA prohibits approval of competitor drugs for the length of the exclusivity grant, which can vary from six months to seven years, depending on the reason for the grant.[\[35\]](#) FDA exclusivity grants provide exclusive marketing rights to a particular company, potentially lengthening the time a drug manufacturer has exclusive access to the market. Exclusivity grants differ from patents, because the FDA grants them (not the Patent and Trademark Office), they protect only marketing rights (whereas patents cover a range of rights), and they must be granted at the time of FDA approval of a NDA or ANDA (whereas patents can be granted at any time during development of a drug).[\[36\]](#) Further, exclusivity grants are not required to run concurrently with the drug's patent term.[\[37\]](#)

The Hatch-Waxman Act also supported the interests of generics drug companies by making it easier for generics to compete in the market. Before the Act, the FDA allowed hastened approval through the Abbreviated New Drug Application (ANDA) for generic drugs originally approved before 1962, and the "paper-NDA" for generic drugs approved after 1962. These expedited review procedures failed to sufficiently spur generic drug competition.[\[38\]](#) The Act added three new policies which further encouraged generic drugs to come to the market. First, it shortened ANDA approval, thereby speeding up the generic drug approval process.[\[39\]](#) Second, the Act created a 180-day FDA exclusivity grant specifically for a generic applicant who is the first to both file an ANDA and challenge an existing patent.[\[41\]](#) Third, and perhaps most importantly, it allowed generic drug companies to litigate patent disputes with brand name drug companies before bringing generic drugs to market, rather than requiring them to enter the market before litigation.[\[40\]](#) Because of this change, generics could now enter the market by challenging a brand name patent during the patent term, or wait until a patent term expired as they had in the

past. When a generic does opt to challenge a brand name patent, it runs the risk of defending itself in a patent infringement suit.

In sum, the Hatch-Waxman Act incentivized innovation by extending new monopolies in the form of FDA exclusivities, while also attempting to spur generic competition by eliminating barriers to entry and providing incentives to enter the market. Unfortunately, some pharmaceutical companies have responded to increased generic competition by employing anticompetitive tactics to delay generic drugs from entering the market after a brand name drug patent expires.

### **3. Generic Delay**

In addition to the inherent characteristics of pharmaceutical markets and the legal systems inhibiting competition, in recent years, brand name drug companies have attempted to prevent competition from generic drugs through anticompetitive practices, known as “generic delay.”[\[42\]](#) Brand name drug companies engage in generic delay because once a drug no longer has patent or FDA exclusivity protection, generic competition will quickly erode monopoly profits.[\[43\]](#) Generic delay may come in many forms. Here, we focus on the following three generic delay tactics: (1) product hopping, (2) pay-for-delay, and (3) Risk Evaluation & Mitigation Strategies (REMS) based restrictive distribution.

#### **a) Product hopping**

Product hopping occurs when a brand name drug company makes minor modifications to a pharmaceutical product with an expiring patent, while also taking actions to reduce or eliminate the market for the original version of the product.[\[44\]](#) By making

even a small change to a product, pharmaceutical companies can receive a new 20-year patent on the product.[\[45\]](#) After re-patenting, brand name drug companies limit or discontinue the older version from the market and encourage physicians to shift patients to the modified version.[\[46\]](#) Pushing patients toward the new modified version of a drug erodes one of generic drug manufacturers main sources of revenue: generic substitution.[\[47\]](#)

Generic substitution laws allow, or in some cases require, pharmacies to automatically switch an individual's prescription from a brand name to a generic equivalent to save costs.[\[48\]](#) But generic substitution laws only apply to generics that are the exact pharmaceutical equivalent of a brand name drug on the market. If a brand name company has "hopped" to a modified product, then no generic equivalent for the modified version exists.[\[49\]](#) In some cases, brand name pharmaceutical companies effectively force doctors and patients to switch to the "new and improved" modified brand name drugs by discontinuing or delisting the original version.[\[50\]](#) By pushing patients toward a new modified product, brand name pharmaceutical companies prevent loss of sales to generics and maintain monopoly profits for another patent term. This revenue is all generated without high research and development expenses or risks because the modifications made to existing products are minor.[\[51\]](#) Perhaps most disconcerting, it is often questionable whether the minor modifications to brand name drugs have any meaningful therapeutic benefit for patients.[\[52\]](#) Thus, consumers end up paying higher prices for a drug with only minor modifications under the guise of a new and better product.

Product hopping came to light in *New York v. Actavis PLC*, an antitrust suit filed by the New York Attorney General, in which the Second Circuit Court of Appeal ultimately held that product hopping can violate federal antitrust law.[\[53\]](#) In the case, Actavis sold a twice-daily Alzheimer drug, Namenda IR.[\[54\]](#) As

Namenda IR was nearing the end of its patent, Actavis introduced a slightly modified version of Namenda IR, called Namenda XR, which was a once-daily extended release version of the drug.<sup>[55]</sup> Eventually, Actavis made a complete switch to the once-daily Namenda XR by discontinuing Namenda IR and requesting that the Centers for Medicare & Medicaid Services remove Namenda IR from their formularies.<sup>[56]</sup> The New York Attorney General sued Actavis, arguing that discontinuing Namenda IR and introducing Namenda XR violated federal antitrust law.<sup>[57]</sup> The Second Circuit concluded Actavis' conduct "forc[ed] patients to switch to the new version [of Namenda] and imped[ed] generic competition, without a legitimate business justification, violat[ing] § 2 of the Sherman Act."<sup>[58]</sup> The Second Circuit aptly recognized that product hopping artificially inflates drug prices by preventing generics from coming in to the market, without providing any meaningful benefit to patients.

More recently, in September 2016, thirty-four states and the District of Columbia filed an antitrust suit involving product hopping in the Eastern District of Pennsylvania.<sup>[59]</sup> The complaint in *State of Wisconsin v. Indivior Inc.* alleges that Indivior tried to force patients to switch from a tablet version of their brand name drug Suboxone, a schedule three drug used to treat opioid drug addiction, to a modified dissolvable oral strip version Suboxone.<sup>[60]</sup> The modification to the oral strip version of the drug occurred just before the patent on the tablet version of Suboxone expired.<sup>[61]</sup> The States argue that Indivior engaged in anticompetitive business practices to maintain its monopoly over Suboxone and prevent generic competition.<sup>[62]</sup> The complaint also alleges that Indivior attempted to delay approval of the generic Indivior tablet by raising "unfounded pediatric safety concerns" about the generic tablet.<sup>[63]</sup> If the states in *Indivior* can follow the success of the New York Attorney General in *Actavis* by showing that the

pharmaceutical manufacturer acted to unreasonably restrain competition, other product hopping cases are likely to arise and further reduce enthusiasm for the practice.

### b) Pay for delay

Pay-for-delay agreements between the brand name and generic drug companies diminish competition through a settlement in which the brand name manufacturer pays a generic manufacturer to stay out of the market. [64] In a pay-for-delay scenario, first a generic drug manufacturer files an ANDA with the FDA to enter the market as a generic version of a particular brand name drug.[65] Then, the brand name manufacturer sues the generic manufacturer for patent infringement.[66] Eventually, the brand name and the generic drug company come to an agreement, in which both parties agree to settle the lawsuit. In the settlement agreement, the generic drug company agrees to not challenge the brand name drug company's patent or sell a generic version of the drug for certain period of time.[67] In return, the brand name drug company pays the generic drug company to stay out of the market.[68] The brand name drug company pays the generic drug company more than what the generic company would have earned if it had been able to successfully challenge the validity of the brand name patent and enter the market.[69]

In some cases, the brand name drug company bringing the infringement suit does not have a valid claim against the generic drug company for patent infringement, because the brand name drug's patent is not valid.[70] Often the brand name and generic companies agree to the settlement because both companies face significant risks if the case goes to trial.[71] If a court holds the brand name drug company's patent invalid, the brand name company will lose profits because the generic drug company can immediately enter the market.[72] Alternatively, if a court finds the brand name drug company's patent valid and infringed

by the generic, the generic drug company will lose its FDA exclusivity and cannot enter the market.[\[73\]](#) When the brand name drug company's patent is invalid, the pay-for-delay settlement artificially extends the longevity of a patent that never should have existed.[\[74\]](#)

The Federal Trade Commission (FTC) brought the anticompetitive harms of pay-for-delay settlements to light in *FTC v. Actavis, Inc.* In that case, generic drug manufacturer Actavis designed a generic version of AndroGel, a brand name testosterone replacement therapy,[\[75\]](#) and filed an ANDA with the FDA.[\[76\]](#) Solvay Pharmaceuticals, who owned the patent for AndroGel, sued Actavis for patent infringement. The two parties ended the case by engaging in a pay-for-delay settlement.[\[77\]](#) The terms of the settlement required Actavis to agree to stay out of the market until the patent expired in nine years, and in return Solvay paid Actavis millions.[\[78\]](#) The FTC sued Actavis and Solvay, arguing that the agreement violated federal antitrust law. The Eleventh Circuit Court of Appeals dismissed the case, concluding that a pay-for-delay settlement did not violate antitrust law unless it extended monopoly rights beyond the normal patent term.[\[79\]](#)

In 2013, the United States Supreme Court heard the case, reversed the Eleventh Circuit decision, and held that pay-for-delay settlements are subject to antitrust law, and can be challenged to determine whether they constitute unreasonable restraints on trade.[\[80\]](#) While agreeing with the FTC's argument that pay-for-delay settlements are not immune to antitrust law simply because they apply during the remaining period of a brand name drug's patent term, the Court rejected the FTC's argument that pay-for-delay settlements are *presumptively* anticompetitive.[\[81\]](#) The Court said that those challenging pay-for-delay settlements will need to show that the settlement harmed competition under the customary "rule of reason"

analysis.[\[82\]](#) Whether a settlement violates antitrust law depends on factors such as “its size, its scale in relation to the payor’s anticipated future litigation costs, its independence from other services for which it might represent payment, and the lack of any other convincing justification.”[\[83\]](#) The decision suggested that “large and unjustified” settlements would likely indicate an unreasonable restraint on trade.[\[84\]](#) The Court also held that the validity of the underlying patent is not normally relevant to the antitrust question.[\[85\]](#) After providing this guidance, the Court sent the case back to the district court to determine whether Actavis’ pay-for-delay settlement indeed violated federal antitrust law.[\[86\]](#) The case is still in discovery as of January 2017.[\[87\]](#)

Finally, in 2015, the FTC [filed](#) a similar suit against Cephalon, Inc. for its pay-to-delay settlement blocking a generic version of its blockbuster sleep disorder drug, Provigil.[\[88\]](#) The FTC reached a [settlement](#) with Cephalon, which required Cephalon to agree to end pay-for-delay agreements and to pay \$1.2 billion in compensation for its conduct.

As these cases demonstrate, both brand name and generic drug manufacturers have engaged in concerted action to prevent competition in the pharmaceutical market, giving brand name manufacturers enormous power over the pricing of their products for long periods of time.

### c) REMS based delay

Brand name drug companies may also prevent generic drugs from entering the market by abusing the FDA’s Risk Evaluation & Mitigation Strategies (REMS) program or by implementing similarly restrictive distribution schemes. Nearly 40 percent of drugs approved by the FDA are subject to the REMS program.[\[89\]](#) The REMS program ensures that drugs with significant side

effects are properly used and administered.[\[90\]](#) The FDA has additional regulatory requirements for REMS drugs which come in many forms.[\[91\]](#) Elements to Assure Safe Use (ETASA), for example, is the most restrictive type of REMS and requires patient monitoring and testing, certifications for prescribers and pharmacies, and limitations on which hospitals and specialty certified pharmacies can dispense the drug.[\[92\]](#) Given that the FDA uses REMS to place limitations on the distribution of a drug, brand name drug manufacturers have abused REMS programs by using them to limit generic drug manufacturers' access to brand name drug samples, which are necessary for ANDA approval and market entry.[\[93\]](#)

When a generic drug company files an ANDA, it must prove that the generic drug is a bioequivalent to (i.e. expected to be the same as) the brand name drug by testing samples of the brand name drug against their generic drug.[\[94\]](#) The FDA requires the two types of bioequivalence testing: in vitro (lab testing) and in vivo (in human testing). REMS gives brand name drug manufacturers an excuse for refusing to give out samples of its drug to generic companies for this testing. Brand name drug companies restrict access by implementing a restrictive distribution system, and only allowing drug to be dispensed by approved hospitals or specially certified pharmacies.

This restraint allows the brand name drug company to refuse to sell its sample to a generic drug company, hindering access. Despite brand name companies claims that FDA policy prevents them from distributing samples, the FDA specifically allows brand name companies to sell samples to generic drug manufacturers.

Even if these access limits are only temporary, such barriers cost generic drug companies time and money.[\[95\]](#) Given that REMS abuse makes it more difficult for some generic drugs to get FDA

approval and enter the market, REMS abuse leaves the brand name drug company as the sole supplier of the drug. This allows the brand name drug company to maintain its monopoly profits and high prices, and raises overall prescription drug spending.[\[96\]](#) One study of forty generic drugs that REMS based delay tactics have prevented from coming to market estimates that \$5.4 billion in annual savings has been lost from REMS based delay.[\[97\]](#) REMS abuse is particularly concerning and dangerous for generic competition because the act is “not linked to patent protection and can continue indefinitely, even after the expiration of all exclusivities.”[\[98\]](#)

REMS based delay came to the public’s attention in 2015, when Turing Pharmaceuticals acquired pyrimethamine (Daraprim), a drug used to treat a fatal parasitic brain infection, and then raised the price of the drug by 5,000 percent.[\[99\]](#) Prior to being acquired by Turing, Daraprim was widely available and sold through wholesalers and drug stores.[\[100\]](#) Shortly before being sold to Turing, the drug suddenly switched to a restricted distribution through only one specialty pharmacy, without any clear or valid safety justification. This switch made it much more difficult for generic competitors to get the samples needed for bioequivalence testing. REMS abuse and REMS based distribution methods, without a legitimate reason to restrict the dissemination of the drug, facilitates these types of price hikes by preventing other manufacturers from entering the market to compete and provide alternative lower-priced options.

## **Conclusion**

High drug prices are associated with a number of factors, one of which is the lack of competition in the pharmaceutical market. This lack of competition is the result of the high costs

associated with developing pharmaceutical products, the approach the United States has taken to granting government-protected monopolies to drug manufacturers, and anticompetitive generic delay practices by pharmaceutical manufacturers.

Generic delay practices are particularly troubling because unlike FDA and patent exclusivity