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### Understanding Pharmaceutical Pricing in the United States

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# Understanding Pharmaceutical Pricing in the United States

By: Ashley Howe

May 4<sup>th</sup>, 2020

## **Abstract**

The issue of high drug prices in the United States is something that could go on forever due to the industry's profit maximizing design. Given the current time with the COVID-19 pandemic, many changes will be made to what Americans have considered a "normal lifestyle" for the past century. This will involve policy changes across many industries to keep Americans safe throughout the duration of this disease, and through any other virus to come. Hopefully, significant changes will be made in the pharmaceutical industry. This industry is unlike any other industry in the world, as all major players: hospitals, insurance companies, the government, middlemen, and pharmaceutical manufacturers act as profit maximizers. This paper gives an insight on how each of these players contribute to pricing pharmaceuticals and how the negotiation process works. Once a basic understanding of this complex industry is achieved, I will explain why and how pharmaceutical manufacturers can charge high prices for their products, even though they are financially burdening many patients. Excessive initial list prices and overprescribing are big issues in the industry, but the biggest problem I found is the ability to increase the price of a drug consistently throughout the duration of its patent, which could be up to 20 years. Now would be the perfect time to make significant adjustments to this pricing system that works in patients' worst interest, but if regulators and law makers choose to do so is a different story.

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## **I. Theoretical Framework**

### **1. What Makes the Pharmaceutical Market Unique?**

The biggest difference in the pharmaceutical industry than in almost any other industry in the world is asymmetric information and the opaque pricing system that results from it. Pharmaceutical companies clearly have more information on the therapeutic effect of drugs than patients do. Doctors may know the efficacy of the drugs, but they may not have the same objectives as the patients. Moreover, when a doctor prescribes a drug to a patient at a hospital or gives a patient a prescription for a drug at a pharmacy, the doctor may not know how much the drug will cost the patient. A drug manufacturing company produces drugs and sells them to middlemen and wholesalers who then sell them to pharmacies and hospitals. These players have to work out a deal with the patient's insurance company, often through Pharmacy Benefit Managers (PBMs), to determine what price the patient will pay. The price is determined through the patient's insurance plan which takes factors such as location, age, and pre-existing conditions into account.

This process is unique to the pharmaceutical industry. Take the clothing industry for example. When someone walks into a clothing store, each item displays a price tag saying exactly how much it will cost them. Imagine if these industries or any other sales industry had an asymmetric information environment where price discrimination was a norm. A person would go to the mall and pick out a shirt not knowing how much it would cost them. The person behind them could buy the same exact shirt. It could cost one person \$50, but it could cost the other person \$100 due to their different "clothing plan" based on their age, residency, occupation, etc. This would cause a whirlwind of issues, as people would see the different prices people are being charged for the same item. In the pharmaceutical market list prices of drugs are available to the

public, but the actual price a patient will pay is undisclosed. This is because each person is charged a different price based on their own personalized insurance plan. Many people in the United States say they are being overcharged for their drugs, but they cannot prove this, as there is no single price to compare it to.

Another difference is the concept of price shopping. In the clothing industry, when someone goes to purchase a dress, they have many different stores to choose from. If the individual chooses to shop at Gucci, the dress will cost on average around \$3,000, but if they choose to shop at Forever 21, the dress will cost on average around \$20. The quality of clothing is definitely better at Gucci, but probably not \$2,990 better. The person who is shopping at Gucci is paying a high price for the brand, while the person who is shopping at Forever 21 is shopping for a practical dress. In the pharmaceutical industry, this is not the case. Different locations will have pharmaceutical drugs available for different prices, even though there is no difference in quality, following the price discrimination policies of the pharmaceutical companies. However, these prices are undisclosed to the consumer and therefore, the patient must pay whatever the prescriber tells them to pay to get the necessary medication, even if it is far out of their price range.

## **2. Inelastic Demand**

Low elasticity of demand means that when the seller changes the price of a product, the demand for the product is not significantly influenced. This means that the percentage change in the price is higher than the percentage change in the quantity demanded. Many pharmaceuticals, especially those in rare disease markets, are necessary for many patients to survive, making them susceptible to predatory pricing policies of pharmaceutical manufacturers. With patents, a

manufacturer has explicit rights to their product, so competition is limited from the initial market date until patent expiration, which could be a twenty-year window. These two claims explain why it is easy and smart for pharmaceutical manufacturers to increase list prices on their products regularly. Their primary motive is maximizing profits, which turns into burdening the lives of many patients.

### 3. High Consolidation

In 2014, almost 2/3rds of the United States population under the age of 65 was enrolled in a private comprehensive health plan. 83% of these people were enrolled in a plan through Cigna, Aetna (now CVS), United, or Anthem/Blue Cross Blue Shield (Dafney 2015 2-3).

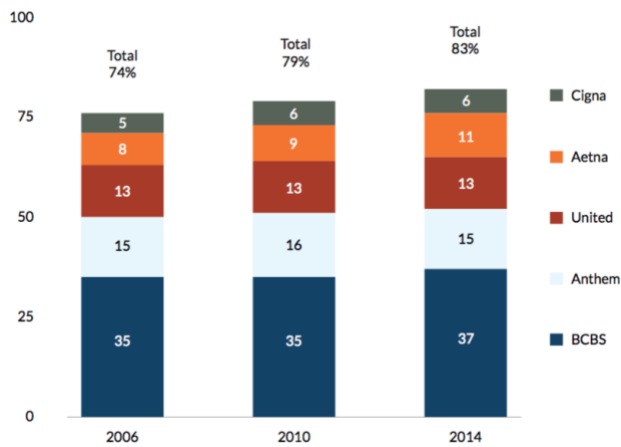


Figure 1: Estimated National Proportions of Market Shares of Top 4 Insurers 2006-2014 (Dafney 2015 2).

The percentage of market share these 4 companies had went up almost 10% in an 8-year window. Since the majority of the United States’ population used one of these four providers, one may think that these companies used their market power to negotiate lower drug prices from pharmaceutical companies. One also may think that hospitals, especially in highly concentrated

areas, have negotiating power for the same reasons. In other industries this would mean being able to negotiate lower prices on products for their consumers, while still achieving high revenue. This is not the case in the pharmaceutical industry as insurance companies and hospitals do not have direct communication with pharmaceutical companies. There are middlemen, often PBMs, that negotiate prices for pharmaceutical manufacturers through communication with hospital directors, pharmacies, and insurance providers. Once a drug is being administered to a patient, the pharmacies and hospitals speak to insurance companies about coverage and costs. Due to this extensive process and no direct communication between players, hospitals and insurance companies in areas with high consolidation have no increased negotiating power.

## **II. Introduction to Four Major Players**

### **1. Hospitals**

Hospitals price discriminate when it comes to their own care, but when it comes to pharmaceutical prices they are not given that “luxury”. Due to a variety of different insurance plans, each drug will cost a different amount for each patient. Even though medical professionals have no impact on how much the drug will cost a patient, they can overprescribe or choose which drug to prescribe if multiple have proven to be effective. Hospitals are profit maximizers, so doctors tend to overprescribe more often than not. Pharmaceutical companies send representatives to hospitals to promote their products and some doctors are incentivized to prescribe their drug. Even if the pharmaceutical companies are not telling doctors directly that they will receive a higher payment from overprescribing, the ones who do often receive money from these companies will continue overprescribing and telling their colleagues. As seen below for a research project done by Harvard University and CNN, out of about 400,000 doctors who



prescribed an opioid to Medicare patients, over half of them received a payment from the pharmaceutical companies directly (Kessler, Cohen, Grise 2018).

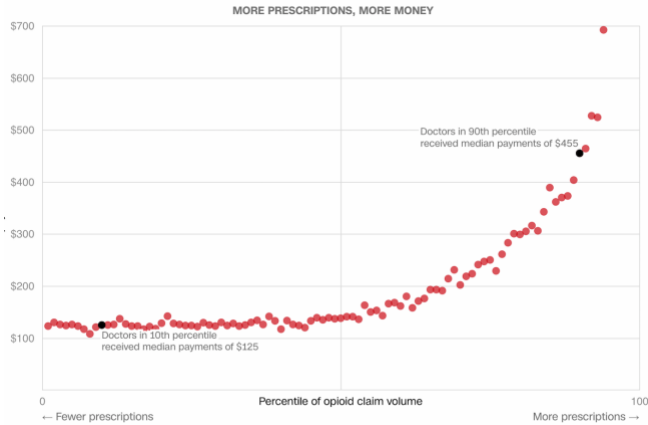


Figure 2: More Prescriptions Lead to Higher Payments (Kessler, Cohen, Grise 2018)

More than 200,000 doctors who wrote opioid prescriptions received payments from pharmaceutical companies that make opioids

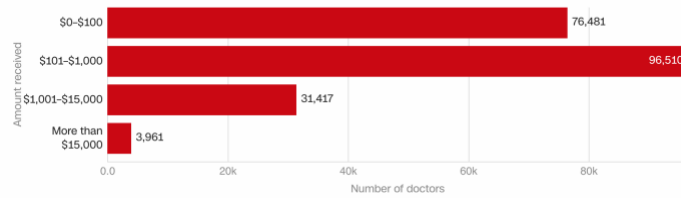


Figure 3: Monetary reward for prescribing opioids (Kessler, Cohen, Grise 2018)

By pharmaceutical representatives having direct contact with medical professionals through marketing their products and delivering financial incentives, they are able to convince some doctors to give out pharmaceuticals even when they aren't necessarily needed. The more pharmaceuticals used, the higher profit for the hospital and the pharmaceutical company, creating a win-win situation.

## **2. The Health Insurance Industry**

Health insurance company employees meet with PBMs to create formularies, which are lists of drugs that the insurance company will choose to cover. Each insurance company will have a different formulary, as well as different plan types for people with different conditions and lifestyles. When a person needs a pharmaceutical, they are either receiving it at a hospital or at a pharmacy. Neither the pharmacy or the hospital will know how much the recipient of the drug will be paying for it. They reach out to the patient's insurance company, directly or through PBMs, to see if the drug is on their formulary and how much of the drug the patient's insurance company will cover.

The pharmaceutical industry is the only industry where insurance works this way. For example, when you are getting a procedure done at the hospital it will cost a certain amount of money at that hospital and they will contact your insurance company to figure out how much the out-of-pocket costs will be. When you go to the dentist and get a cavity filled, the dentist can tell you how much the procedure will be before insurance, and then they send the information to your insurance company and you are given an out-of-pocket amount for the procedure. With pharmaceutical drugs, you are being prescribed a product where the list-price is likely unknown or astronomically high, and the out-of-pocket costs are calculated by many different players behind the scenes. There are rebates and discounts to help patients with costs, but many individuals believe patients are not given their full discount due to hospitals and PBMs wanting to maximize their profits, and their ability to relay imperfect information to the patient and their insurance company.

### **3. Government**

There are two government regulations that heavily contribute to high prices of pharmaceuticals in the United States, lack of negotiability and patents.

First, there is no direct communication between manufacturers and any players in the healthcare industry, besides middlemen, to establish pharmaceutical prices. This makes it so hospitals, government programs, pharmacies, and insurance companies cannot negotiate prices of pharmaceuticals for themselves, their patients or their members. This gives pharmaceutical manufacturers the ability to list their drugs at whatever price they choose and consistently raise them, as people have no choice but to administer their drugs to save lives. Negotiation limitations affect everyone involved, but Medicare gets hit hard, being one of the largest buyers of prescription drugs in the United States. This government-run program cannot negotiate drug prices with pharmaceutical companies by law, allowing pharmaceutical companies to charge highly unaffordable prices to one of the country's neediest populations (Cubanski 2019).

Second, in 1995 patent limits were extended to 20 years in order to be consistent with Trade Relations Aspects of Intellectual Property Rights (TRIPS) (Montalvo, 1996). This allows pharmaceutical producers to have exclusive rights to their product for 20 years. Acting as profit-maximizers, they charge high list prices for their products. They are able to consistently increase these list prices throughout the duration of their patent, as there is no threat of competition. Patent lengths have luckily not increased since 1995, as pharmaceutical companies could charge even higher prices for a longer period of time.

Both of these regulations act in the best interest of the pharmaceutical manufacturers which allow them to easily charge high prices with no consequence.

#### **4. Middlemen**

Now we know that along with drug manufacturers, hospitals, government regulations, and insurance companies are part of the pricing process for what a patient will pay. But how is this process of negotiation working?

When a patient goes to a hospital or doctor's office, the doctor does not know the price of the drug they are prescribing. When a patient goes to the pharmacy to fill a prescription the pharmacist does not know what the patient is going to be charged. A doctor fills out a prescription for a certain pharmaceutical and the pharmacy negotiates the price of this drug with the patient's insurance company. This is where PBMs come into play which refers to the middlemen who are the only people who know how much a patient will be charged for treatment. These people are negotiating directly with the drug manufacturers for the insurance companies, hospitals, and pharmacies to decide how much the insurance company will cover for each patient, how much of a co-pay each patient will have, and how the profits are split up between players. This is known as an oligopoly, where a market is "dominated by several businesses that administer drug benefits provided to most Americans by health-insurance plans. By negotiating with drug manufacturers on behalf of the insurers, these companies set the terms for most prescriptions, and they've gained further leverage through what economists call vertical integration: merging or forming partnerships with insurers, wholesale distributors, and chain pharmacies" (Tierney 2019). This is how well known pharmacies such as CVS can charge higher prices than a locally owned pharmacy.

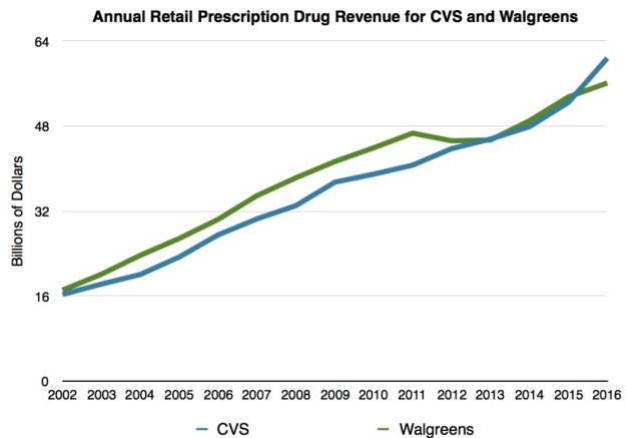


Figure 4: Annual retail prescription revenue for CVS and Walgreens (Belk 2018)

As seen from the figure above, CVS and Walgreens both were on track to quadruple their annual prescription drug revenue in about 15 years. This is due to the increased volume of prescriptions and the consistent rise of drug prices from the pharmaceutical companies.

PBMs are a main reason pharmaceutical companies are having their list prices be high, especially for pharmaceuticals that are curing rare-diseases. Drug manufacturers create high list prices and then coupons, rebates, and insurance come into play so that a patient does not have to pay the list price. There has been great discrepancy on if rebates and coupons are being used honestly. Annabelle Samimy, an analyst at Stifel Financial who covers Horizon says, “What you see between the gross price and net price is a big bubble – and we don’t know where the savings are passed on to.... the System in the U.S has created warped pricing. Everyone points fingers at each other and nothing gets fixed” (Egan 2018). Manufacturing companies have historically had issues negotiating with PBMs due to them believing PBMs finagle large discounts, keeping most of the money for themselves, and passing the leftover to the patients. While PBMs voice the same problems with hospitals and pharmacies saying they are giving patients less of a rebate

then agreed on, and pocketing the difference. Unfortunately, those outside of the industry cannot confirm or deny these claims due to the pricing information being private.

### **III. Pricing A New Drug**

There is a strict approval process from the FDA before a drug can be brought to market. Drugs have an initial screening phase, three phases of clinical trials and research, and then a New Drug Application (NDA) review. A drug becomes more and more expensive for the manufacturer each time it enters a new phase (FDA). Researchers at the MIT Sloan School of Management found that about 14% of drugs that make it to the first clinical trial stage will make it to market (Hale 2018). Pharmaceutical Research and Manufacturers of America, PhRMA, claims these drugs that make it through all phases cost about \$2.6 billion each to produce (PhRMA).

Once a drug is approved, the manufacturer needs to construct a list price to market the drug at. But how is this constructed? This is one of the biggest questions in America right now that no one seems to have a concrete answer to. The Kaiser Family Foundation conducted a study in 2019 that resulted in 79% of Americans thinking drug prices were too high. (Kirzinger 2019). The research and development (R&D) costs of developing new drugs are high, giving some reason for pharmaceutical producers to charge high amounts to make up for the high cost of production. The former CEO of Pfizer, Hank McKinnel has a different argument documented in his book, *A Call to Action*. He states, “How do we decide what to charge? It’s basically the same as pricing a car ... A number of factors go into the mix. These factors consider cost of business, competition, patent status, anticipated volume, and, most important, our estimate of the income generated by sales of the product. It is the anticipated income stream, rather than

repayment of sunk costs, that is the primary determinant of price” (Emanuel 2019). The former CEO of Merck, Raymond Gilmartin, believes pricing is based on the projected outcome of the drug, telling the Wall Street Journal, “The price of medicines is not determined by their research costs. Instead, it is determined by their value in preventing and treating disease” (Emanuel 2019). The former CEOs of two pharmaceutical companies in the United States, had two very different views on how pharmaceuticals are priced. Leaders in the pharmaceutical industry are known for making claims on how their drugs are priced, but fail to show data to back up their claims, leaving the true answer to how they price their drugs unknown. The most likely strategy, which pharmaceutical companies refuse to acknowledge, is drugs are priced unfairly to maximize profits. Each drug has a long gestation period and a low chance of succeeding, which is risky for producers. It makes sense that these manufacturing companies want to make the highest profit they can on drugs that are marketed because they do not know when their next success will be. Dr. Peter B. Bach, the Director of Memorial Sloan Kettering’s Center for Health Policy and Outcomes, agrees by saying high prices are directly correlated to drug companies being profit maximizers (Emanuel 2019).

## **1. Price Fluctuation**

The highest costing pharmaceuticals are those that cure rare diseases. The people taking these drugs are the ones that need the drug to survive, so it is a flawed system that these drugs would be priced the highest. It does make sense though as pharmaceutical producers need to make money off of their products and if only a couple new patients a year or every few years are going to use their product, it needs to be priced high to make up for production and R&D costs.

By drug producers continually increasing the price of their products, they can make up for the potential of lost revenue due to lack of usage in any given year.

In quarter one of 2019 over 500 drugs saw price increases according to FierceHealthcare GoodRx researchers found that among these drugs, it was not just rare disease medications that had price increases, generics and brand-name drugs increased by 2.9%. Also, the location where drugs are being sold has an impact on their cost. In New York drugs cost about 17% more than the national average, in San Francisco they cost about 14% more than the national average, and in Atlanta and Houston they cost about 20% below the national average. (Minemyer 2019). A city like New York City with high cost of living can have pharmacies charge more for pharmaceuticals than a city like Atlanta with a low cost of living. The average American is not going to shop around to find where they can get a drug for the cheapest in different towns, cities, or states, they will go to their local pharmacy and pick up what they need.

Any person can look on a website such as GoodRx and get coupons for almost any pharmaceutical drug on the market. A question I had when doing my research was why don't drug manufacturers charge less for drugs so then coupons aren't needed and insurance can just step in. Originally, the only answer I could come up with is that some patients may not know these coupons are available, so these drug companies, insurance companies, hospitals, and pharmacies could maximize profits. This may be a small part of the reason, but the answer is much more complex than that. Coupons are used as a price discrimination tactic giving consumers the ability to self-soothe. For drugs with substitutes, patients are driven towards the one that costs less each month, which is often the drug that has a coupon attached. Also, the producer of the coupon can discontinue the coupon at any time, leaving many patients without access to a drug they have been using for some time. Even though patients are spending less each month,



insurers are left to pay the difference which is often flipped into patients paying higher premiums.

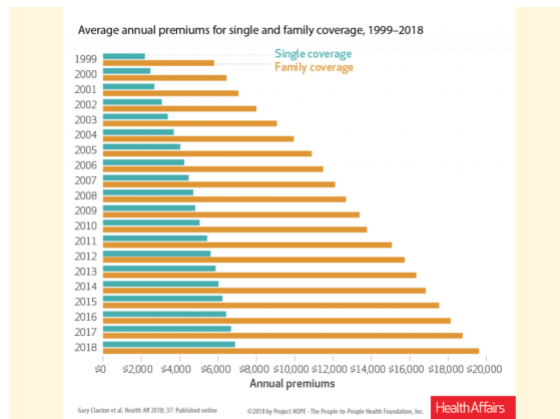


Figure 5: Average annual premiums for employer based single and family coverage 1999-2018 (NCSL 2018)

The average annual health insurance premiums for employer based insurance policies have increased every year from 1999-2018. Gradual market increases must occur to keep up with inflation, and individual plan prices change due to the conditions of the patients. The cost of overall family premiums doubled in about 15 years (NCSL 2018). The previous two criteria should not be enough to increase the prices this much, therefore I believe the increased use of coupons and dishonesty are greatly contributing. Patients think they are getting a great discount, but in reality they may not be better off, as the insurers are getting slammed, causing higher premiums for patients.

The Journal of the American Medical Association, JAMA, explored an example in 2013 of how coupons are affecting insurance companies regarding pharmaceuticals that lower cholesterol. Lipitor has an average of a \$30 co-pay per month, while Simvastatin has an average co-pay of \$10 per month. Pfizer produces a Lipitor Savings Card, which allows consumers to pay \$4 per month for the drug. This sounds like the best deal, as it is the cheapest for the

consumer, but the affect this \$26 price decrease has on insurance companies is shocking. The average insurer pays \$18 a month for Simvastatin, but \$137 per month for Lipitor (Schultz 2012). The prices of these cholesterol drugs are very cheap compared to many of the other drugs in this study, so imagine how big of an impact a coupon for thousands of dollars would have for insurance companies.

## 2. United States Drug Pricing Model

How pharmaceuticals are priced in the United States has been a question studied for centuries that has not yet been answered. The only pricing model that I have come across in my research was created by Z. John Lu and William S. Comanor. Their goal was to see a pattern in their sample of 144 drugs that came to market between 1978 and 1987 in the drug's initial price compared to existing substitutes and the drug's price 8 years after introduction. Through their research they developed the following two regression equations:

$$1) \text{ LREL P} = \beta_0 + \beta_1 \text{RATEA} + \beta_2 \text{RATEB} + \beta_3 \text{ACUTE} + \beta_4 \text{LNUM}(0) + \beta_5 \{ \text{DGEN or LPGN} \} + \varepsilon$$

$$2) \text{ LRATIO}(t) = \delta_0 + \delta_1 \text{RATEA} + \delta_2 \text{RATEB} + \delta_3 \text{ACUTE} + \delta_4 \text{LNUM}(t) + \delta_5 \text{DALP} + \delta_6 \text{DBLP} + \delta_7 \text{DCLP} + \delta_8 \{ \text{DCHGEN}(t) \text{ or } \text{LCHPGN}(t) \} + e$$

(Lu, Comanor, 1998, 110-111)

These equations do not state how a drug is priced, but how a drug's price can change over time. This model may have more accurate back in 1998 when it was introduced, but drug prices now are fluctuating more than ever, with no apparent pattern. Lu and Comanor separate drugs

into four different categories of severity to determine the price of them: acute pain, chronic conditions, topical agents, and emergencies. Each category has a different pricing method determined by their FDA ratings. FDA ratings shown by the “RATE A”, “RATE B”, and “RATE C” variables in the model correspond to FDA ratings of A, B, and C, where A is important therapeutic gain, B is modest therapeutic gain, and C is little to no therapeutic gain. The variation in importance of therapeutic gain refers to how essential this drug is compared to others of its kind, if there are any others. So, for example high therapeutic gain means this product is either the only treatment for a disease or it has leverage over others in terms of healing faster or more efficiently.

The chart below shows how drugs treating acute conditions varied in price over time. It can be seen that drugs with rating A were priced the highest and had price decreases over time. Drugs with rating B increased for the first 6 years and then stayed constant, while drugs with rating C rose for the first 4 years and then fell constant. It makes sense that drugs with rivals would continually raise prices, especially if their drug was most useful. Then, their competitors would adjust their prices, creating an ongoing circuit until they reached a common ground. These were drugs that were only used in the short-term by patients, so price adjustments made sense to adjust to the different number of patients each year.

FIGURE 1—REAL PRICES FOR NEW DRUGS INDICATED IN ACUTE CONDITIONS  
(SEMILOG SCALE)

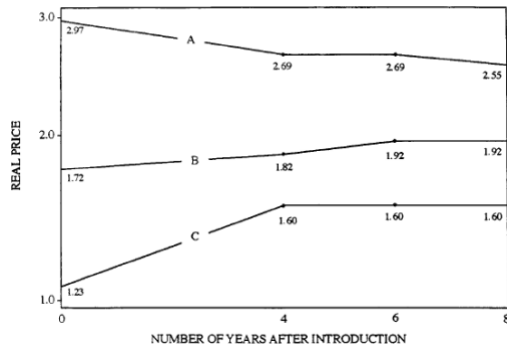


Figure 6: Real price changes for drugs for acute conditions introduced between 1978 and 1987 (Lu, Comanor, 1998, 110-111)

The next chart shows how drugs treating chronic conditions varied in price over time. Drugs with rating A were priced the highest and had slow price decreases over time. Drugs with ratings B and C rapidly increased until year 4, then essentially fell flat with slight decreases for the next four years. When a new drug is marketed people catch an interest in it and doctors are probably incentivized to prescribe it. The producers of this drug can maximize their profits by continually increasing prices during the drugs early stages, until usage starts to decline.

FIGURE 2—REAL PRICES FOR NEW DRUGS INDICATED IN CHRONIC CONDITIONS  
(SEMILOG SCALE)

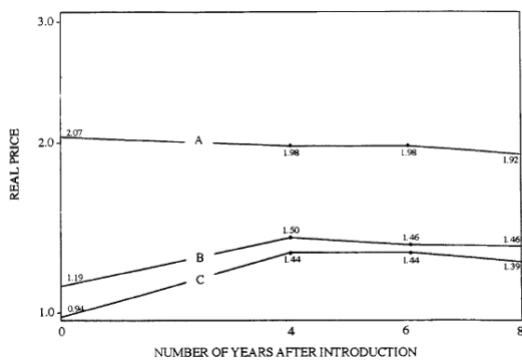


Figure 7: Real price changes for drugs for chronic conditions introduced between 1978 and 1987 (Lu, Comanor, 1998, 110-111)

Keep in mind that these charts represent drugs that were introduced between the years of 1978 to 1987. The TRIPS law was not implemented until 1994 and the patent on pharmaceuticals became 20 years in 1995. Prices were much cheaper and the market was not at its high competitive nature that it is at now. Comparing these charts to today, I would say drugs with B and C ratings in both markets show a similar trend, increasing for many years and then staying constant or decreasing based on usage. With the increased patent length, they tend to increase for a longer amount of time and at a varying pace. Drugs with a higher therapeutic gain still are priced higher than those with moderate or low therapeutic gain, as pharmaceutical companies are profit maximizers who want to make as much money as possible off of their unique product.

The biggest change in the industry today is the trends of drugs with high therapeutic gain, especially those that cure chronic diseases. These charts show a high initial list price, but a gradual decrease in price over time each year. My paper shows that drugs, especially the ones that cure rare diseases, have rapid continual price hikes, primarily due to profit maximization and patent length. The producers of the drugs want to make as much money as possible, while there are no other competitors in the market. Therefore, they establish a continual increase in price in drugs for many years, possibly for the entirety of their patents. These drugs increase over time, but there is no steady pattern to how this is happening or how the drugs were priced originally. Nicholson Price, an assistant Professor at Michigan Law School claims, “We don’t have a good model for pricing pharmaceuticals in this country and, as a result, we keep spending a lot more money... We avoid thinking about it, or avoid dealing with it, and as a result things get more problematic” (Luthra 2018). In Lu and Comanor’s paper we at least had insight into the pricing fluctuation trends, but now each drug has different trends, or lack thereof, so the average would not be a good representation.

An example of this is when the former CEO of Turing Pharmaceuticals, Martin Shrekli, increased the price of Daraprim from \$13.50 a pill to \$750 a pill overnight in 2015. It is a false assumption that Mr. Shrekli is in jail due to this incident, as he is actually in jail due to an unrelated securities fraud. Shefali Luthra from Kaiser Health News said, “On average, Medicaid programs in 2017 paid \$35,556.48 per Daraprim prescription, according to a Kaiser Health News analysis of federal data covering that year’s first three quarters”. Matt Salo, executive director of the National Association of Medicaid Directors, adds to this by exclaiming Medicaid is getting ripped off by covering Daraprim and with the still high costs of the pill and dosage of two to three pills per day, the costs for the drug are most likely higher now than they were when it had the price hike (Luthra 2018). Turing Pharmaceuticals, now Vyera Pharmaceuticals, is still charging high prices for their product because no generics have been brought to the market and they want to continue maximizing profits.

#### **IV. Case Studies of Pharmaceutical Manufacturers**

In 2019, seven of the twelve most expensive drugs in the United States were produced by one of three companies. Horizon Pharma produced two, Actimmune and Ravicti, Aegerion produced two, Myalept and Juxtapid, and Shire produced three, Cinryze, Takhzyro, and Firazyr (Paavola 2019). Seven out of the eleven most expensive drugs in the United States are currently produced by one of three companies. Amryt Pharma produces two, Juxtapid and Myalept, Horizon Therapeutics (formerly Horizon Pharma) manufactures two, Ravicti and Actimmune, and Takeda produces three, Takhzyro, Cinryze, and Gattex (Marsh 2020). The changes from 2019 to 2020 are: Shire got bought out by Takeda and Aegerion got bought out by Amryt, Firazyr is no longer on the top twenty list of most expensive drugs in the United States, and

Gattex moved its way into the top twelve after not being in the top twenty in 2019. This led me to want to answer two questions.

- 1) How can companies that produce the most expensive drugs in the United States get bought out?
- 2) Why are these companies pricing their drugs the highest?

## **1. Amryt**

Amryt Pharma, with a global headquarters in Dublin, Ireland and a U.S headquarters in Boston, completed the acquisition of Aegerion in September of 2019 after Aegerion filed for chapter 11 bankruptcy. This gave Amryt Pharma ownership of two of the most expensive drugs in the country, Myalept and Juxtapid, which generated \$136.5 million in revenue in the year 2018 for Aegerion. As high as this number is, it was not enough to make up for the \$35 million in debt Aegerion acquired falsely marketing Juxtapid, also known as Lojuxta in Europe, as well as annual R&D costs (Keown 2019). The FDA approved Juxtapid to cure the disease of homozygous familial hypercholesterolemia (HoFH), a rare disease causing high cholesterol that is inherited by the mutation in both parents being passed down to the child (The FH Foundation). Aegerion was also marketing this drug as a cure for high cholesterol not caused by this disease, being dishonest about the true benefits and side effects one may experience from taking it. According to the Wall Street Journal, this led to Aegerion being involved in a lawsuit in 2017 totaling \$40.1 million, where they still owe \$26.4 million in installment payments through the year 2021 for two misdemeanor violations of the Federal Food, Drug, and Cosmetic Act (Fitzgerald 2019).

The Chief Executive Officer of Amryt, Joe Wiley, believes “the acquisition of Aegerion accelerates (their) ambition to become a global leader in treating rare conditions to help improve the lives of patients where there is a high unmet medical need. By delivering two substantial revenue-generating products and an enhanced pipeline of promising development opportunities, this will significantly strengthen (their) growth in highly attractive markets globally”. He also added that this acquisition will allow Amryt to “deliver significant shareholder returns” (Keown 2019). When logging onto the Amryt Pharma’s website, the first words one will see are “Hope for those with the greatest need” (Amryt). Considering they are a company in the rare disease market, this is true, but how much hope are they really giving a patient when helping them survive could bankrupt them. Wiley touched briefly on helping those in need in his interview, but mainly discussed the profits this acquisition would grant his company. Aegerion had developed two of the most expensive drugs in the United States that were benefiting numerous people, but they were so caught up in profits, that they ended up becoming bankrupt due to their dishonest behavior. If Amryt stays out of legal trouble, they have a chance to help many people and be a huge power in the industry.

From 2019 to 2020, the list price of Juxtapid increased from \$40,671 per month to \$44,714 per month and the list price of Myalept increased from \$46,329 per month to \$71,306 per month, including a 9.9% price increase from December 2019 to January 2020 (Paavola 2019, Marsh 2020). The increase in price of Juxtapid is pretty significant, as it raised about \$50,000 per year over the course of 12 months. The price increase in Myalept is astronomical and there is no reasonable explanation for it. How Amryt employees price Myalept to be \$855,672 a year is insider information, but outsider hypotheses can be made to decide they want to maximize profits.



Lipodystrophy is an irregular spread of fat throughout the body and there are three different ways it can be acquired: generalized, inherited, and attained through different diseases including HIV. Myalept is the only treatment for generalized and inherited lipodystrophy. There are other treatments for acquired lipodystrophy if the patient is not experiencing leptin deficiency. Generalized lipodystrophy, on average, affects less than one out of every one million people and there have been about 250 cases of acquired partial lipodystrophy (MedicineNet). This means that Myalept is not a popular drug among the U.S population and it can be inferred that this is why the price has increased so much. Amryt wants to maximize profits in a small target market.

It is not public knowledge how much Amryt is charging the wholesalers and PBMs who buy their products, or how much Amryt and these middlemen are charging pharmacies, insurance companies, and hospitals. What we do know is each player is a profit maximizer. This implies that Amryt will charge the highest possible price to each player and in turn these players will charge the highest possible price to their consumers. Luckily, there are insurance companies that do not allow their patients to pay \$855,672 a year for Myalept treatment. Amryt offers co-pay assistance programs for those with insurance and free drug assistance programs for those without insurance and those whose insurance does not cover Myalept (Myalept). These assistance programs do not apply for those with Medicare or Medicaid and according to GoodRx, only 38% of Medicare Part D and Medicare Advantage Plans cover Myalept and there is still a co-pay of up to \$5,857 a year for this drug on these plans (Myalept GoodRx). The programs and insurance companies will make the drug as affordable as they can for patients, while still keeping their optimal profit in mind, meaning patients will still be charged very high prices.

Amryt Pharma has recently created a drug titled AP101 that is a cure for Epidermolysis bullosa, which is “a group of rare diseases that cause fragile, blistering skin” (Mayo Clinic). Amryt was not satisfied with their enrollment numbers for trial, so it delayed the target date of this trial back by a year. Investors are not convinced this drug will be a success due to their inability to increase trial enrollment by 25% in a year (Taylor 2019). However, if Amryt is able to do this in 2020, *EvaluatePharma* predicts when the drug goes to market in 2024, it will create \$193 million in revenue (Pleith 2019).

## **2. Takeda**

In January of 2019, Takeda Pharmaceutical Co. out of Japan completed the acquisition of Shire PLC out of Dublin for about \$62 billion. AbbVie Inc.’s attempt to buyout Shire fell through giving Takeda the opportunity to improve their wide range of pharmaceutical with rare disease curers (Terry 2018). Now, Takeda distributes 53 innovative pharmaceutical drugs in different market areas (Takeda), including three of the most expensive drugs in the United States in 2019: Takhzyro, Cinryze, and Firazyr (Paavola 2019). From 2019-2020, Takhzyro has increased from a list price of \$44,140 per month (Paavola 2019) to \$45,646 per month (Marsh 2020). and Cinryze has stayed constant at \$44,141 per month (Paavola 2019, Marsh 2020). Takhzyro is “a prescription medicine used to prevent attacks of hereditary angioedema (HAE) in people 12 years of age or older” (Takhzyro). According to the U.S HAE Association, this disease affects between 1 in every 10,000 people and 1 in every 50,000 people. Cinryze is a biosimilar drug for people age 6 or older (HAEA). Takhzyro was put on the market in 2018 and has had positive results for Shire and now is having the same result for Takeda. This drug is projected to be the top treatment for HAE. This explains why Cinryze has not had any price fluctuation due to

another drug of its kind made by the same manufacturer dominating the market, leaving Cinryze only for treating those between the ages of 6 and 12. In 2019, Firazyr had the 12<sup>th</sup> most expensive cost in the United States, but this drug did not make the top 20 in 2020 (Paavola 2019, Marsh 2020). This drug is a treatment for HAE in those age 18 or older (Firazyr), therefore the rapid price decrease is explained by the new, more effective drug, Takhzyro.

Gattex came in at the 11<sup>th</sup> most expensive drug in the United States in 2020 costing \$40,450 per month (Marsh 2020). Gattex is used to treat short bowel syndrome (SBS), which is a rare condition causing severe malnutrition (Shire US Inc.). The sudden price increase does not come by surprise, as in 2019 Gattex got approval by the FDA to expand their cliental to patients of one year of age or older with SBS (Takeda 2019). With this increase in demand, it can be assumed that Takeda increased the price to maximize profits from this larger pool of patients.

### **3. Horizon Therapeutics**

In 2019, Actimmune was listed as the most expensive drug in the United States at \$52,322 per month (Paavola 2019) and in 2020 it was listed as the fourth most expensive drug in the United States at \$52,777 per month (Marsh 2020). This drug treats osteopetrosis, a disorder causing abnormal bone development, and chronic granulomatous disease, a rare disorder resulting in complications to the immune system that affects about one in every 250,000 children (Actimmune). It has a patent expiration in 2022 (U.S SEC 2014). Ravicti, listed as the tenth most expensive drug in the U.S in 2019 costing \$33,572 per month (Paavola 2019), is listed in 2020 as the second most expensive drug in the U.S costing \$55,341 per month (Marsh 2020). Its purpose is to treat urea cycle disorders, which are “genetic conditions that result in high levels of ammonia in the blood” (GoodRx). It is used to treat the disorder that occurs in about one out of

30,000 newborns once they reach two months of age (Cincinnati Children's). At the end of 2018, the U.S Patent and Trademark Office issued two patents covering rights to Ravicti with expirations of 2030 (Business Wire 2018).

Actimmune is used by few people, as the disease it treats is rare, and the price has stayed consistent in the past two years. Ravicti is more common and has increased by a price of \$261,228 per year from 2019 to 2020 (Paavola 2019, Marsh 2020). The large price increase of Ravicti could be due to many different factors, but most likely they are taking advantage of the large profitability window they have for this drug for the next 10 years. However, while both of these diseases are rare and the treatment costs are very high, Horizon offers Horizon Patient Services which allows patients of certain diseases connect with others with that same disease, get financial information, and become educated on what the disease is and how to treat it. Almost all of the drugs they offer have their own savings programs that one must qualify for based on factors such as income level, location, and qualification for government funded programs. Even if a patient does not qualify for one of these programs, Horizon still works with insurance companies and provides financial assistance to insure affordability. They have provided \$1 billion in support every year since 2015 and take pride in knowing that no patient will be unable to afford the treatments that they offer (Horizon). Therefore, even though there was a large increase in the list price of Ravicti, this most likely did not greatly affect the amount patients are paying, more so what pharmacies and hospitals are paying to access this drug.

Horizon's primary products are medications that do not treat specialty diseases, so they are able to charge competitive prices in the specialty drug industry that do not greatly overcharge patients. However, even the non-specialty drugs that Horizon manufactures are part of the patient assistance program and some patients pay very little for them. Horizon manufactures Krystexxa,

a medication to treat gout, which was approved by the FDA in 2010 under the manufacturer Savient. Savient had to file bankruptcy and then sold the rights to Crealta, who sold the rights to Horizon in 2016. Crealta raised the price by 2.5 times once they obtained ownership and still did not see the results they were looking for. Horizon is taking a different approach to the drug by keeping a consistent price to Crealta, but also increasing their marketing efforts. They are marketing this drug alongside other drugs they manufacturer for maximum usage and to educate doctors on its reliability. They are ensuring patient cost reimbursement and they created a new dosing schedule to help eliminate side effects. Krystexxa gathered over \$300 million in profits in 2019, which exceeded the estimated \$250 million (Helfand 2016).

Horizon cleared a new treatment for Thyroid Eye Disease (TED) called Tepezza with the FDA in January of 2020. Tepezza was developed by River Vision through stage two and then was bought by Horizon for \$145 million in 2017. Horizon has spent about \$100 million during 2019 on research and development (R&D). This drug is projected to cost \$14,900 per vial, which equates to \$200,000 for a six-month treatment. After an 82.9% effective rate for 2-mm or greater reduction in proptosis during trial, it is projected that between 15,000 and 20,000 patients will seek treatment resulting in profits between \$30 million and \$40 million (Blakenship 2020).

Horizon CEO Tim Walbert claims, “We have the right balance sheet, we have two billion-dollar medicines to drive growth, and that will allow the cash flow to fund acquisitions that will help develop our portfolio” (Blakenship 2020). They want to use Krystexxa and Tepezza as their leading cost drivers. Acquiring drugs in their later trial stages will avoid high R&D costs, leaving more room for marketing and sales. Not developing their highest profiting drugs allows them to focus their attention on research and helping patients without worrying about going bankrupt. They are looking in the best interest of their patients by ongoing efforts to

limit side effects and educate all parties involved on what their products do. They are looking in their own best interest to maximize profits, but doing in a way with maintaining reasonable prices and reimbursement programs, so patients are not severely affected.

From all of this information, it is no surprise that Horizon Pharma's stock has continued to rise since May of 2017 from \$10.19 to \$36.04 per share, as of April 2020 (Yahoo Finance). Another factor contributing to Horizon's successes business is them "cheating" insurers by having people pay for the convenience of a product, not for the quality and manufacturing costs. They manufacture a drug called Vimovo, which was created by combining brand name drugs Aleve and Nexium. Aleve is a painkiller and Nexium treats stomach pain from pain relievers. If a patient bought these two products it would cost about \$36. Horizon claims that even though they are marketing Vimovo at a list price of \$2,979 per bottle as of 2018, about 98% of patients are paying less than \$10 out of pocket per bottle. Companies such as CVS Caremark and Express Scripts put bans on this drug from being in their pharmacies, so Horizon has negotiated with these companies through rebate programs to lower the cost for these parties (Egan 2018).

#### **4. Pfizer**

When looking into the company with the highest revenue in 2019, there was discrepancy between different sources. This was no surprise due to imperfect information in this industry. A pharmaceutical company that consistently ranked the top three is an American pharmaceutical company based in New York City. Pfizer obtained \$51.8 billion in revenue in 2019, with the help of their highest profiting drugs, Enbrel, Eliquis, and Prevnar (Pfizer 2019).

Enbrel is a drug that helps reduce joint pain and damage and improves physical function in individuals with severely active rheumatoid arthritis. The list price for Enbrel is \$1,389.24 per

50 mg dose, which is the recommended weekly dose for adults and the maximum amount for pediatric patients. Therefore, Enbrel costs about \$72,240.48 per year for the average user before insurance and copay programs. Pfizer is transparent with the cost of Enbrel and explains the average cost of a prescription with different types of insurance. For patients with commercial insurance, 76% of prescriptions cost \$50 or less per month, while the other 24% cost an average of \$469 per month. Through Medicare, 77% of prescriptions cost \$50 or less per month, while the other 23% of people are paying an average of \$415 per month. Through Medicaid, 93% of prescriptions cost \$10 or more per month and the remaining 7% of prescriptions cost on average \$239 per month. For those without insurance or have a plan that excludes Enbrel, the Amgen Safety Net Foundation will help patients gain access to the medication (Enbrel).

Eliquis is a drug that treats those with Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). It is listed at a list price of \$471 for a 30-day supply which is equivalent to about \$5,652 per year. Through insurance and co-pay programs, no patient will be paying this price. Patients with commercial insurance pay on average \$42 per month with 50% paying \$15 or less per month. Patients with Medicare pay on average \$46 per month with 50% paying \$35 or less per month and patients on Medicaid pay on average \$5 per month with 50% paying \$0. If a patient does not have insurance or their insurance does not cover Eliquis, the patient will have to pay the list price minus pharmacy discounts they can receive on the drug (Eliquis).

Pevnar 13 is a vaccine to prevent against diseases resulting from one of the thirteen strains of *Streptococcus pneumoniae* in those over the age of 18 and under the age of 65 (Pevnar 13). Many states require the students in their schools to have all four shots that are a part of this vaccination. In 2018, each shot cost almost \$180, which is over a 50% increase from their initial list price of \$109 per shot in 2010 (Sagonowsky 2017). With insurance, most patients are paying

no-out-of-pocket costs, so the cost increase may not seem to affect them, but this rise in price is contributing to increased premiums, deductibles, and overall government health spending. Sally Beatty, a spokeswoman for Pfizer, claims that the increase in price is necessary to cover research costs which is a common cover up by pharmaceutical companies (Sagonowsky 2017). In *The Ratcheting Price Of The Pneumococcal Vaccine: What Gives?*, a health policy professor at Johns Hopkins University, Gerard Anderson, has a different idea claiming Pfizer is raising costs to maximize profits on a Centers for Disease Control and Prevention (CDC) recommended patented product (Luthra 2017). This is a common case of conflicting information where those associated with a pharmaceutical company say high prices are necessary to counter high R&D costs, while researchers bring attention to the more likely case of being self-interested.

Pfizer also produces a drug called Vincristine, an injectable chemotherapy drug approved by the FDA in 1963. This is one of the country's oldest chemotherapy drugs that treats different forms of leukemia, lymphoma, and brain tumors in patients of all ages. In July of 2019, Teva Pharmaceuticals decided to stop manufacturing the drug due to its lack of profit making Pfizer the lone supplier (ASH Clinical News). Dyane Bunnell, MSN, APRN, clinical nurse specialist in hematology/oncology at Nemours/Alfred I. duPont Hospital for Children and secretary of the Association of Pediatric Hematology/Oncology Nurses and chair of their Drug Shortages Task Force, believes that this shortage could reduce the 5-year 90% event free survival rate in children in the United States (Healio 2019). This shows that Teva is self-interested because they discontinued a drug due to it not producing enough profits, not taking into account that lives could be lost because of it. Pfizer is taking the necessary steps to speed up production and make up for the shortage, but it will take time. According to Peter C. Adamson MD, professor of pediatrics at Children's Hospital of Philadelphia and chair of the Children's Oncology Group,



“the average sales price of a vial of vincristine right now is \$10.” (Healio 2019). It is listed on the World Health Organization’ list of essential medicines at \$42.60 per dose in the United States which is much higher than the average list price in developing countries at \$1.80 a dose (Kuttner 2019). This proves that even though a drug manufacturer is in the United States, it does not mean that a drug they manufacturer will be cheaper in the United States.

Pfizer is transparent with the list prices of their products and the increase in prices year after year, while other companies try to hide their massive price hikes. Pfizer advertises the list prices of their products along with the average price different patients with different insurance coverages would pay. They are raising the price of their drugs fairly and transparently and are still getting backlash. What these critics are failing to accept is in order to stay competitive in the pharmaceutical market, they need to raise prices over time. Pfizer’s profit maximizing products are not cures for rare diseases, so they do not need to worry about lack of usage. One could argue that the more transparent a company is with their prices, the more healthcare professionals will utilize their products. This could be true, as Pfizer is the most transparent company I came across in my research and they are creating high revenue. No matter if this statement is true or not, if it was used in advertisements, more companies may be willing to become more transparent with the prices of their products, helping solve our imperfect information problem.

## **V. Can the Overpricing Problem Be Fixed?**

The problem of high drug prices in the United States is not something that can be changed overnight and before the outbreak of COVID-19, I may have made the argument that it could never be changed. But due to the current state of our country and our healthcare system during the outbreak of this disease, it may be possible for changes to be made to help point us in

the right direction to lowered drug prices. Three primary issues in the pharmaceutical industry in the United States are lack of affordability, accessibility, and availability. By making it easier for patients to afford pharmaceuticals, the drugs become more accessible. The demand will become higher, making the manufacturer want to make the drug more readily available to make a greater profit. Through my research, I have developed a list of the top five changes I believe will make the biggest impact on the pharmaceutical industry, so that all players and patients can benefit.

Arguably the most important, but not currently feasible with our market structure, is perfect information regarding pricing policies and trends. The issue right now is that pharmaceutical manufacturers want to hide how they develop a list price for each of their products because they do not want each player and patient to see how much they are being overcharged. If pharmaceutical companies were transparent about how they priced a product, it would be clear to see if they were being fair or not. Pharmaceutical manufacturers should develop pricing models for each of their products and show how they plan to increase this price over time to keep up with inflation and still profit. All five major players are at fault in the overcharging scheme, but the pharmaceutical producers are at the top of the chain. Having the player at the top of the chain price fairly, could trickle down into each of the other players being forced to charge fairly. Due to the competitive profit maximizing industry, most companies would most likely not be willing to do this, so it may take government regulation to force this into existence.

An easy adjustment would be the length of patents and exclusivity. With the current laws, a drug can have a patent of up to 20 years, which cannot be renewed, and an orphan drug can have an exclusivity of 7 years which can be renewed. Some drugs have patent and exclusivity protection, while some have one of the other, and few have neither (FDA). With our current drug pricing regulations, or lack thereof, having pharmaceutical manufacturers create drugs that

cannot be replicated for 20 years allows them to increase the price of their drug on a regular basis for those 20 years. These companies have nothing, but maximizing profits on their minds, and have no incentive to think otherwise. There should be a reduction in patent length and a restriction on how much a drug price can increase each year. Drug prices must increase over time to match inflation, but there is no reason for them to increase 10% or 20% or even 50% in a given year, which currently happens. With this imposed restriction, drug companies will be tempted to market their drug at a higher price than usual, so they can still incur maximum profits. If this was combined with the symmetric information solution, drug companies would not price their drugs as high and would be forced to minimize price increases.

The Trump administration has continually discussed changing the 340B Drug Pricing Program which allows hospitals to get rebates for treating patients who are uninsured and patients who are on Medicaid. The idea of this program is for the pharmaceutical companies to provide drugs at cheaper prices to those who cannot afford them at their current costs. With the current pricing program, there is once again a lack of symmetric information. Pharmaceutical companies believe that hospitals are pocketing some the rebates, while hospitals say the patients are receiving the full rebates. Due to the pricing information not being public, there is no way of knowing if this is true or not. This can be solved through a legislation change where drug companies can negotiate directly with health and human-services representatives to work out reasonable prices that benefit each party involved and The Health Resources and Services Administration (HRSA) releasing 340B drug ceiling prices (Lim, Abraham 2018). With this change, the list price of these drugs can still be significantly higher than what pharmacies, hospitals, and ultimately patients pay, while being reasonable and affordable. Having these

prices be accessible to all players will be the only way to determine how reasonable the prices are, but this will take time to achieve.

Next is getting rid of rebates to PBMs and insurers. This would lower individual co-pays and allow players to have clearer information on the drug price. Keep in mind this would not directly decrease the high list prices pharmaceutical companies are charging. This would allow a smoother communication between players and not allow them to give the next player in line a smaller discount than decided on, causing more symmetric information. With more symmetric information in the industry, pharmaceutical companies will not create such high list prices, allowing increased accessibility for patients.

Lastly, an idea coming from *Making Medicines Affordable: A National Imperative*. The summary at the beginning of the book discusses changing legislation behind Medicare Part D drugs to regulate Medicare patients' out-of-pocket costs. With new legislation, insurance benefits would be redesigned to put a limit on out-of-pocket costs for Medicare patients, so that once patients reach their catastrophic coverage limit, they would not have any more out-of-pocket costs. Ideally, the insurance industry would calculate the patients out-of-pocket cost from the net price of the drug, not the list price, since that is an accurate depiction of what the patient is being charged. If insurance companies are currently calculating their coverage based on the list price of the drug, they are making a lot of money on Medicare patients. This is because the patient's out of pocket cost would be much greater when calculating using list price, rather than net price. The imperfect information problem would need to be changed for this to work efficiently, so that patients could see the cost of the drug, the cost and risks of implementing the drug, the overall cost of care, and if applicable, the cost of drug alternatives. The only way that insurance

companies would be willing to do this is if it was enforced by the government and new laws were in place enforcing out-of-pocket pricing guidelines and pricing transparency.

Having all five of these policies work together would be able to decrease pharmaceutical drug costs in the United States. Solving our asymmetric information problem should be the country's number one priority to start the journey of reducing pharmaceutical prices. Along with patients, pharmaceutical companies, insurance companies, and hospitals would all benefit in some way, even if they had a reduction in annual revenue. During the Covid-19 pandemic, there is going to be a change in regulations in almost every industry in the world, which will likely include the pharmaceutical industry. If adjustments are not made now regarding astronomical prices, then it will be even more difficult to adjust them in the future because we will be trying to change a newly implemented platform too soon.

## **VI. Closing**

To eliminate the high cost of pharmaceutical drugs in the United States, there needs to be accessibility to pricing information and a limit to price increases. The solution to the problem is quite simple, but the implementation is complex. Every player in the industry is a profit-maximizer, besides the patient who needs the pharmaceutical to treat a medical issue. It bottles down to ignorance that making the maximum amount of money is more important than saving as many lives as possible. The following chart developed by Pharmaceutical Executive shows the revenue of the highest profiting manufacturers in 2018. Different researchers have found slightly different numbers, which once again is caused by pharmaceutical companies not releasing all of their pricing information.

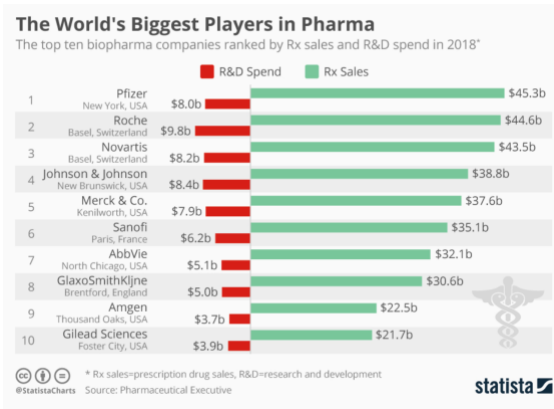


Figure 8: Sales and R&D costs of the top 10 pharmaceutical manufacturers in 2018 (Buchholz 2019)

The difference in sales and R&D for the company with arguably the greatest revenue in 2018 is about \$37 billion. The argument commonly made by pharmaceutical manufacturers is that they need to charge high prices for their products to make up for high R&D costs. As shown by the chart, this is clearly not the case as all companies are profiting over 4x their R&D costs. They can afford to have much lower prices and still make a profit of say 2x or 3x what they are spending on research and development. If a company does this and is vocal about what they are doing to improve patients well-being, doctors should be more willing to prescribe the product and patients will be more willing to use the product. This may be different for the rare disease market, as sometimes patients have no choice but to take a medication, but in markets where there is a choice, pharmaceutical companies may make up for their reduction in revenue with increased usage. Looking in patients' best interests may look like a losing battle for the pharmaceutical industry, but with increased regulation and price transparency, it would not have to be.

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