

The Complexities of the Pharmaceutical Industry and the Drug Pricing Challenge

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Abstract

The pharmaceutical industry, a dynamic sector integral to healthcare, is a highly complex field valued at nearly 1.5 trillion dollars. The sector encompasses the research, development, production, and marketing of drugs. Noteworthy companies like Pfizer and Bayer have played pivotal roles, tracing their origins to the 19th century. Presently, the industry is globally centralized, with developed and developing nations both participating. The industry's growth potential is vast, though developments face competition and challenges. The advent of COVID-19 has significantly impacted the industry, prompting both positive and negative effects. The drug pricing dilemma underscores the balance between profit and accessibility, spotlighting intricate ethical dilemmas. Regulatory systems like drug approval processes and pricing controls attempt to address these concerns. Government intervention seeks to strike equilibrium, but tensions persist between health and economics. Ethical controversies arise and are furthered by corrupt events such as the Thalidomide Scandal. Countries employ divergent pricing systems - the U.S. wrestles with private insurance, Medicare, Medicaid, and 340B programs, while European nations emphasize healthcare efficiency. The UK navigates compulsory licensing, global trade, and equity pricing. The pharmaceutical industry's multifaceted landscape traverses history, economics, ethics, and health, influencing and being influenced by global policies and perspectives. By analyzing varying strategies employed around the world and the evolution of the industry, leaders can progress towards a solution for the various challenges involved in drug pricing and the pharmaceutical industry as a whole.

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The Pharmaceutical Industry and its Origins

Author Elise VanDyke from Michigan State University writes, “The pharmaceutical industry is defined as the discovery, development, and manufacture of drugs and medications” (para. 1). VanDyke further explains that at the time of her article in late 2019, 119 million Americans relied on prescription drugs (para. 5). This number has only grown since, not to mention the millions of others who use prescription drugs worldwide. In 2019, approximately 1.7 million people worked in the pharmaceutical industry (Kristensen, 2:40). A video report from Xerfi Global states “The World Pharmaceutical Market exceeded the \$1 trillion euro threshold for the first time in 2017” (Mc Farland, 0:30). This same report predicted that over the next five years, from 2017 to 2022, the market would expand by a compound annual growth rate (CAGR) of 4%. However, a Yahoo Finance report found that “The global pharmaceuticals market had total revenues of \$1,112.6bn in 2020, representing a compound annual growth rate (CAGR) of 5.6% between 2016 and 2020” (“Global Pharmaceuticals Industry Report 2021: Market Had Total Revenues of \$1,112.6 Billion in 2020 - Forecast to 2025.”, 2021). This shows that the growth rate was even greater than expected.

This evidence proves the incredible size and role of the pharmaceutical industry in the global market, even before the recent COVID-19 pandemic. But how did such an expansive industry come to be? The pharmaceutical industry is very young compared to other primary markets in our world today. The origins of the industry can be traced back to the second half of the 19th century, when the ideas of the Scientific Revolution of the 17th century and the mechanical advancements of the Industrial Revolution were finally coupled. This 19th century development primarily occurred in three nations: Germany, Switzerland, and the United States.

The pharmaceutical boom in Germany is primarily represented by three companies: Merck & Co., GlaxoSmithKline, and Bayer. Merck & Co. originated from a pharmacy in Darmstadt, Germany, founded in 1668. In 1827, Heinrich Emanuel Merck inherited the pharmacy. A Pharmaphorum article written in 2020 explains that Heinrich Emanuel Merck revolutionized the company by shifting focus towards the manufacturing and sale of alkaloids (“A History of the Pharmaceutical Industry”, para 3). Alkaloids are organic compounds derived from plants with physiological effects on humans. Morphine is one such alkaloid. GlaxoSmithKline was another key company. Although the company originated in 1715, it wasn’t until “the middle of the 19th century that Beecham became involved in the industrial production of medicine, producing patented medicine from 1842, and the world’s first factory for producing only medicines in 1859” (“A History of the Pharmaceutical Industry”, para 4). Bayer is arguably the most notable of the early German pharmaceutical companies. Younger than GlaxoSmithKline and Merck, Bayer was founded in 1863, in Wuppertal, Germany. Although the company was originally founded as a dye maker, it soon moved into medicine, creating one of the most successful and well known pharmaceuticals at the start of the 20th century, aspirin. After major growth for the company in various parts of the world, Bayer’s aspirin trademark was stripped from the company after the first world war.

Prior to the rise of major pharmaceuticals, Switzerland was one of the leading textile producers in Continental Europe. Swiss printed cotton was unrivaled within Europe, akin to the finest found in the far east. As successful pharmaceutical manufacturers arose in Germany, Swiss textile manufacturers found that much of their dye materials had antiseptic and medicinal properties. Thus, they began to market them as pharmaceuticals. Pharmaphorum recognizes Sandoz, CIBA-Geigy, Roche and the Basel hub as key companies that arose from this trend in

mid 19th century Switzerland (“A History of the Pharmaceutical Industry”, para. 7). As mentioned earlier, Bayer has similar origins.

Across the Atlantic, the United States also played a key role in establishing the pharmaceutical industry. Pfizer, one of the most established and famed companies in today's industry, was founded in 1849 by two German immigrants in New York City, Charles Pfizer and Charles F. Erhart. The company was first founded as a fine chemicals business. Pharmaphorum reports that business boomed during the American Civil War as the demand for painkillers and antiseptics increased drastically (“A History of the Pharmaceutical Industry”, para 5). Colonel Eli Lilly is another patriot who can be described as a founding father of modern pharmaceuticals. Lilly served in the Union Army and established his own pharmaceutical business, one of the first to focus on research and development as well as manufacturing. Edward Robinson Squibb also became known as a leader in American pharmaceuticals during the mid to late 19th century. In 1856, Squibb invented an ether still apparatus which provided better quality ether, a form of anesthetic, and was much safer than previous strategies as it did not require exposing the highly flammable ether to a flame (“Squibb, Edward Robinson (1819-1900)”, para. 1). Squibb left the U.S Navy in 1857 to commit himself to improving pharmaceuticals after being exposed to impure medicine all throughout his military career. Ultimately Squibb established his own laboratory in Brooklyn, playing a major role in the supply of necessary drugs during the American Civil War and further advancements such as a new lightweight pannier box, a medicine chest used by doctors in the field. Beyond this, Squibb set a great example for future leaders in the pharmaceutical industry. The biographical report by the University of Alabama cited above further explains, “Edward Squibb was also known for what Lawrence Blochman calls his “rugged idealism”. He was committed to pure, quality pharmaceuticals manufactured and

distributed to high professional and ethical standards. Never patenting his discoveries and inventions, Squibb held onto the notion that anyone who wished to use them to benefit mankind should have the ability” (“Squibb, Edward Robinson (1819-1900)”, para. 3).

In the early ages of the pharmaceutical industry, there was almost no distinction between the “chemical” and “pharmaceutical” industries. Companies focused as much on prescription drugs as they did on other products such as oils, toothpaste, hair gel, and citric acid. In reality, the regulations we are familiar with today would not emerge until after World War II, when nations began introducing healthcare systems and after controversies such as the Thalidomide scandal of 1961. PharmaPhorum explains “After the war, the arrival of social healthcare systems such as the UK’s National Health Service (NHS) in Europe created a much more structured system, both for prescription of drugs and their reimbursement” (“A History of the Pharmaceutical Industry”, para. 12). For example, in 1957 the NHS declared a pricing plan which guaranteed reasonable returns on investment for drug manufacturers, incentivizing further research, while simultaneously maintaining reasonable pricing for consumers.

The Thalidomide scandal of 1961 caused severe birth defects and even death in thousands of newborns globally. Medical Doctor Ann Dally explains that after Thalidomide was first synthesized in 1953, the drug was highly praised, prescribed, and advertised as a safe sedative most effective in the treatment of morning sickness in pregnancy (Dally, para. 1). However, due to a lack of sufficient research on the drug's side effects, it was found to cause horrible abnormalities and deformities in unborn children. This tragedy prompted new legislation in the pharmaceutical industry including the Kefauver-Harris Amendment to the U.S Food and Drug Administration (FDA) in 1962 and the 1964 Declaration of Helsinki. These rulings mandated

proof of efficacy and clear declaration of side-effects and put greater emphasis on the ethics of clinical research, creating a distinct line between pharmaceuticals and chemicals.

The period between these reforms and the start of the 20th century, the interwar era, was critical for the development of the pharmaceutical industry. The interwar era was a period of international collaboration, prompting major developments and advances like none the industry had ever seen to that point. These key developments include the finding and development of insulin and penicillin, the globalization of the industry, and interbusiness partnerships.

In 1921, Frederick Banking and his colleagues successfully isolated insulin in order to treat diabetes, up until then a fatal disease. “In collaboration with the scientists at Eli Lilly that they were able to sufficiently purify the extract and industrially produce and distribute it as an effective medicine” (“A History of the Pharmaceutical Industry”, para. 13). This is just one example of interbusiness collaboration in the pharmaceutical industry during the early 20th century.

In 1928, Alexander Fleming first discovered the penicillin mold which exhibited antibiotic properties. Ernst Chain and Howard Florey took Fleming's discovery and expanded upon it in the early 1940's, further characterizing it and eventually producing a pure form of the antibiotic. After these developments, “a government-supported international collaboration including Merck, Pfizer and Squibb worked on mass producing the drug during World War II, saving thousands of soldiers' lives” (“A History of the Pharmaceutical Industry”, para. 14). This is another example of the trend of collaboration between independent companies to further pharmaceuticals during the period of both world wars. New drugs including analgesics also arose from this trend prompted by the war-time.

Surprisingly enough, both World Wars actually helped to bring the Pharmaceutical Industry together around the globe. As explained above, the growth in research observed both during and after the world wars prompted the teamwork of different companies, often between different nations, and even continents. Furthermore, after the war “in the UK, import duties incentivised many foreign companies such as Wyeth, Sandoz, CIBA, Eli Lilly and MSD to set up subsidiaries in Britain in the post-war years” (“A History of the Pharmaceutical Industry”, para. 14). This development foreshadowed the international span of the pharmaceutical industry today.

While the pharmaceutical industry does play a key role in the economy of every nation on the planet, the key companies of the industry are almost entirely centralized in a few nations. These nations largely have not changed since the industry first developed. In a lecture on the pharmaceutical industry, Kristoffer Kristensen, PhD, explained that today about fifty percent of the major companies of the pharmaceutical industry are located in the U.S including, Genentech, Amgen, Merck, and Pfizer (Kristensen, 2:50). An additional forty percent is located in Western Europe between Switzerland, Germany, and France including companies such as Sanofi-Aventis and Novartis. The final ten percent is spread throughout Eastern Asia and the rest of the world. Ultimately, the foundation of pharmaceuticals has not changed since the industry’s origin.

Developing nations with emerging pharmaceutical industries rely heavily on these established pharmaceutical companies. For example, Iran is an example of a developing country with a pharmerging market. Iran’s pharmaceutical industry is controlled by a national drug policy which focuses on generic-based medicines, price control, and the promotion of local production, with the policy last being updated in 2014. A research article from the Daru Journal of Pharmaceutical Sciences states, “Although more than 95% (in terms of sale volume) of marketed pharmaceuticals in Iran are produced locally, the dependence of the production of these

medicines on the import of raw materials is a challenging issue. Currently, more than half of the active pharmaceutical ingredients (API) are produced in the country, and the remaining are supplied by reputable companies in India and China, and in some cases by some European and eastern European companies” such as France, Germany, and Switzerland (Ayati et. al, para. 7). An article from Michigan State University further states “The increasing quality of life standards in developing nations has created another trend for pharmaceuticals as they focus on penetrating developing markets that have high growth. The exportation of research and formation of in-country pharmaceutical and biotech industries has become an important development for the industry. With ever-advancing technology allowing rapid innovation, companies are able to enter these markets more profitably” (“Pharmaceuticals: Background”, para 8). Essentially, already established pharmaceutical companies take over the industries within these regions, capitalizing on the nation's growth to benefit the company. This is a key reason why major change has not occurred in the leaders of the pharmaceutical industry since its origins in the 19th century.

This reality, paired with the colossal expense of modern research and the complexity of approval processes, limits the possibility for new findings from small, developing nations such as Iran. This creates a trend which furthers the centralization, even described as the “monopolization”, of the pharmaceutical industry.

Emerging companies and startups often make important findings from new, innovative ideas. However, these youthful and inexperienced companies often face difficulty funding their projects and in the approval process. At the same time, big pharma-companies with financial stability and approval experience often have difficulty constantly innovating. This provides the perfect opportunity for the two groups to pair, with the startup’s research being carried out but the final product being recognized as the property of big pharma. While there are exceptions, this trend

ultimately builds up big-pharma companies, ensuring their stability while also eliminating competition, explaining why the leading pharmaceutical companies in the 19th century still head the industry today.

This practice was essential during the peak of the Covid-19 pandemic. A University of Pennsylvania article explains “Drew Weissman, a professor of medicine in Penn’s Perelman School of Medicine, and Katalin Karikó, an adjunct professor at Penn and a senior vice president at BioNTech, together discovered that exchanging one of the four building blocks of messenger ribonucleic acid (mRNA) molecules could greatly increase its therapeutic potential” (para. 1). The research of these scientists proved key in 2020 during the search for a Covid-19 Vaccine. While Weissman and Karikó were most strongly connected to the young company BioNTech throughout their research, when demand for a Covid-19 vaccine emerged, their research was utilized collaboratively with the more established, global pharmaceutical leaders Moderna and Pfizer. This partnership allowed for the vaccination of over 5.55 billion people worldwide, approximately 72.3% of the Earth’s global population (Holder, para. 1).

In general, Covid-19 had a major impact on the pharmaceutical industry. Nayyareh Ayati and her team at the Tehran University of Medical Sciences in Iran stated “COVID-19 may be seen as a century’s opportunity for the pharmaceutical industry, as it increases the demand for prescription medicines, vaccines and medical devices” (2020). As a whole Covid-19 increased demand for pharmaceutical production and innovation while making the general population significantly more aware of the need for the goods which the industry produces. The global pandemic prompted staggering growth in the industry. A market research report from Fortune Business states “The global pharmaceuticals market size was valued at \$1,494.67 billion in 2021. The market is projected to grow from \$1,585.05 billion in 2022 to \$2,401.22 billion by 2029,

exhibiting a CAGR of 6.1% during the forecast period” (2021, para. 1). A similarly positive effect of Covid-19 was experienced in research and development. “According to the 2021 annual report of AstraZeneca, the total R&D spending in 2020 was \$ 5,991.0 million, which was increased by 62.5% in 2021, wherein the total R&D spending was valued at 9,736.0 million.” (Fortune Business, 2021) A study from IQVIA recognizes that clinical trial activity for a variety of conditions including COVID-19 witnessed an increase of 14% through the pandemic, from 4,891 trials in 2020 to 5,578 by the end of 2021 (Childs et. al, 2023). Despite the immense tragedy it entailed, the coronavirus pandemic acted as a true spur for the pharmaceutical industry which developed momentum and has continued to catalyze growth in 2023.

Despite augmentation to a variety of facets of the pharmaceutical industry, Covid-19 did hurt other spaces. The coronavirus caused supply-side disruptions for complete pharmaceuticals and pharmaceutical ingredients. A research article from the Samuel Neaman Institute for National Policy Research from March of 2020 explains “Drug makers are struggling to get vital raw ingredients for common antibiotics and vitamins from Chinese factories, which were closed for weeks as China battled to contain the coronavirus” (Maital et. al, p. 7). As a result of this many governments blocked specific pharmaceutical exports including those of keystone nations such as India. According to the India Brand Equity Foundation, India exported about \$19 billion worth of drugs in 2019, the year before Covid-19 fully emerged, and accounted for about one-fifth of the world’s exports of generics by volume. These pandemic period policies had cascading effects on economies throughout the world. Today in 2023, some nations are still working to recover from the harsh limitations imposed during the more threatening years of the coronavirus pandemic.

The Drug Pricing Challenge

Drug pricing is a complex and contentious issue that intersects with healthcare economics and patient access to medications. The current challenge of drug pricing revolves around the rising costs of certain medications, making them unaffordable for many patients. To understand this issue, it is essential to explore the drug approval system, which ensures safety and efficacy standards are met before medications reach the market. Fundamentals of drug pricing involve considerations such as research and development costs, production expenses, and anticipated demand, but striking a balance between affordability and profit remains challenging. Pricing control systems and payer cost control mechanisms, including government regulations, aim to maintain access and affordability. Perspectives from payers, companies, and consumers provide insights into the complexities of drug pricing, while market access considerations shed light on barriers and facilitators influencing pricing dynamics. Moreover, the interplay between health outcomes and economics emphasizes the need to develop pricing policies that prioritize both financial sustainability and population health.

The drug approval system in today's pharmaceutical industry is a rigorous and multi-stage process that ensures the safety, efficacy, and quality of medications before they can be brought to market (U.S. Food and Drug Administration [FDA], 2017). This system involves several key steps, including preclinical testing, clinical trials, and regulatory reviews. In preclinical testing, potential drug candidates undergo extensive laboratory and animal studies to assess their pharmacological properties and identify any potential safety concerns. Subsequently, drugs that show promise in preclinical testing advance to clinical trials, which consist of three phases involving human subjects. These trials evaluate the drug's effectiveness, safety profile, dosage, and potential side effects. The gathered data is then submitted to regulatory authorities such as

the FDA or the European Medicines Agency (EMA) for review and approval. Regulatory agencies assess the submitted data, examining the drug's benefits and risks to determine whether it can be granted market authorization. This meticulous drug approval system works to ensure that medications meet stringent standards and safeguards patient health and well-being during the pharmaceutical development process.

Fundamentals of Drug Pricing encompass various factors that contribute to the pricing of medications. Pharmaceutical companies take into account research and development costs, production expenses, marketing expenditures, and anticipated demand when determining drug prices (Lichtenberg, 2019). Additionally, they consider the need to generate profit and return on investment. However, striking a balance between ensuring affordable access to medications and allowing companies to recoup their investments remains a significant challenge.

Pricing control systems and payer cost control mechanisms play a crucial role in shaping drug pricing dynamics. Governments often implement control mechanisms to regulate drug prices and ensure affordability. These mechanisms can include price negotiations, reference pricing, and the establishment of formularies that determine which medications are covered by insurance plans (Danzon et al., 2019). The aim is to control rising healthcare costs and promote equitable access to essential medications. However, finding the right balance between controlling prices and maintaining incentives for innovation can be a delicate task.

The issue of access and profit arises from the tension between ensuring patient access to necessary medications and pharmaceutical companies' need to generate revenue. High drug prices can create barriers to access, especially for those who are uninsured or underinsured. This poses ethical and public health concerns, as individuals may be unable to afford critical treatments. However, pharmaceutical companies argue that high costs reflect the investment

required for research and development, clinical trials, and obtaining regulatory approvals (Hernandez et al., 2020).

Despite claims supporting the current drug pricing system, in practice it is clear that the benefits of drug research and pharmaceutical access are not shared equally throughout the world. A Yale study analyzing newly approved drugs between 2012 and 2014 found that of 563 trials in which location information was available, only 15% of drugs were approved in every country which hosted trials five years after their approval. Furthermore, this same study found that “among the 70 countries that contributed research participants, 7% (five countries) received market access to the drugs they helped test within a year of FDA approval and 31% (22 countries) did so within five years” (Cummings, 2021). Drug approvals were expedited in wealthier nations like Germany and Canada, whereas accessibility was significantly limited in Africa, with the exception of South Africa. The study explains that in Africa, none of the medications were accessible anywhere else, and even in South Africa, access to only 24% of the drugs was granted after a five-year period (Cummings, 2021). This lack of accessibility turns already dire situations worse, with focuses being turned away from a hopeless pharmaceutical industry and towards other expenditures. This lack of pharmaceutical focus directly contributed to the breakout of HIV and subsequently AIDS from Central Africa as well as a variety of other epidemics. These nations continue to be ravaged by a poor pharmaceutical system today, relying on the charitable works of organizations such as the Red Cross rather than an established system.

Pharmaceutical corruption in regards to the drug pricing challenge however is by no means limited to struggling third world countries. In September of 2015, American Investor Martin Shkreli and his company Turing Pharmaceuticals obtained the manufacturing license for Daraprim, a life saving drug for parasitic infections. After attaining full control of the

manufacturing license, Shkreli and his team increased the price of the drug by over 5,000% overnight. The U.S Federal Trade Commission states that Shkreli's team's "anticompetitive scheme prevented generic competition and allowed them to protect their Daraprim price increase from \$17.50 per tablet to \$750 per tablet" (Vedova, 2023). For his violations of free trade principles Shkreli was finally tried and sentenced to seven years in prison in 2018, but was released from a low-security prison after four years in May of 2022. In the period from 2015 to 2018, Turing Pharmaceuticals is reported to have made \$64.6 million in excess profits. Furthermore, despite Shkreli's trial and subsequent fining and imprisonment, a rebranded Turing Pharmaceuticals, now known as Viera Pharmaceuticals, still maintains rights to the manufacturing of Daraprim. The price for Daraprim still has not shifted from \$750 a pill. There has been a repeal of many of Turing's initial monopolistic policies that has opened the market to generic versions of Daraprim for cheaper prices and better market access. Many insurance policies still supply Daraprim to customers rather than newer generics. These policies continue to support the rebranded Viera Pharmaceuticals, a subject of major ethical controversy.

Ethical Controversy

The ever-controversial drug pricing challenge is rooted in ethical debate. Contention arises in issues such as the right to patient access, the funding of new technologies, and compulsory licensing. Government policies further the controversy; arguments arise over how much control the government should have in economics as a whole and the extent to which the government should be able to limit a particular part of the market. Ed Schoonveld describes this controversy in his book *The Price of Global Health* saying "an industry that should be hailed for bringing great improvements in patient well-being has stunningly slipped in image to or below the ranks of tobacco and gun manufacturers" (p. 227).

The issue of patient access seems to have a clear answer: everyone deserves access to healthcare, no matter income, nationality, race, and other demographics. This patient access challenge is nowhere near this simple. The true issue is found in who can pay and for those who cannot, what should be prioritized. Struggling groups such as third world, developing countries simply cannot provide citizens with access to healthcare as other nations such as Canada and the United States have proven able. Solely looking at healthcare expenses within these countries, funding must first be provided for acquiring clean water, doctors, nurses, and developing healthcare infrastructure. Furthermore, many of these nations push funding away from the healthcare and pharmaceutical industries for other economic and political reasons.

These ideas are clearly evidenced in the nation of Libya. Libya is a North African nation plagued by civil war. In 2011, author Richard Sullivan stated that “Libya has been justifiably feted as one of the world's great success stories in public health. Its ability to deliver low cost healthcare with good outcomes is held as a model for other developing countries... But all this is changing. The conflict in Libya is already altering mortality and morbidity rates as well as degrading public healthcare systems” (paras. 1-2). As seen by Sullivan’s text, the extent to which Libya’s civil war would affect the healthcare system was still unknown several years ago. Today, we can see that the civil war has decimated the once-successful Libyan healthcare system. Fighting has destroyed countless hospitals and clinics. Water and electricity shortages are widespread, limiting the range and quality of care. Government funding is pushed towards weaponry rather than rebuilding the healthcare system. All of this was furthered by the Covid-19 pandemic. Not just Libya, but many nations deal with such issues damaging and preventing the rebuilding of their healthcare systems.

Situations such as that in Libya also further the debate over the funding of research and new drug technologies. In recent years, great progress has been made in fields such as gene therapy, Artificial Intelligence and machine learning, cloning, and personalized medicine. All of these fields will revolutionize the treatments of diseases such as cancer and diabetes. However, their promise of immense success is paired with funding burdens, funding burdens that many would argue are unnecessary at this current time.

Many believe that the distribution of “essential drugs” should be prioritized over studying new, unproven technologies. A major impetus for this argument was the deficient response to the HIV and Aids pandemic around the world. According to the World Health Organization, this pandemic has killed about 40 million people and about 38 million people are currently infected with it worldwide. Drugs to treat and prevent these diseases have long been a topic of debate primarily due to pricing issues (Table 1). In the same text mentioned above, Schoonveld explains “Drug companies have been hesitant to supply HIV / AIDS drugs at lower prices because of past issues related to global price differences” (p. 226). Disagreements over pricing, an insufficient supply, and a distribution effort with a major lack of communication prevented the drugs from getting to areas where they were needed most. With so many complexities already present in the pricing and distribution of previously researched and proven drugs, many say we cannot prioritize new research and technologies.

Many nations, such as Brazil and South Africa supported compulsory licensing as a solution for pricing and distribution challenges with HIV / AIDS treatments. Compulsory licensing is seen by many as a solution to the drug pricing challenge as a whole. The World Trade Organization explains “Compulsory licensing is when a government allows someone else to produce a patented product or process without the consent of the patent owner or plans to use the

patent-protected invention itself' (para. 1). Article 31 of the Agreement of Trade-Related Aspects of Intellectual Property (TRIPS) outlines the issuing of compulsory licenses for patented pharmaceuticals. For a reasonable license fee determined by the government, the government is authorized to produce a version of the patented product when necessary. For obvious reasons, the idea of compulsory licensing is greatly controversial.

While producing non-branded cheaper alternatives is beneficial for increasing supply and reducing the price of pharmaceuticals it sparks moral debate over the extent to which the government should be able to interfere with the patents and productions of individual companies. Furthermore, pharmaceutical companies directly oppose price differences between nations and products as it often forces them to reduce the price of their own, previously established products. While government interference appears to be the most direct and authoritative way to solve the drug pricing challenge, it furthers the complexities of the moral and ethical debate.

In Canada and Australia, tight restrictions have been placed on health economics adhering to the set guidelines of each province. The governments within these nations strictly follow the positions of drug prices and often force limitations upon independent companies and their products. Germany's implementation of the Arzneimittelmarkt-Neuordnungsgesetz (AMNOG), a price control legislation, clearly illustrates governments further involvement in the pricing of drugs. This directly opposes ideals of free trade which many support and believe should command the pharmaceutical industry. Government interference policies create major debate between nations such as the U.S, where free trade and trends of laissez faire economics are idolized and important.

Restrictions on prices further contention between governments and pharmaceutical companies. When prices are forced to be reduced in particular regions, issues over pricing develop

elsewhere. This idea was evidenced by the Clinton administration in the 1990's. The administration reprimanded companies for supplying essential children's vaccines to developing countries for less than the prevailing prices in the U.S (Schoonveld, p. 230). The administration argued that not all Americans had equal access to key drugs, facing similar challenges to citizens of those developing nations.

Suspicious and lenient punishment for crimes in the pharmaceutical industry represent arguably the most daunting disputation in regards to pharmaceutical morality. Rofecoxib, marketed as Vioxx, was a drug first introduced by Merck & Co as a safer anti-inflammatory, pain-relieving drug as treatment for disorders such as arthritis. Vioxx was on international markets for five years from 1999 to 2004, with nearly 107 million prescriptions being distributed in the United States alone (Kruhmholz, para. 17). From the initial stages of Vioxx's development, certain scientists within Merck expressed apprehension regarding the potential negative impact of the drug on the cardiovascular system. This concern was furthered by a variety of internal tests during the research paper including one which recognized a 79% greater risk of death or serious cardiovascular events as a result of treatment (Kruhmholz, para. 5). However, recognizing the lucrative potential of Vioxx, leaders at Merck sought to conceal this harmful reality. Primary tests were directed away from the cardiovascular system and readings on the affects to the cardiovascular system were taken from loosely related analysis. Similarly, in order to soften the interpretations of Vioxx's effects, Merck swayed the literary techniques of authors in academic manuscripts - "for example, they changed "systemic biosynthesis of prostacyclin ... was decreased by [rofecoxib]" to "Cox-2 may play a role in the systematic biosynthesis of prostacyclin"" (Kruhmholz, para. 4).

This manipulation continued to grow during the infamous VIGOR study. In January 1999, Merck initiated the Vioxx gastrointestinal outcomes research (VIGOR) study, marking their most extensive investigation of rofecoxib to date. The primary objective of this study was to demonstrate that rofecoxib, as a treatment for rheumatoid arthritis, would result in fewer gastrointestinal side effects compared to naproxen, a similar drug. A key part of this study was that the board would be independent, with no personal bias in the monitoring of the trial. Despite this, “the head of the VIGOR board was awarded a two year consulting contract two weeks before the trial ended and as the trial was concluding disclosed family ownership interest in Merck shares worth \$70,000 (£37 000; €55 000)” (Kruhmholz, para. 9). The report ultimately emphasized the false safety of rofecoxib and promoted the production and distribution of Vioxx.

From 1999 to 2004, the distribution of Vioxx was devastating, directly causing the deaths of tens and possibly even hundreds of thousands of people. A study conducted by D.J Graham and his team revealed that Vioxx users faced a 34% higher risk of heart attacks compared to non-users. The study also found a significant increase in the risk of ischemic strokes among Vioxx users (2005). These alarming findings led to the voluntary withdrawal of the drug from the market by Merck in 2004.

After Vioxx’s withdrawal from worldwide markets, Merck & Co. was set to face punishment. An article from the United States Department of Justice states that the American pharmaceutical company “agreed to pay \$950 million to resolve criminal charges and civil claims related to its promotion and marketing of the painkiller Vioxx (rofecoxib)” (2011). This plea includes a civil settlement of over \$650 million. Of this civil settlement \$426,389,000 was recovered by the United States, and the remaining share of \$201,975,000 was distributed to the participating Medicaid states (USDJ , 2011). While at first this punishment seems reasonable, under closer

examination a more corrupt reality reveals itself. The Wall Street Journal recognizes that Merck profited over \$11 billion dollars from Vioxx ; all of these profits beyond the first billion required for the plea were kept by the company. Furthermore, the civil settlement placed the money into the hands of the U.S government, which funds a large portion of research done by companies such as Merck and provides major tax breaks for large pharmaceutical companies, and to Medicaid systems. Pharmaceutical companies profit from Medicaid partnerships as doctors are more likely to prescribe their drugs to a wider range of Americans. Ultimately, when Merck & Co.'s punishment for the production and distribution of Vioxx, a drug that seriously affected millions around the world, is fully analyzed, it is clear that the retribution was by no means adequate, with a large portion of the relatively nominal payment being returned to the company.

While ethical challenges of the drug pricing debate are clearly based in arguments over the importance of life saving drugs in comparison to profit, they run much deeper. The seemingly basic issues quickly become more complex, initiating debates over political and economic ideologies. These disagreements slow the process of solving the drug pricing problem and prevent the implementation of a global strategy. It is unclear whether the disputes between certain nations will ever allow for the success of a global plan to combat the drug pricing challenge.

Global Pricing Systems

In order to better assess the global pharmaceutical and pricing systems it is important to understand the unique systems in nations around the world.

The pharmaceutical pricing system in the U.S is complex, influenced by a variety of federal systems, independent entities, and separate factors. Medicare is the federal health insurance policy, specifically for people over the age of 65 and some younger people with disabilities.

Most people who are covered by Medicare do not pay (or pay only copays) as they paid Medicare taxes while working. Medicare was first established in 1965 during the presidency of Lyndon B. Johnson as part of his “Great Society” domestic programs. Just recently in August of 2022, President Joe Biden passed the Inflation Reduction Act (IRA) of 2022 which made key improvements to Medicare. According to the Centers for Medicare & Medicaid Services (CMS), the law provides Medicare with the ability to negotiate the prices of certain high expenditure, single source drugs without generic or biosimilar competition (2023, para. 2). This is key as it promotes positive communication between federal policies and pharmaceutical companies, which was previously limited.

The Medicaid system is a joint federal and state program that provides health coverage to low-income individuals, families, and certain vulnerable populations. Contrary to Medicare, Medicaid is directed as a free form of healthcare for adults and children who otherwise could not afford health insurance. Medicaid is supported by beneficiaries so price negotiations are key to secure more favorable pricing for covered medications alleviating some financial burdens. The program's ability to negotiate drug prices contributes to its mission of ensuring affordable and accessible healthcare for eligible individuals and families. While prior to President Biden’s legislation price negotiations were a key difference between Medicare and Medicaid, the U.S Department of health and human services recognizes that now the most stark contrasts are seen in the population the programs apply to and federal vs. state support (2023, para 6).

Private health insurance companies have continued to grow as the pharmaceutical industry developed. A dissertation from Wharton Faculty Research at the University of Pennsylvania states that the overall percentage of drug expenditures paid by insurance rose from about 40% in 1990 to over 75% by 1999. Similarly, “The share of outpatient drug expenditures paid out-of-

pocket declined from 69.4 percent in 1980 to 59.1 percent in 1990, with a more rapid decline to 33.4 percent in 1999” (Danzon, 2002). This trend has continued throughout the 21st century. However, one key issue in the spread of American private insurance has been a lack of a growth in depth to insurance policies. As a result, it has proven difficult for Americans afflicted with rare diseases that affect a small portion of the population to find coverage for their necessary drugs. This often leads to major out of pocket expenses.

Hospitals and Accountable Care Organizations (ACOs) also contribute to the pharmaceutical pricing landscape. Hospitals negotiate prices with drug manufacturers for medications administered in healthcare settings. Additionally, the 340B Drug Pricing Program allows certain healthcare providers to purchase medications at discounted prices. According to the U.S Health Resources & Services Administration, "The 340B Drug Pricing Program is a federal program that requires drug manufacturers to provide outpatient drugs to eligible healthcare organizations and covered entities at significantly reduced prices. The program aims to stretch scarce federal resources to reach more eligible patients and provide them with access to affordable medications. The 340B program allows covered entities, such as qualifying hospitals and clinics serving underserved populations, to access discounted medications and enhance their ability to serve vulnerable populations” (2023). The 340B program has proven to be a key achievement in the U.S healthcare system, playing a key role in limiting expenses and improving access in the pharmaceutical industry.

In France, the drug pricing system is structured around comprehensive assessments of both medical benefit and added benefit. These assessments are conducted by regulatory bodies to ensure that only effective and valuable drugs are included in the reimbursement system (French National Authority for Health [HAS], n.d.).

The Medical Benefit Assessment Program is overseen by HAS. This evaluation process thoroughly examines the therapeutic value and clinical benefits of a drug. Factors such as efficacy, safety, and improvement in patient outcomes are carefully considered (HAS, n.d.). The goal is to determine whether the drug should be included in the list of reimbursable medicines.

The outcomes of these assessments play a crucial role in determining the reimbursement rates for drugs in France. Drugs that demonstrate significant medical benefit and added value are more likely to receive favorable reimbursement rates, making them more accessible and affordable for patients. This comprehensive approach ensures that the drugs included in the reimbursement system are of high quality, effective, and provide significant benefits to patients in France (HAS, n.d.).

The United Kingdom (U.K) faces its own challenges in drug pricing due to rising costs and their impact on the National Health Service (NHS). High prices of patented drugs strain the NHS budget and limit patient access to vital medications. To tackle this, the U.K. employs health technology assessments by the National Institute for Health and Care Excellence (NICE), which evaluate the clinical and cost-effectiveness of drugs (NICE, 2022). This system parallels the French system as described above.

The U.K. healthcare system, the NHS, offers universal coverage funded through taxation (Department of Health and Social Care, 2021). However, increasing demand, rising costs, and limited resources pose ongoing challenges. Budget constraints may affect drug availability and prioritize treatments based on clinical need and cost-effectiveness. The NHS aims to balance patient access and system sustainability (Department of Health and Social Care, 2021). Efforts are underway in the U.K. to address drug pricing challenges and improve healthcare affordability while upholding the principles of universal coverage. The system in the U.K is

continually utilized to exemplify a system of universal coverage against systems such as the system in the U.S with differing ideals. Both the U.S and U.K systems illustrate particular benefits and disadvantages to differing healthcare principles.

These contrasting views are evidenced endlessly in global pharmaceutical systems. Notable debates have emerged over compulsory licensing, as described earlier, and global trade vs. equity pricing. Advocates of equity pricing argue for fair and uniform drug pricing across countries to ensure equal access. Equity pricing seeks to promote fairness, but systems so far have experienced challenges in balancing economic capacities.

Conclusion

The drug pricing challenge is a multifaceted issue that cannot be solved with a single solution. The pharmaceutical industry is youthful and flexible. Many nations recognize this, making policies more open to change. Increasing price transparency could prevent excessive pricing and promote competition. Advances in negotiation, as seen by the Inflation Reduction Act of 2022 in the U.S, paired with pharmaceutical regulation could ensure affordability and accessibility. Intellectual property reforms that balance incentives for innovation with the need for affordable access to medicines, such as compulsory licensing or patent pooling, can help to support innovators while also limiting destructive monopolies. By streamlining the generic drug approval system, governments could encourage generic competition, reducing exorbitant prices. By studying the most effective funding models around the world, as well as health insurance and reimbursement systems, governments can determine the most effective systems for their particular demographics and pharmaceutical environments. International collaboration such as initiatives like the World Health Organization's Access to Medicines Program can help to support industries in struggling third world nations and promote global accessibility. While

issues such as the war in Ukraine delay international advancements, ingenuity from the leading nations in the pharmaceutical industry could help promote positive change elsewhere, as we saw during the coronavirus pandemic. While the drug pricing challenge and issues in the pharmaceutical industry may seem daunting now, the future is hopeful and resolutions are already underway.

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