

Issues of an Insular Insulin Industry

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Before the discovery of insulin therapy, children with type 1 diabetes resorted to counting calories, weighing food, and implementing starvation diets to stay alive (Beran et al., 2016). About 50% of type 1 diabetics died within two years of developing diabetes and more than 90% died within five years. An article written by Harvard's Chief Medical Editor, Howard LeWine, reports that due to insulin therapy advances over the past years, people with type 1 diabetes now have life expectancies of over 50 years (LeWine, 2015). Although far less deadly, type 2 diabetes also affects millions of people and can lead to serious health problems. In 2021, in the US alone, 38.4 million people were diagnosed with diabetes accounting for 11.6% of the population, with another 8.7 million adults going undiagnosed according to the National Institute of Diabetes and Digestive and Kidney Diseases (*Diabetes Statistics - NIDDK*). Today, diabetes is a global epidemic that over 420 million people worldwide (6% of the world's population) are dealing with everyday, and this number is expected to increase to 700 million by 2045 (Siew & Zhang, 2021).

With this projected rise comes the increased demand for insulin. However, affordability and accessibility of insulin remains a challenge in many parts of the globe (Beran et al., 2021). Some countries have made efforts to regulate insulin prices, but insulin price regulation in the U.S. has remained a challenge, as indicated by a report from the Office of the Secretary for Planning and Evaluation (ASPE) that states that “the average gross manufacturer price for a standard unit of insulin in 2018 was more than ten times the price in a sample of 32 foreign countries: \$98.70 in the U.S., compared with \$8.81 in the 32 non-U.S. Organization for Economic Co-operation and Development (OECD) countries for which we have prescription drug data” and that “the U.S. prices for the mix of insulin used in the U.S. were 8.1 times prices paid in all non-U.S. OECD countries combined” (ASPE, 2020). With such a large price

differential, it is evident that there are unique circumstances that contribute to high prices of insulin in the U.S and that the actions taken to reduce insulin costs in the U.S. have proved ineffective.

The current state of the insulin industry is a large problem for many Americans. This paper outlines the different factors that contribute to the high prices of insulin in the U.S. and the attempts to reduce costs by applying the actor-network theory. Actor-network theory describes how the shifting relationships of human and non-human actors shapes the social and technological world, which this paper utilizes to analyze high insulin costs (Latour, 1992). This paper analyzes domestic policies and historical attitudes of insulin manufacturers in order to investigate the high prices of insulin in the U.S. The actors are categorized into three distinct categories: insulin manufacturers, the US government, and illegitimate insulin distributors.

Historically, insulin companies are known for setting the prices of insulin at expensive rates. Many pharmaceutical companies take advantage of the process called “evergreening” which is defined as “the practice of making incremental, patentable innovations for medicines without corresponding benefit, particularly if patients are aggressively or forcibly transitioned to the new product” (Beall, 2016). After a firm’s patent expires on an insulin product, competition from generic drug manufacturers can drastically reduce profit margins for the firm. A study by the International Review of Intellectual Property and Competition Law (IIC) reports that generic entry into a market leads to a loss, on average, of 80% the market share and a 20% to 30% reduction of drug price, and that each additional generic entry leads to further loss (Gurgula, 2020). Evergreening extends the patent life on a product, preventing generic drug manufacturers from entering the industry as a competitor. Diabetic patients are forced to pay a substantially more expensive price for insulin because generic drug manufacturers are prevented from entering

the market. Generic drugs are much more affordable than brand name medication, but the status quo in the insulin industry is protected by patent laws as insulin manufacturers continue exploiting patent law loopholes like evergreening.

Evergreening is commonplace through the pharmaceutical industry as a whole, but the insulin industry is especially problematic because its products can be considered under the classification of a “medicine/device” combination product, and the patents on the devices often outlast the patents on the medicinal components. In the case of the insulin industry, the medicinal component is the insulin itself while the device is the delivery system. For insulin, the most common medical device comes in the form of insulin pens to facilitate drug delivery. A study conducted by researchers sponsored by the Canadian Institutes of Health Research found that 90 percent of the 49 medicine/device products selected for the study had unexpired device patents, and that for 14 of the 49 products the device patents were the only unexpired patents (Beall, 2016). It was discovered that market competition was very limited for similar products. The motivation for an insulin firm to employ evergreening is to “maintain their profitability and dominance in the market” (Bala, 2020). The synergistic nature of the medicinal and device components of insulin is used to prolong the market exclusivity of insulin products, making it even more difficult for new parties to enter the insulin market and make prices more competitive.

Diabetics are negatively affected by this process due to the lack of competition in the insulin industry. This has led to high insulin market prices going unchallenged, allowing insulin manufacturers to increase their products’ prices in order to maximize profits. Insulin companies argue that patent protection is “essential for recouping their investments, as well as for incentivising them to engage in further innovation” (Gurgula, 2020). While this may be true, insulin companies have been reaping the benefits of tight patent laws for almost a century.

T1International, a diabetic advocacy group, reports that a vial of insulin costs \$3 to \$6 to produce today and that since the 1990s, the cost of insulin has increased by over 1200%

(T1International). So while it is important that companies gain and maintain a profit from their products to incentivize further innovation, it's clear based on the insulin cost increase that insulin companies are seeking to maximize profits by setting high prices in a tightly controlled market.

In the US and the EU, the traditional approach to strategic patenting prevents competition law involvement. Patents and competition laws exist to incentivize innovation, but because these patent strategies have demonstrated the negative effect on competition and consumer welfare, action needs to be taken against patent strategies such as evergreening. Despite the perceived negative effects, it is difficult to clearly define the insulin industry's actions as evergreening. The key phrase in the definition for evergreening is "corresponding benefit". If incremental changes in a device's patent is justified by the corresponding benefit that follows, then the action cannot be labeled as evergreening. The benefit that follows the incremental changes to insulin devices is highly debatable, but since there is no clear cut answer, insulin manufacturers are permitted to continue their practices. However, regardless of whether these actions are officially labeled as evergreening or not, the IIC reports that the evidence surrounding current strategic patenting suggests that these types of patents reduce innovation and should raise competition law concerns due to the practices acting against public interest (Gurgula, 2020). The insulin industry is at fault for abusing patent laws, but they are not solely at blame. Existing patent laws have allowed insulin companies to take advantage of loopholes which have allowed them to maintain control over the insulin market. However, the U.S. government is currently attempting to make insulin more affordable and considering proposals to increase affordability of insulin.

It's evident that without an incentive to reduce prices, insulin manufacturers will continue to sell their products at a high cost and potentially even raise prices. The historic and current attitudes of insulin manufacturers show no indication or intention of change. In order to control the price of insulin, action must be taken by a party outside of the insulin industry. The insulin industry continues to regulate their own product prices, but the government has the ability to step in to place limits on the industry. The cost of insulin has caught the attention of many people in the US, eliciting discussion of multiple future reforms to stem insulin prices. A popular proposal is taking advantage of international insulin companies and introducing them into the U.S. insulin market through a reciprocal approval policy (Knox, 2020). A reciprocal approval policy allows the U.S. to allow the FDA to approve drugs based on approvals from comparable regulatory authorities globally. Studies have shown that reciprocal approval policies would greatly increase the number of drug products in the U.S. including insulin. Such a policy would not only increase supply in the U.S., but it would also increase competition in the insulin market. An increase in competition would drive insulin costs down while promoting innovation, greatly benefiting diabetic patients. However, a reciprocal policy runs the risk of lowering the global supply of insulin and incentivizing foreign insulin companies to raise the price of their own products. A reciprocal policy substantially lowers the cost and duration of the FDA's drug approval process.

The second proposal is insulin importation. Many diabetic patients travel from the U.S. to foreign countries such as Mexico or Canada to gain access to significantly lower prices abroad. Current legislation prevents the importation of medicines not approved by the FDA, which makes insulin importation challenging. The drug approval process associated with importation is longer and more costly than implementing a reciprocal policy. Despite the legality and costs of importation, senior research fellow at the Solomon Center, Ryan Knox, claims that supporters of

prescription drug importation assert that “Americans would save \$50 billion over 10 years” (Knox, 2020). However, this idea is not sustainable for either the U.S. or the global markets due to supply disruption as well as providing markets incentive to increase their own insulin prices at a global scale. An increase in demand in foreign insulin markets would lower the insulin supply for the supplier’s domestic market. Furthermore, an increase in demand in foreign insulin markets could encourage these markets to raise their own prices to meet the supply demands and to push their own profits.

The final proposal is through price capping, which is defined as a government required limit or discount on prices. A price capping law has been passed in Colorado and similar laws have been proposed in many other states. This proposal differs from the first two proposals due to its goal of directly increasing affordability rather than promoting competition. A peer reviewed article published in *Health Affairs* stresses the importance of price capping by asserting that biologics are a natural monopoly because of the high entry cost in the insulin market, meaning that competition-based proposals would be ineffective at lowering insulin prices (Trusheim et al., 2019). For this reason, established insulin suppliers have such a large advantage over new entrants in the insulin market that it would not be financially feasible for these entrants to enter the market. The government needs to step in to allow new entrants to be able to compete with the established insulin manufacturers who currently dominate the market.

A price control on insulin would have an immediate effect of enormous savings for consumers. However, a price control could lead to insulin manufacturers looking for ways to recoup their losses by withdrawing products or raising prices in less regulated markets resulting in higher prices and drug shortages globally. Knox warns that capping insulin prices may cause more problems than it solves and that it is important to consider how legislation would affect

global markets as well as U.S. markets. The insulin market presents many unique challenges including “limited competition, regulatory challenges for approval and interchangeability, and practical challenges with trade secrets, anticompetitive behavior, and pricing of biologics” (Knox, 2020). It is important for lawmakers to understand the nature of the insulin market and the circumstances that led to limited competition in the market in order to create laws to increase accessibility to insulin. However, it is equally important for policymakers to consider the implications and potential outcomes of their actions. Regardless, action is required because the uncontrolled costs of insulin have incentivized diabetic patients to seek alternative and cheaper sources of insulin from unverified vendors.

Although there is limited competition in the legitimate insulin market, there are lots of illegitimate insulin distributors. Illegitimate insulin sources are characterized by a lack of regulation and license to distribute insulin. However, due to the high costs of insulin set by insulin companies, diabetics patients have turned to look for lower cost and alternative methods of obtaining insulin. These methods include purchasing insulin from friends, across borders, or from internet pharmacies. A peer reviewed study published in the Journal of Medical Research reports that diabetic patients are incentivized to find alternative sources of insulin due to ease of access and because prices from alternative sources are substantially reduced (Penley et al., 2022). However, the shift from legitimate insulin sources to illegitimate insulin sources poses a significant problem. Patients are at risk of receiving poor quality medication and services resulting in poor diabetes control. The government has made attempts to better regulate the insulin market, but it has proven to be a challenging task, especially with the high quantity of and large demand for illegitimate internet pharmacies services.

Internet pharmacies in particular have become a popular source of prescription drugs demonstrated by the sheer number of internet pharmacies making their services accessible. A report from the Center for Safe Internet Pharmacies cited by Penley's study reported that in 2016 there were 30,000 to 35,000 pharmacies making themselves accessible through the internet (Penley et al., 2022). Of the 30,000 internet pharmacies, 96% operate illegitimately (Penley et al., 2022). The World Health Organization reports that 50% of all internet pharmacies that do not advertise a physical location are counterfeit and illegitimate (Penley et al., 2022). Internet pharmacies by nature are easily accessible which poses a problem since the rising cost of insulin from legitimate sources serve to make safe and reliable insulin products less accessible. Despite the associated risk, diabetics are likely to turn to these illegitimate sources because of the accessibility and affordability of their products.

Patients who purchase medication from illegitimate sources are subject to dangerous risks. High quality is necessary in high risk medications such as insulin in order to have their intended effects on patients. Incorrect insulin administration can lead to serious health risks including transient and serious hypoglycemia/hyperglycemia, wide glycemc excursions, and diabetic ketoacidosis. However, the risk of obtaining insulin from illegitimate sources goes beyond the poor quality of medication (Penley et al., 2022). The lack of services offered by alternative sources compared to the services provided by traditional healthcare providers is equally concerning. Insulin dosage is reliant on blood sugar, weight, physical activity, and diet, among other factors. There are many considerations that are weighed when administering insulin dosages and instructions. Patients are unable to receive medication counseling, monitoring, and drug-drug interactions that legitimate health care services provide. These resources have been proven to improve patient health, but illegitimate outlets of insulin medication strip patients of

these services (Penley et al., 2022). In Penley's study, 57% of illegitimate pharmacies did not require a prescription, 43% did not display medication information or warnings, and only 21% offered access to pharmacists (Penley et al., 2022).

The US government recognizes the dangers presented by these illegitimate sources of insulin. Several states require internet pharmacies to be accredited with the National Association of Boards of Pharmacy in order to receive licensure. The FDA partners with companies such as LegitScript in order to assess and monitor internet pharmacies. There are multiple national organizations with the purpose of combating internet pharmacies such as the FDA's BeSafeRx campaign and the Alliance for Safe Online Pharmacies' Buy Safe Rx campaign which help patients identify illegitimate internet pharmacies. There are multiple ongoing regulatory and legal actions against illegitimate internet pharmacies (Penley et al., 2022). Interpol in conjunction with the FDA and US Department of Justice has removed thousands of illegitimate internet pharmacies, but illegitimate pharmacies continue to find ways to continue their operations. The enforcement of rules and regulations is very complicated because of the intricate e-commerce environment composed of a number of stakeholders. The complex and anonymous nature of e-commerce allows illegitimate internet pharmacies to avoid detection and reopen operations under new web addresses.

It is evident that the high prices that plague the insulin industry pose a major problem of accessibility for many Americans. Insulin is a life saving drug, yet millions of people struggle to access it due to the high prices. The issue is not an easy one to diagnose or solve. There is an intricate network of actors who all play a part in the high prices of insulin that must be taken into consideration when examining the circumstances surrounding the insulin industry. The insulin industry bears responsibility for setting high prices for their products through their tight control

on the insulin market and their abuse of patent laws through evergreening. The US government has not taken sufficient action to regulate the prices set by insulin manufacturers which has allowed the insulin industry to maintain their grasp on setting insulin prices. There are many alternatives proposed and discussed, but these potential solutions are limited by the lack of research into the unintended side effects of implementing new policies. However, the US government bears responsibility for finding solutions to lower the price of insulin. Many Americans are turning to illegitimate distributors in order to gain access to insulin. Diabetics who turn to these illegitimate sources endanger themselves by risking incorrect dosages, low quality drugs, and a lack of traditional medical services. However, many diabetic patients have no choice because they are unable to afford the prices of insulin from traditional sources, so they are likely to accept the risks of obtaining insulin from illegitimate sources. While the US government has made attempts to stifle illegitimate drug vendors, the US must take action by addressing the root issue, which is the high cost of insulin. While the issue is a complex one that requires lots of research and consideration, it is necessary to explore alternative solutions because the current state of the insulin industry is not conducive to increasing the accessibility and affordability of insulin.

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