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«An overview of the pharmaceutical market: Structure, behavior, returns, and government intervention»

Damdas Ioannis

Under the supervision of Professor *Filippiadis Eleftherios, PhD*

School of Economic and Regional Studies, Department of Economics

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Abstract

The pharmaceutical industry has been a subject of a lot of academic research, not only because of its high research & development activity, but because of the high profits that the firms have achieved through the last decades, through patent competition, marketing strategies and, sometimes, overpricing of certain pharmaceutical products. This thesis is an attempt to determine how the pharmaceutical industry operates as a whole, and how this affects the society's welfare as a whole, by examining the structure of the market, in terms of concentration, barriers to entrance through patent diplomas, and pharmaceutical benefit management. The market behavior is also in question, and more specifically, how the firms decide on optimal research & development activity, as well as expenditures in marketing, and the price the final product will have. Finally, after examining the returns of the pharmaceutical market, in terms of products and firm profits, the intervention of government agencies is examined, and more specifically the refunds the companies ought to pay, in the form of clawback payments.

1. Introduction

The health industry consists of the pharmaceutical industry, the industry of medical services, the industry of hospital services, the industry of long-term care, as well as the private insurance industry. These health sectors generate a lot of interest regarding their markets' structure, behavior and returns, since health as an economic good is somewhat differentiated from others, due to the characteristic of uncertainty, the generation of both positive and negative externalities, and of course, every individual's right to it. The application of microeconomics, and more specifically industrial organization, is essential in understanding the health industry, in order to achieve market efficiency and social welfare through proper policies. Emphasis is put on the pharmaceutical industry, because of its profitability, as well as the relationship between market structure and the attempts in patenting and Research & Development (R&D).

The pharmaceutical market has been the center of many previous analyses, because of the industry's size, profits that amount to billions of dollars, values that add up to trillions of dollars, as well as concerns regarding the affordability of pharmaceutical products due to high pricing. High prices are the factor that results in the growth of the pharmaceutical industry, and could be attributed to various factors, such as the existence of barriers in the market to prevent entrance, through patent diplomas for certain drugs, the role of Pharmaceutical Benefit Managers (PBMs), the expenditures in R&D and marketing, as well as how the market is distributed among the firms in it. All these elements affect the monopolistic power that each firm has in the pharmaceutical market, and, consequently, the level of prices. Given the fact that health is a necessity for every person, rather than a common good, the prices of drugs, a product crucial to "producing" health, ought to be considered when the welfare of the consumers - patients is analyzed.

Should the government intervene in the pharmaceutical market? And if so, how? The primary concern of public policies should be establishing basic, yet not simplistic, regulations for patent approvals and drug reviews before entering the market, as well as preserve the stability regarding various macroeconomic factors. However, in the case of excessive profitability for big pharmaceutical firms, perhaps higher intervention is needed, always taking into consideration the welfare of the society as a whole.

A possible way for the government to reduce the percentage of expenditure covered by public funds or patients would be to impose a refund, in the form of clawback payments, for the pharmaceutical companies, in order to maintain a balanced budget. When clawbacks are in effect, if the revenues of the firms exceed the clawback threshold on aggregate, the difference is covered by them. Since their profits are reduced, the firms usually reduce the quantity supplied in the market, as a response. However, given that the final price of each product is usually defined by the government agencies, this can be done by reducing their marketing expenditure. The model described in chapter 5 discusses the consequences of imposing a clawback threshold in a duopoly market, when firms decide on their marketing levels and the price is set by the government.

2. Pharmaceutical Market Structure

A very important aspect of the theory of Industrial Organization is the analysis of a market's structure, behavior and performance. In the pharmaceutical sector, the market structure describes the competition under which a pharmaceutical company has to operate. The most important characteristics of the pharmaceutical market structure are the number of companies in the market, concentration in both the supply and the demand side of the market, and the existence of entry barriers in the market, mostly created by the existence of patent diplomas. An industry characterized by relatively high competition has few to no entrance barriers, as well as a high number of both pharmaceutical suppliers and buyers. These features could induce a situation under which the firms in the industry cannot achieve monopolistic power, and thus cannot price their products highly.

2.1. Market Concentration

A common assumption regarding the pharmaceutical industry is that there are relatively few companies in the market, and only a handful of them, the so called pharmaceutical "giants", have acquired very high market shares and enjoyed high revenues. That is partially true, since the top companies in pharmaceuticals do make billions in revenues, however the number of those is not that low and the market shares are not that high.

Table 1 presents the total revenue and the market share for the top 10 pharmaceutical companies worldwide, for the year 2018.

Table 1: **Top 10 Pharmaceutical Companies by Market Share (2018)**

#	*Company*	*Revenue (US$ billion)*	*Market share (%)*
1	Pfizer Inc	53.60	5.60
2	Novartis	51.90	5.44
3	F. Hoffmann - La Roche Ltd	44.68	4.69
4	Merck & Co Inc	42.30	4.44
5	Johnson & Johnson (J&J)	40.70	4.27
6	GlaxoSmithKline Plc	40.00	4.19
7	Sanofi	39.23	4.11
8	AbbVie Inc	32.73	3.43
9	Bayer AG	27.10	2.84
10	Eli Lilly and Co	24.55	2.57

Source: ***Pharmaceutical Technology, https://www.pharmaceutical-technology.com/features/top-pharmaceutical-companies (Accessed 6/2/2020)***

According to these data, the concentration in the market is not that high. The four biggest pharmaceutical companies produce around 20% of the total output, while the eight biggest produce around 36%, as depicted by the CR index:

$$CR_4 = 5.60 + 5.44 + 4.69 + 4.44 => CR_4 = 20.17\%$$

$$CR_8 = 5.60 + 5.44 + 4.69 + 4.44 + 4.27 + 4.19 + 4.11 + 3.43 => CR_8 = 36.17\%$$

However, in order to achieve a better understanding of the differences and the inequalities between the sizes of the pharmaceutical companies, the Herfindahl - Hirschman index, or *HHI*, is used. Using the data from Table 1, we find an HHI index around 181, which is a relatively low number:

$$HHI_{10} = 5.60^2 + 5.44^2 + 4.44^2 + 4.27^2 + 4.19^2 + 4.11^2 + 3.43^2 + 2.84^2 + 2.57^2$$

$$=> HHI_{10} = 181.7798$$

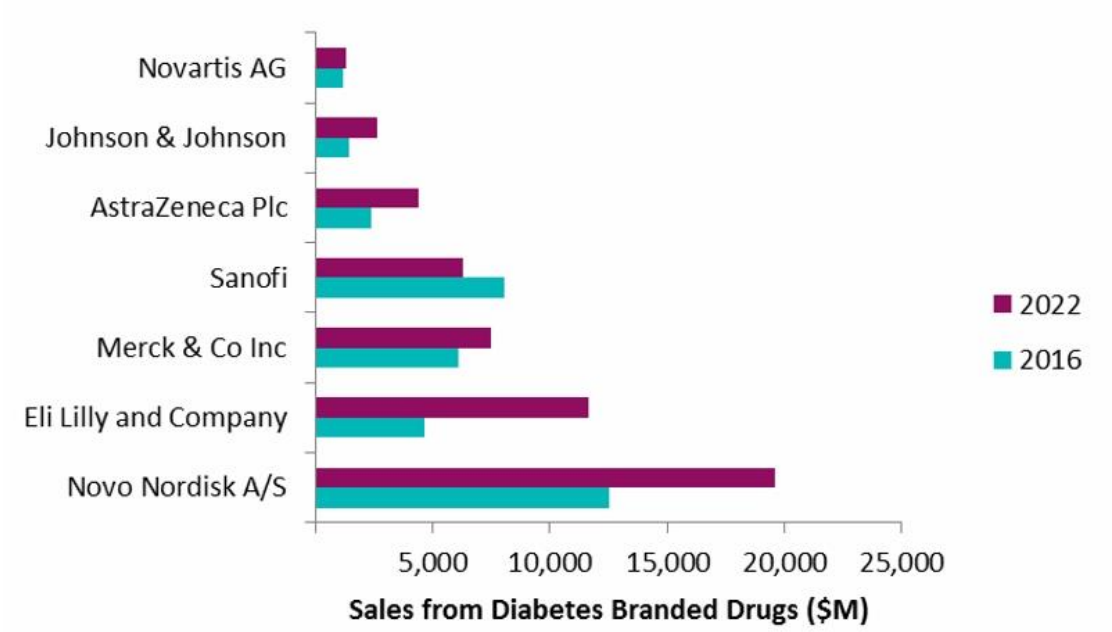
These indices indicate that the pharmaceutical industry is characterized by a significant number of large companies, and therefore the competition in the market can be considered as relatively high.

The pharmaceutical market's concentration is properly calculated only under the hypothesis that, even though a lot of individual drugs are used, the market for all of them is relevant, known as the Relevant Product Market, or *RPM*. An examination of the RPM ought to include a possibility that a pharmaceutical company be threatened from another, and its ability to develop a substitute drug (Santerre & Neun 2012, p. 400). RPM can be defined either narrowly or widely.

According to Stigler (as cited in DiMasi, 2000), the definition of the relevant market scope has to take into account possibilities in substitution, both production and consumption. DiMasi (2000) argues that an allocation of resources to new therapeutic programs, or an expansion of the already existing, without substantial retraining or new hiring, could be possible. In a relatively short period, that could suggest a fairly broad measurement of concentration in innovation. However, if barriers in production do exist, then a more narrow approach in defining the RPM for drugs is preferred. A narrower definition means that most drugs cannot become substitutes, because of more specific properties (Santerre & Neun 2012, p.401).

An indicative example of market concentration in individual pharmaceutical products is the market for anti-diabetics, one of the top therapeutic classes. Diabetes is a chronic disease that, according to the World Health Organization, has an extremely increasing prevalence - over 400 million people had diabetes in 2014. Given their importance, it comes as no surprise that anti-diabetics, according to data from Statista, generated 40 billion dollars in revenue globally in 2018.However, there is little to no change in which pharmaceutical companies have the highest market share in pharmaceutical products for diabetes. The following data suggests a high concentration in the diabetes market:

Figure 1: **Sales from Diabetes Branded Drugs (US$ million) (2018)**



Source: ***Pharmaceutical Technology, https://www.pharmaceutical-technology.com/research-reports/researchreportseven-kings-of-diabetes-will-remain-in-power-for-years-to-come-5773644/ (Accessed 10/2/2020)***

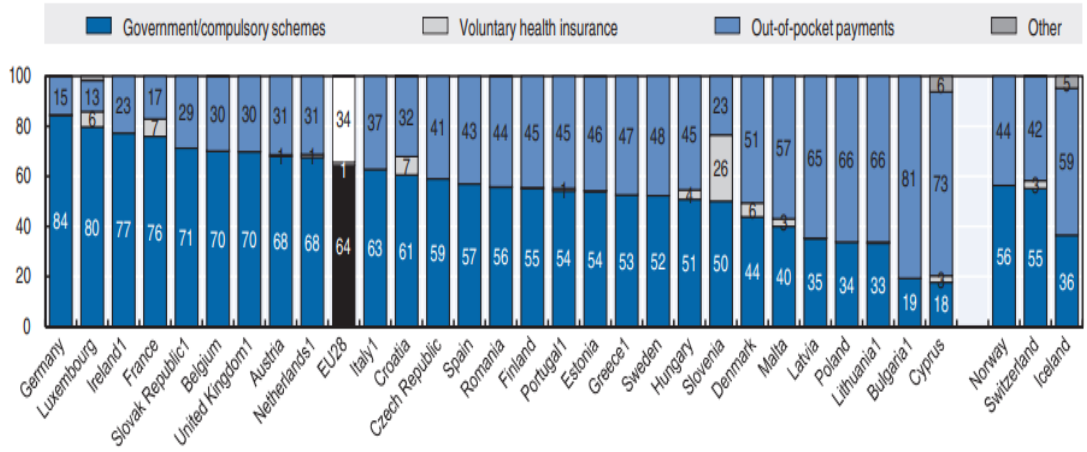
Given its increasing prevalence, diabetes can be considered as a high lucrative market for large pharmaceutical companies. However, despite the motives for entrance or investment in the market, it appears that only 7 companies have individual revenues over 1 billion dollars, and are expected to continue to dominate in the market in the foreseeable future. Similar data for other top therapeutic classes suggest that in most markets only few companies have the majority of the market share, suggesting a relatively high concentration.

In general, it appears that the supply side of the pharmaceutical market, can be considered as concentrated, but not in a way that the dominant companies will continue to maintain their top positions in the industry. Therefore, additional information ought to be taken into account in order to draw proper conclusions regarding the pharmaceutical market structure, as well as the pharmaceutical companies' power in the particular market.

Another important aspect of the market for pharmaceutical products is the concentration in demand, and more specifically, the number and distribution size of the buyers (Santerre &

Neun 2012, p.402 - 403). The following data depicts the various sources of expenditure in European countries, for the year 2016:

Figure 2: **Expenditure (%) on retail pharmaceutical by type of financing (2016)**



Source: ***OECD/EU (2018), Health at a Glance: Europe 2018: State of Health in the EU Cycle, OECD Publishing, Paris. https://doi.org/10.1787/health_glance_eur-2018-en (Accessed 11/2/2020)***

In Europe, the cost of pharmaceuticals is, for the most part, covered by government or mandatory insurance schemes. On average, these schemes cover around 64% of all retail pharmaceutical spending. Financing the remaining part is covered by out-of-pocket payments at 34% and voluntary private insurance at 1%. *(Note: The percentages do not add up to 100% due to rounding)*

In the United States of America, 73% of the expenditure on retail pharmaceuticals is covered by government or compulsory insurance schemes, and the rest is covered by out-of-pocket expenses (OECD Statistics 2019). It is evident that government and compulsory insurance schemes cover the majority of pharmaceutical expenditures. Since the government's intervention in the market is considerably high, it is assumed that the prices of the pharmaceutical products could be regulated, to a certain extend. Therefore, the fact that around 2/3 of the demand are covered by insurance, and around 1/3 is covered by out-of

pocket payments could suggest a relatively concentrated demand side of the pharmaceutical market.

2.2. Entrance barriers - Patents

An important characteristic of the pharmaceutical industry is the entrance barriers that exist in the market. The ownership of patents and the establishment of a brand could offer advantages to the companies already existing in the market against potential entrants. In theory, these advantages could increase market power and share, thus maintaining higher prices.

The acquisition of drug patent diplomas is a company practice that is directly connected to the firm's investment activity in Research & Development. Patent diplomas, or simply patents, are related to the protection of a company's innovation against its competition. Therefore, the dilemma that arises when it comes to the level of access to information, is whether or not encouragement towards monopolies through incentives for R&D is preferred over the efficiency achieved by making the innovation available for all.

The motives for innovation that are due to patent diplomas create monopoly profits, since the company that owns the patent can behave as a monopolist. However, a monopolistic situation in the drug production is considered a better alternative than a production absence, in the sense that without a patent, the drug may not enter the market at all (Santerre & Neun 2012, p.407).

The profit created is considered motive for investment in pharmaceutical R&D itself, however at the same time the total surplus is reduced, since the market is contained. Therefore, the question asked previously actually concerns the relationship between the protection of the

innovator - owner of the patent and the consumers' protection, which is when the former is preferred over the latter. In order to answer that, the patent's structure, and more specifically its duration and the variety of products covered by it, is examined.

Regarding the patent's duration, the time period in which a patent diploma can be legally valid is 17 years (Santerre & Neun 2012, p.407). However this period is not necessarily optimal. The Nordhaus model (as cited in Pepall, Richards, & Norman, 2017) describes the equilibrium between the return of an investment in R&D and the consumer gains that exist after the expiration of the patent, when there is no monopoly and competition increases. In this model the industry is competitive, and every company studies an innovation. From this attempt at innovating there is cost of unit c. Investment in R&D with intensity x results in an expected operating cost $-x$. The cost of R&D with intensity x is $r(x)$.

However, Research & Development is expensive; cost $r(x)$ grows with an increasing rate. In other words, $r'(x) > 0$ and $r''(x) > 0$. Competition is assumed, therefore price is equal to c and quantity is equal to Q_0^C. If the company's innovation is successful, two options are possible. It can either set a marginally lower price than the current, and therefore discourage its competitors, or provide licenses to use this innovation, subject to a cost of $c - x$ per unit. In any case, the market price and quantity are not changed, even though the company earns $\pi = x * Q_0^C$ for the time period T that the patent is valid.

After the patent is no longer valid, the competition created by the free access in technology reduces the price to $c - x$ and increases the quantity, to Q_1^C, for example. The profit made by the company is now the consumer surplus, a surplus that is increased by the increase in quantity.

Of course, the higher the *duration of the patent* (T), the higher the *profits* (π) for the company, and therefore there are more incentives to invest in R&D. The Present Value of this investment will be:

$$V_i(x,T) = \sum_{t=0}^{T-1} R^t \pi^m(x,T)$$

Therefore the Net Value of Research & Development will be equal to:

$$NV_{R\&D} = V_i(x,T) - r(x)$$

The company, given T, chooses a level of $x^*(T)$ so that net value is maximized. That choice makes the marginal cost of the profit in present value equal to the marginal cost of R&D.

The patent's duration T is decided by the Patent Office, which, after taking into consideration that their choice affects the company's choice (for $x^*(T)$), makes their decision aiming at the maximum total welfare. At first, there has to be an estimation of the increase per period in the total welfare created by the innovation after it is available for free. The Present Value of this increase is:

$$CS(x,T) = \sum_{t=T}^{\infty} R^t cs(x,T) = \frac{R^T}{1-R} cs(x,T)$$

Therefore the net total welfare from the innovation is:

$$NS(x^*(T),T) = NS(x^*(T),T) + V_i(x^*(T),T) - r(x^*(T))$$

Assuming that the immediate existence of replicas does not create a surplus and that the activity in Research & Development has diminishing returns, maximization of the net present total welfare can only be achieved if the optimal duration of the patent is a positive and finite number. Therefore, patent diplomas must not last forever, in order to place emphasis on the consumer surplus, not just the profits of the monopoly.

When it comes to the width of the patent diplomas, there are many different opinions. Given that there is no internationally acceptable way of measuring (Pepall *et al.* 2017, p. 792), each situation falls under judgment by the corresponding patent office, and always with discretion. Each patent policy is decided after taking into consideration not only the width, but the duration as well. The choice is between patents with high duration, but low coverage, and its opposite, patents with low duration but high coverage. Optimal patent policy should keep the balance between maintaining the motives for investment in innovation and a broad distribution of the benefits created by innovations (Pepall *et al.* 2017, p. 793).

Economists' opinions differ on the matter; some favor the narrower patents, like Gilbert & Shapiro (1990), and state that the most appropriate way to apply patent policy is by choosing longer patent lives, very narrow in terms of breadth, under careful provision, because of increasing costs in terms of deadweight loss in a patent characterized by breadth. However others, like Klemperer, suggest that a wider patent is optimal. In particular, Klemperer (1990), advises for width in the patents because it results in lower distortion of the choices the consumers make between patented brands and unpatented varieties.

In the pharmaceutical industry, the situation is more complicated, due to the nature of the products. More specifically, a drug patent diploma is granted for the drug's novelties in its chemical composition rather than its therapeutic characteristics, as Lu and Comanor (1998) suggest. Therefore the protection that the patent ensures for its owner does not necessarily guarantee that the company will not face any competition in the market, because new drugs might not be affected by the patent, due to different chemical compositions, even though they have the same therapeutic properties as the patented ones (Santerre & Neun 2012, p.407). Thus, the patent does not fully limit the choices between pharmaceutical products and cannot be considered as a certain way of achieving a monopoly in the market.

However, a patent could help a company achieve a first-mover advantage in the market by creating brand loyalty to the specific product. If the early entrant in the market has a significant lead time over their rivals, the market advantage will be significant. Data in the drug markets are consistent with this particular hypothesis, even though entry by competitors is not very delayed (Grabowski & Vernon 1992, p.346). An innovative pharmaceutical product would probably be considered as a first mover advantage, because its quality is more known in comparison to the generic drugs that will follow it. On the one hand, the doctors do not have the economic motives to compare their choices between generic drugs, due to costs from a possible wrong diagnosis. On the other, patients lack the necessary knowledge to properly estimate the advantages and disadvantages of switching to generic drugs (Santerre & Neun 2012, p. 408).

2.3. Mergers & Acquisitions

The structure of the pharmaceutical industry is considerably dependent on any occurrence of mergers and acquisitions between the companies that participate in the market. Mergers and acquisitions are an essential part of any analysis regarding the behavior of the pharmaceutical sector, since most of the motives for a union between two companies lie in optimizing their operations.

In general, there are several reasons for mergers and acquisitions in an industry. For example, companies want to take advantage of economies of scale and scope in order to reduce their production costs. Other reasons include the improvement of information flow, the acquisition of assets of significant importance, and, perhaps the most important, increasing the market share and gaining its control (Danzon, Epstein & Nicholson, 2007). However, a merger or an acquisition could be a way of creating a cartel in the market (Pepall

et al. 2017, p. 532) in order to achieve monopolistic profits, something that raises the question of whether or not is that merger against any anti-monopolistic regulations that may exist.

Mergers and acquisitions are usually classified by the nature of the relationship between the companies that decide to proceed in this manner (Pepall *et al.* 2017, p. 533). Firstly, horizontal mergers are those that take place when the companies used to be competitors in the same market. In other words, horizontal mergers involve companies that produced goods that were substitutes in consumption (Pepall *et al.* 2017, p. 533). Horizontal mergers are the most common kind in the pharmaceutical sector. Secondly, vertical mergers involve companies that belong to different stages of a production process. They also apply to any combination of companies that produced goods that were complementary in consumption (Pepall *et al.* 2017, p. 533-534). Vertical mergers usually occur between pharmaceutical companies and pharmaceutical benefit management companies, or PBMs. Finally, conglomerate mergers are those that concern companies with products that cannot be characterized either as substitutes or complements (Pepall *et al.* 2017, p. 533 - 534). Those mergers are not common in the pharmaceutical market.

Mergers and acquisitions occur in every industry. In the pharmaceutical sector, however, M&A deals are as old as the industry itself. For the most part of pharmaceutical history mergers and acquisitions could be characterized as “commonplace”. However, since the late 80’s, the so-called “blockbuster mergers” started to appear. (Richman, Mitchell, Vidal & Schulman, 2016). For example, in 1989, SmithKline merged with Beecham in a $7.7 billion deal, in 1995, Glaxo merged with Wellcome in a $15 billion deal, and in 2000, Glaxo-Wellcome merged with SmithKline-Beecham in a $76 billion deal.

The following table presents a recent history of large pharmaceutical mergers.

Table 2: **Pharmaceutical mergers**

1. Pfizer • 2009: Acquired Wyeth (which resulted from 1994 merger of American Cyanamid and American Home Products). • 2003: Acquired Pharmacia (which acquired Upjohn in 1995). • 2000: Acquired Warner-Lambert.
2. Johnson & Johnson (no major mergers).
3. Novartis • 2011: Acquired Alcon. • 1996: Resulted from merger of Ciba Geigy and Sandoz.
4. Roche • 2009: Consolidated 1990 acquisition of Genentech. • 1995: Acquired Syntex.
5. Bayer (no major mergers).
6. Merck • 2009: Acquired Schering-Plough.
7. Sanofi-Aventis • 2011: Acquired Genzyme. • 1999: Name changed after merger of Rhone-Poulenc and Hoechst. • 1995: Hoechst acquired Marion Merrell Dow. • 1995: Rhone-Poulenc acquired Fisons. • 1990: Rhone-Poulenc acquired Rorer.
8. Glaxo SmithKline • 2000: SmithKline Beecham merged with Glaxo. • 1995: Wellcome merged with Glaxo. • 1989: Beecham merged with SmithKline.
9. Abbott (no major mergers).
10. Astra Zeneca • 1999: Zeneca Group merged with Astra AB.
11. Eli Lilly (no major mergers).
12. Bristol-Myers Squibb • 2001: Acquired duPont Pharmaceuticals. • 1989: Bristol-Myers and Squibb merged; name change

Source: ***Danzon et al. (2007)***

The ranking is according to the sales in 2010, worldwide.

The blockbuster merger trend continued through 2008; fifteen megadeals occurred, each totaling over $1 billion. The highest deal was the Roche's acquisition of Genentech for nearly $100 billion.

In recent years, historic highs gave been achieved in the pharmaceutical industry when it comes to mergers, both in numbers and values of deals (Richman *et al*., 2016). It is evident that, given the number of firms in the market before and after a significant number of merger deals, that mergers and acquisitions result in a relatively more concentrated pharmaceutical market, and therefore play a very significant role in its structure.

The importance of mergers in the pharmaceutical industry's structure and behavior raises concerns regarding certain aspects of drug production and supply. These concerns mainly regard the changes in research & development operations after the M&A deals.

More specifically, a scenario in which two large pharmaceutical companies merge could result in more concentrated market for discoveries, as well as less competition, less experimentation and fewer novelties in general, as Richman *et al.* (2016) point out. Other possible problems that may occur in a pharmaceutical merging are related to the competition in the market, since the merged companies have more power in terms of promoting possibilities, like marketing, sales and distribution, in comparison. This power inequality results include a weakened competition, which in turn reduces any pressures in pricing and increasing the barriers to competitors (Richman *et al*., 2016). In general, the concerns about mergers and acquisitions are related to the effect those deals have on the pharmaceutical market's structure and behavior. If the proper market authorities fail to hedge this effect with proper regulations regarding M&A deals, the results will include price increases, less innovation and consequently, structural and behavioral problems for the pharmaceutical industry, as well as unfair treatment for the consumers.

However, it is evident that mergers and acquisitions do not have exclusively negative consequences for the pharmaceutical industry; were that the case, public policies would forbid them through proper regulations. Possible advantages include, as mentioned before, the economics of scale and scope that result in reducing production costs for drugs. Therefore, activity in development could increase, thus new, innovative entrants could appear (Richman et al., 2016). If production improvements, both in terms of drug quality and in terms of cost reductions, can generate increases in the consumers' welfare, besides additional profits for the companies, then mergers and acquisitions in the pharmaceutical industry can have an overall positive impact. Obviously, it is the public policymakers' responsibility to determine the circumstances under which a merging deal should be approved or stopped, based on the current market's situation, as well as the consequences for its structure and behavior.

2.4. Pharmaceutical Benefit Management

Apart from the pharmaceutical companies, the doctors, the patients and the government, the Pharmaceutical Benefit management companies, or PBMs, play a significant role in the drug market's structure and behavior. The pharmaceutical benefit managers do not manage, per se, the prescribed drugs, but rather act as mediators between the pharmaceutical companies and the pharmacies (Santerre & Neun 2012, p. 406). Even though the existence of PBMs is not that widespread in Europe, in the U.S. the pharmaceutical benefit managers operated in association with various private and public health insurance plans, like union or employer plans for example, towards reducing drug prescription costs for the consumers. More specifically, PBMs, under contracts with these plan sponsors, work towards negotiating rebates from drug manufacturers and discounts from drugstores, while at the same time they

offer more affordable pharmacy channels and they encourage the use of generic products, in order to produce savings for the consumers (PCMA, 2020)

Many pharmaceutical benefit managers have been merged with pharmaceutical companies since the 90's, but then they were sold up, like in the case of Merck and Medco (acquisition in 1993, sell up in 2003) (Santerre & Neun 2012, p.406). Merging deals between PBMs and pharmaceutical companies fall under the vertical merging category, as mentioned before, since the stages in the production process are different for each company; pharmaceuticals are involved with the production of drugs, while PBMs with their distribution. However, the existence of vertically integrated companies in the pharmaceutical benefit market poses questions regarding the monopolistic power that they gain. Two are the main concerns. First of all, the PBM could favor the pharmaceutical products of its own company over their counterparts, which could be less costly for the consumers. In doing so, the competition is affected, prices rise and quality is doubted (Santerre & Neun 2012, p.406). Additionally, through their PBMs, pharmaceutical companies can share information regarding the drugs' prices with their competitors in the production, in order to facilitate a collusion between them (Santerre & Neun 2012, p.406). Thus, it is evident that, given the role a PBM plays in the pharmaceutical market, a vertical merging with a pharmaceutical company could have a significant effect on the market's distribution and behavior.

However, the existence and the importance of pharmaceutical benefit managers is based on their advantages. As separate entities, PBMs exist, in association with various health plans, in order to help consumers increase their savings on pharmaceutical products. The need for this kind of mediation in the market is sustained when one takes into account the pharmaceutical price levels; outpatient prescription drug expenditures surpassed $360 billion in 2019 (PCMA, 2020). Since the development of new pharmaceutical products and the existence of the insurance plans with higher coverage are expected to increase drug

expenditures, PBMs will continue to play a highly important role in the pharmaceutical market. However, even though merging with pharmaceutical companies could create various problems, PBMs in vertically integrated entities can theoretically be more efficient, since a merging results in an internalization of externalities, due to singular management (Pepall *et al.* 2017, p.586). More specifically, not only does the company refrain from transaction and negotiation costs, since those procedures are not required, but it also protects itself from the possibility of contract incompleteness (Santerre & Neun 2012, p.407). Because of the integrated company's effectiveness, pharmaceutical products enter the market without the double profit margin, since the pharmaceutical company does not impose a profit margin in the price they set for the benefit manager. Thus, the consumers face lower prices.

Undoubtedly, pharmaceutical benefit managers have played, and will continue to play a very important role in the pharmaceutical industry. Given the amount of information regarding drug pricing and quality they manage, PBMs could, in theory, succeed in making pharmaceutical products more affordable to patients, in association with their respective health plans, of course. However, since PBMs work very closely with Pharmaceutical producers, and sometimes even merge with them, every procedure ought to be strictly regulated by public policies, so as to avoid negative consequences in the market's structure and behavior.

3. Market Behavior

Firms in the pharmaceutical industry develop their strategies in three dimensions: the process of developing innovative pharmaceutical products, the promotion of these products through marketing practices, and their pricing. According to Santerre & Neun (2012), in order to properly estimate the competitive behavior of the pharmaceutical companies, four issues need to be addressed. More specifically, the pharmaceutical industry's issues that fall under the microscope are the relationship between drug prices and competition, the relationship between entrance in the market and high profits created by patenting, the way marketing affects the market structure, as well as the relationship between the company's size and innovation initiatives.

3.1. Pricing strategies

The pricing of the products in the pharmaceutical industry is essentially the center of an analysis at the market level. First, it helps the understanding of the relationship between drug prices, profits and competition. Second, it provides helpful insight in the ways that patenting and market barriers affect the structure of the market.

Given that the pharmaceutical market is not perfectly competitive, one should expect prices to be set higher than the marginal cost of the products, as basic microeconomic theory suggests. However, as the number of firms increases, prices should approach marginal costs, because the market starts to behave more and more like a perfect competition. Moreover, the relatively high concentration in the supply side, combined with the existence barriers due to patent diplomas, could induce a dominance from the firm with the patent. This dominance over the firms producing generic drugs is further established by the first-mover

advantages. Generally, differences in prices both with and without the existence of patents, as well as relatively higher prices from the companies already in a product's market, should be expected. Various researches have been conducted in order to analyze the pricing practices in the pharmaceutical industry, for the cases where a patent has expired and entry barriers have been lifted.

A seminal research regarding pharmaceutical competition was conducted by Hurwitz & Caves, in 1988. Their research was based on a regression associating the leading company's market share with the relative prices, the costs of promotion and other variables associated with brand loyalty. Hurwitz & Caves (1988) expected a negative relationship between the relative prices, which is defined as $(P_L - P_F) / P_F$ (P_L & P_F being the weighted average prices of the Leader and the Followers, respectively), and the leader's market share, in accordance with the law of Demand.

Findings from this research confirm that a positive price difference is associated with a decrease in the leader's market share, *ceteris paribus*. However, the fact that a 10% increase in the leader's price premium results in nearly a 0.5% loss of market share for the leader suggests a very small sensitivity to changes. Moreover, Hurwitz & Caves (1988) have found that the longer a company owns the patent, the more "robust" its market share is. That robustness in the market share is attributed to brand loyalty and low price sensitivity from the buyers' side. However, the companies that follow can, to a small extent, achieve a higher market share by increasing promotion costs for their generic products.

Caves et al. (1991) have also analyzed the effect that the entrance of generic drugs in the market has on the pricing practices for both branded and generic products, after the patent diploma has expired. In doing so, they have found that limit pricing policy is not evident, since after the patent is no longer valid, the innovator's price actually rises until a generic competitor appears. Thus, entrance in the market is not limited. Moreover, an increasing number of

generic drug companies entering the market results in a decreasing price on the innovator's side, even though that decrease is not that high, at 4.5% on average. It is worth mentioning that the higher the entrants' number, the lower the sensitivity of the innovator's price; after the first entry the price decreases by 2%, but with 20 generic competitors the decrease is 22%. According to Caves et al. (1991), this behavior can be considered as regular when the innovators face new competitors in the market.

The producers of generic drugs enter the market with much lower prices in comparison with the companies owning the brand, and these prices decline with the entrance of more competitors in the market as well. Prices could fall up to 17% of the branded product's price before the entrance of competitors. However, Caves et al. (1991) point out that despite these discounts in price, generic drug companies cannot gain a higher market share. It is worth mentioning that the effect that additional generic competitors have on the prices is higher on the generic products than on the branded ones.

Grabowski & Vernon's research (1992) has proven that the prices of generic drugs decline as well. However, a somewhat unusual finding was that the price of the branded product actually increases, due to a "segmented market dynamic". In other words, when generic drugs enter the market, consumers either switch to the lower priced generic product, or remain loyal to the original brand. The second category has a more inelastic demand curve, and thus prices can be increased. However, Grabowski & Vernon point out that despite that increase, the drug's average price is 21% lower 2 years after the new companies enter the market, because on average, branded products keep only half the market; the rest is gained by the generic ones.

In their findings, Lu & Comanor (1998) also confirm that a higher number of branded substitutes could result in lower prices. However, there is a difference in the pricing strategies used by companies producing therapeutically innovative and imitative pharmaceutical

products. More specifically, innovative drugs are usually launched under a *skimming* strategy that suggests a moderate price decrease over time. This strategy is employed since consumption of the product usually offers significant advantages in comparison to previous alternatives for those who do so. However, imitative drugs enter the market under a *penetration* strategy, which leads to a price increase curve over time. This strategy is preferred given that the product is only marginally improved compared to its counterparts. The type of products already in the market also affect the prices on the time of entrance. If the competition that the new product will face is more generic and there are not many branded products then the launch prices for new products will be relatively higher. However, their price will increase with lower rates in comparison to a more branded competition.

The research of Reiffen and Ward (2005) in pharmaceutical competition is consistent with the aforementioned ones, since their empirical findings indicate a fall in generic drug prices when the amount of competitors in the market is relatively higher. More specifically, Reiffen and Ward have shown that the profit margin, which is the difference between prices and marginal costs, is initially around 20% to 30% for the market monopolist. When the number of products is increased, a steady decline is observed in generic prices; the existence of 10 or more competitors results in marginal profits very close to 0, since prices approach the long-run marginal cost. Reiffen and Ward have also argued that an increasing flow is observed when it comes to generic industry profits, a flow that begins to fall after 5 to 12 months, since companies entering the market results in reduced profit margins.

Taken all of the researches above into consideration, the assumptions made regarding price policies when patent diplomas exist can be confirmed to a certain point. The companies that produce the pharmaceutically innovative products and enter the market earlier usually keep their prices relatively higher, since they have first-mover advantages, even after patents have expired, due to inelastic demand, which translates into brand loyalty from the consumers.

Pharmaceutically imitative products enter the market with lower prices, and earn a share of the market due to the existence of price-sensitive consumers. Finally, a basic prediction of microeconomic theory is confirmed, as both innovative and imitative products have lower prices, when more substitutes are available and competition is increased.

3.2. Research & Development

The sector of Research & Development in the pharmaceutical industry is, essentially, its core, since the basic function of the pharmaceutical companies, which is the supply of pharmaceutical products for those in need, cannot happen without proper researching and continuous developing. The production of a drug is a process that requires a lot of time, and it is not without its risks. Those two characteristics of pharmaceutical R&D highlight the importance of the sector, not only for theoretical analysis, but for real-life applications as well.

Given the aforementioned characteristics, the development of new pharmaceutical products is a multi-staged process. At several points in the process a pharmaceutical firm will review the research status and its development potential and decide accordingly on whether to proceed on the next stage or not. That decision depends on the net expected profits that the new drug will make, therefore a cost-benefit analysis is conducted, taking into account the potential therapeutic benefits, the expected frequency and severity of adverse reactions, projected additional development, costs related to marketing, distribution, and production and estimates of a future revenue stream. The market's situation in terms of size and competition must also be taken into account (DiMasi et al., 1991).

DiMasi et al. (1991) have also described the sequential process for the drugs that have completed all the stages and have acquired FDA marketing approval. It should be mentioned that many of the procedures to approve drugs in the EU are similar to those of the FDA (Van

Norman, 2016). However, there are differences in various issues, the most important of which are, according to Van Norman (2016), the time required for the approval of a drug, as well as the transparency of data on drug trials that have not been published.

The period from concept to market for a drug is important to patients and firms alike, since it generates costs for a product that is not available yet. Given that these costs can amount to billions of dollars (or euros, for that matter), the time spent in clinical trials and the time used by the agencies to conduct their product reviews are critical (Van Norman, 2016). Regarding clinical trials, an earlier market release, after Phase II of clinical trials and constant evaluations afterwards could be considered as a possible solution, and has been proposed in Europe already (Cooksey, 2006). Even though, however, Europe seems to be less strict when it comes to clinical trials, the situation is different in the reviews conducted. Despite popular belief, processes by the FDA are faster than those of the EMA. According to an analysis by Downing et al. (2012), completion of the first review is around 2 months earlier for the FDA, with the median total review time being shorter as well. Moreover, of the approved drugs in total for both Europe (either by the EMA or through mutual recognition by the member countries) and the United States, 63.7% were first approved in the U.S. (Downing et al., 2012)

The issue of transparency of data on trials and drug approval concerns both the FDA and the EMA, since it could be a source of publication bias, the phenomenon in which studies with positive results are more likely to be published than studies with negative results (Begg & Berlin, 1988). Transparency of data is an issue that is closely related to public safety and health, through the production of systematic reviews and meta-analyses (Van Norman, 2016). However, the FDA and the EMA do not deal with it in the same way. While at the FDA, any not-published data regarding drug applications is available (online, by request), at the

EMA, data is not available to the public, with the exception of overriding public interest (Van Norman, 2016)

Clinical testing is consisted of three separate phases. Phase I testing is performed on a small number of (usually healthy) volunteers. These trials are used to obtain useful information regarding toxicity, safe dosing, the drug's absorption, distribution and elimination in and from the human body, as well as its effects in metabolism. In phase II, the drug is administered to a larger number of people. The selected groups consist of patients for whom the drug is intended to be of benefit, in order to measure the drug's efficacy and obtain additional safety data. Success in the phase II trials means that there is significant evidence of efficacy. Finally, phase III, involves large-scale trials on patients. Larger sample sizes should result in statistically significant actual benefits. Because many patients are typically enrolled in the trials, not only the benefits found will be statistically significant, but infrequent adverse reactions can also be detected. Phase III could also serve as a proxy in order to determine how the drug would be utilized after marketing approval.

During the three phases of the clinical period, long-term stability testing, dosage formulation work and manufacture in sufficient amounts for clinical testing also occur. Additionally, experimentation on animals is continued to be conducted for long-term assessments of teratologic and carcinogenic effects. Upon completion of the clinical development phases, and if the firm believes that its evidence for approval is sufficient, it will submit a New Drug Application (NDA) to the FDA for review. Marketing for approved uses may begin upon notification from the FDA.

The completion of those sequential stages, as mentioned before, is a highly time-consuming process. More specifically, DiMasi et al. (1991) have found that it takes 98.9 months, on average, for a drug to be approved by the FDA, since the beginning of Phase I, while just the FDA approval lasts 2.5 years on average. In general, from synthesis to marketing approval,

the average length is 12 years, even though overlaps might exist in between stages. Obviously, the R&D process could last even more, if one takes into account the research before synthesis, which has been known to last even longer. The complexity of the pharmaceutical substances used in the synthesis, as well as the importance of proper testing and trialing, in order to ensure the drug's safety and efficacy, can reasonably account for the length of these procedures, and thus the length of the drug's development in sum.

Evidently, research & development in the pharmaceutical industry is a procedure not only time-consuming, but also expensive. According to data from Statista (2020), the R&D expenditure of U.S. leading biopharmaceutical research companies reaches nearly $80 billion worldwide. It is estimated that the development of a new drug costs around $2.6 billion. Therefore, a company that desires to invest in R&D ought to take into account the net present value (NPV) of the costs and the net present value of the revenues, in order to determine whether this investment will yield profits or not. The value of the investment in R&D concerns not only the company, whose aim is to maximize its profits, but the policymakers as well, since they aim at maximizing the social welfare.

For and R&D investment to be profitable, one has to evaluate the pharmaceutical market's structure and behavior first. In his revolutionary work, Capitalism, Socialism, and Democracy (1942), the famous economist Joseph Schumpeter laid the ground for research in the relationship between a market's structure and the trends in research & development. More specifically, Schumpeter (1942) states that:

> *On the one hand, largest-scale plans could in many cases not materialize at all if it were not known from the outset that competition will be discouraged by heavy capital requirements or lack of experience, or that means are available to discourage or checkmate it so as to gain the time and space for further developments (p.88-89)*

In other words, Schumpeter assumes that a more concentrated market, where competition is not that high, could be a better environment for research and development of innovative product. However, the question is whether this applies to the pharmaceutical industry or not; does a concentrated pharmaceutical market favor R&D in drugs?

Assuming that a pharmaceutical company invests in R&D, the application of the Dasgupta - Stiglitz model (as cited in Pepall *et al.*, 2017) in the pharmaceutical sector provides useful insight in the relationship between the market's structure and the investments in R&D. The model assumes Cournot oligopoly, with n identical firms. Each firm chooses its quantity q_i and the amount spent in R&D x_i. Even though R&D has its costs, it reduces the cost per unit of production c. More specifically, the cost per unit is a function of the amount spend in R&D; $c_i = c(x_i)$, $c'(x_i) < 0$. Therefore, the firm's net profit will be:

$$\pi_i = P(Q)q_i - c(x_i)q_i - x_i$$

If the R&D expenses are given, x*, then each firm's cost per unit is c(x*), and the firms' and market's equilibrium quantity can be determined. In Cournot analysis, the Lerner index in equilibrium is:

$$\frac{(P - c(x^*))}{P} = \frac{si}{\eta}$$

P is the price, si is the market share for firm I and η is the demand elasticity. Given that the firms are identical, $x_i^* = x^*$ for every i = 1, 2, …, n. Additionally, $s_i = {}^{1}/_{n}$. Therefore, the Lerner index can be rewritten as:

$$P\left(1 - \frac{1}{nh}\right) = c(x^*)$$

However, the optimal R&D expenses cannot be derived from this equation. In order to derive those, one has to compare the marginal benefit and the marginal cost from an increase in x,

dx. Since the marginal benefit is equal to $(-{}^{dc}/_{dx_i})$ qi and the marginal cost is $({}^{dx_i}/_{dx_i}) = 1$, the equilibrium holds for:

$$-\frac{dc}{dx_i} q_i = 1$$

Finally, given the fact that all firms are symmetric, the index i can be omitted, and thus the equation becomes:

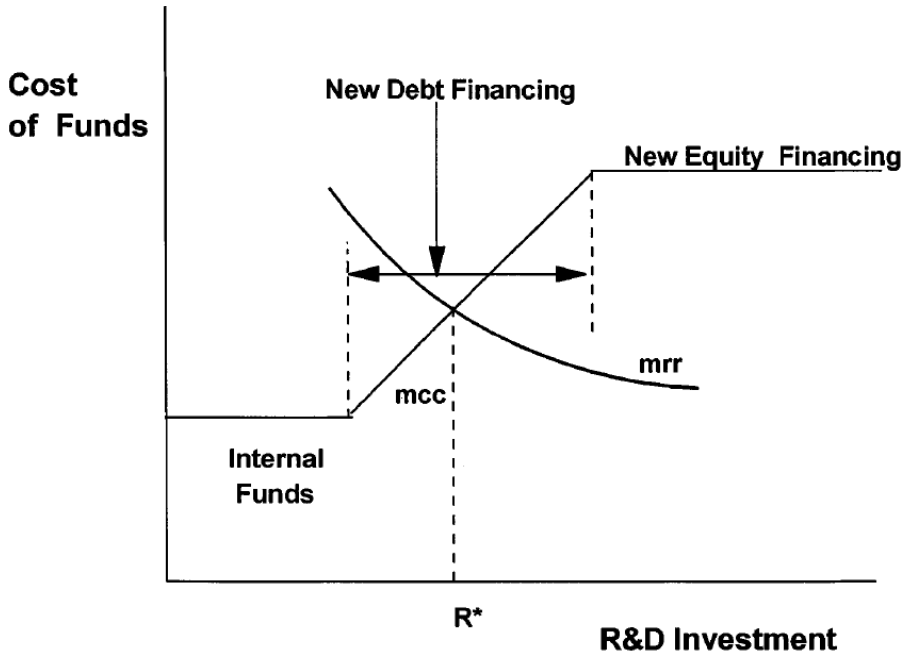
$$-\frac{dc}{dx} = 1$$

Through the equilibrium equations, it is proven that the higher the number of firms in the pharmaceutical market, the lower the amount spent on R&D by an individual company, and vice versa. Moreover, since the marginal benefit of R&D expenses is positively related to the company's production levels, a decrease in those levels, created by the increase of the number of firms, results in a decreased marginal benefit, and thus, a lower equilibrium level of expenses. However, the total R&D expenditure will not necessarily be decreased with additional firms; it could even be increased. In order for this to happen, the elasticity of demand should be relatively high, in order to avoid a significant reduction in prices when the quantity increases, due to increased production. Since R&D is funded by the price-cost margin, the firms' behavior regarding investment depends on the elasticity. Evidently, the Dasgupta - Stiglitz model support's Schumpeter's work, since it is proven that innovation is more favored in less antagonistic markets. In other words, if the industry is competitive in its nature, less effort is put into R&D, *ceteris paribus*.

In their work, Grabowski and Vernon (2000) provide a more focused approach on the determinants of research and development in the pharmaceutical industry. More specifically, they state that the decision for R&D investment is determined by the *marginal rate of return*

on investment schedule (mrr) and the *marginal cost of capital* schedule (mcc). The mrr is calculated by an arrangement of potential R&D projects in order of decreasing rates of return, and the mcc schedule reflects the opportunity cost of alternative investments. Figure 3 depicts how the optimal amount of investment R* is determined in the equilibrium:

Figure 3: **The R&D investment decision**



Source: ***Grabowski, H., & Vernon, J. (2000). The determinants of pharmaceutical research and development expenditures. Journal of Evolutionary Economics, 10(1-2), 201-215.***

The mcc schedule here consists of two horizontal segments. The lower one shows the cost of internal funds, while the higher ones the cost of new equity financing; their connection is the cost of new debt financing. Reasons for the difference in the cost of internal and external funds possibly include transaction costs, tax advantage, agency problems, costs of financial distress, and asymmetric information (Grabowski and Vernon, 2000)

Mathematically the optimal level of investment, R*, is obtained by:

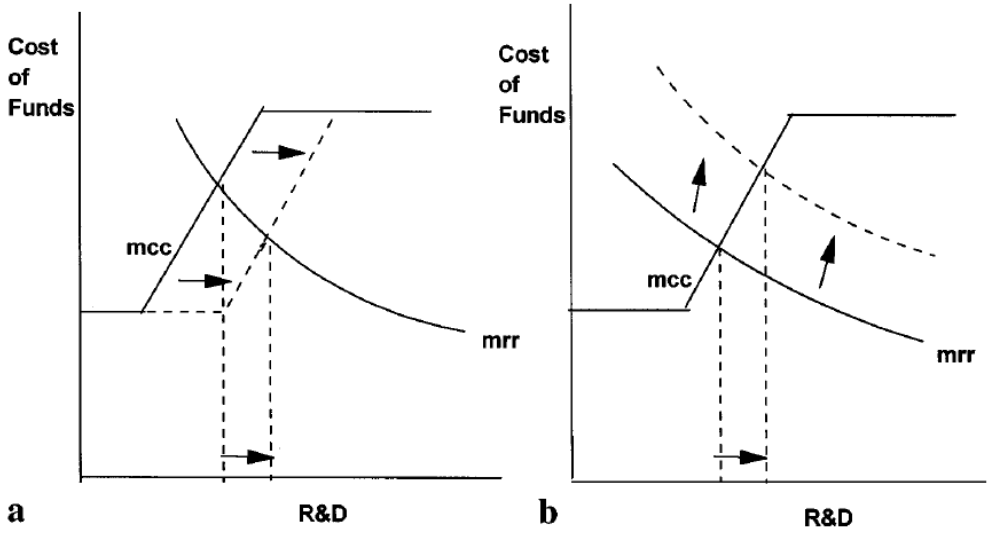
$$\mathrm{mrr}(\mathrm{R},\mathrm{X}) = \mathrm{mcc}(\mathrm{R},\mathrm{Z})$$

R is investment expenditures in R&D, X is a vector of (exogenous) variables influencing the return from new drug R&D and Z = a vector of (exogenous) variables influencing the opportunity cost of investing in new drug R&D. Solving for R:

$$R^* = f(X, Z)$$

If more internal funds, or cash flow, are available, optimal R&D investment is increased. Increased expected returns have the same effect on optimal R&D investment as well. This is depicted graphically in Figure 4:

Figure 4: **Two effects on R&D investment: (a) Increased cash flow - (b) Increased expected returns**



Source: ***Grabowski, H., & Vernon, J. (2000). The determinants of pharmaceutical research and development expenditures. Journal of Evolutionary Economics, 10(1-2), 201-215.***

By estimating this equation in a regression analysis, using data from 11 firms in a 20-year period (1974-1994), Grabowski & Vernon (2000) have confirmed that both expected returns and cash flow are essential characteristics in the pharmaceutical R&D. This is important, since it indicates that a relatively stricter public policy could actually reduce R&D. Government

interventions affect both the returns from R&D activity and the supply of funds in many ways. These mostly include pre-market regulatory controls, drug price and reimbursement controls, tax policy etc. (Grabowski & Vernon, 2000). Thus, when the government makes decisions regarding all those policies, it should take into account that the negative effect they have on present and future research and development could actually result in decreasing social welfare in the long run.

Finally, besides the market's structure and the government's policy, the decision for investment on pharmaceutical research & development depends on the firm's size. However, the relationship between these two is not that clear. While many economists assume that the bigger the firm, the more the activity in R&D, there are some who disagree. The importance of defining that relationship lies in the need for determining what the proper public policy regarding mergers & acquisitions between pharmaceutical companies should be; if bigger firms are more innovative, then the law ought to be less strict.

In theoretical level, there are adequate arguments both for and against the idea that bigger firms invest more in R&D. The advantages of bigger firms include a higher availability of funds to put into investment, the ability to hedge higher levels of risk through diversification in R&D activities, as well as economies of scale in research, since research is conducted more efficiently and the cost per unit of R&D activity decreases. (Santerre & Neun 2012, p.419). However, a big firm size is not without its disadvantages. Many analysts argue that big firms that operate in a "top-down" model, under central authority, face the problem of bureaucracy, which in turn creates communication issues, disruption in the information flow and, consequently, less creativity and innovation (Santerre & Neun 2012, p.419).

Since economic theory cannot provide the answer to this problem, research has turned on the empirical analysis. In their work, Acs and Audretsch (1987) have concluded that bigger firms have the R&D advantage when an industry is capital-intensive, marketing-intensive and has a relatively concentrated market. However, smaller firms are more productive in industries characterized by not too many big firms, in which the role of innovation and labor is essential. The pharmaceutical industry might be marketing-intensive, but since innovation is important, the work of pharmacologists and biochemists is necessary and the market is characterized by some big firms and many smaller ones, the safest conclusion is that optimal pharmaceutical innovation is achieved when there is a variety in the market, in terms of firm size (Santerre & Neun 2012, p.420). It appears that, despite their advantage, innovation by the small firms can be improved by the dominance of bigger ones in the industry. That occurs because each category operates based on its advantages; smaller firms are better in research and discovery, but bigger are better in development and marketing. Thus, both are necessary for pharmaceutical R&D to progress as a whole.

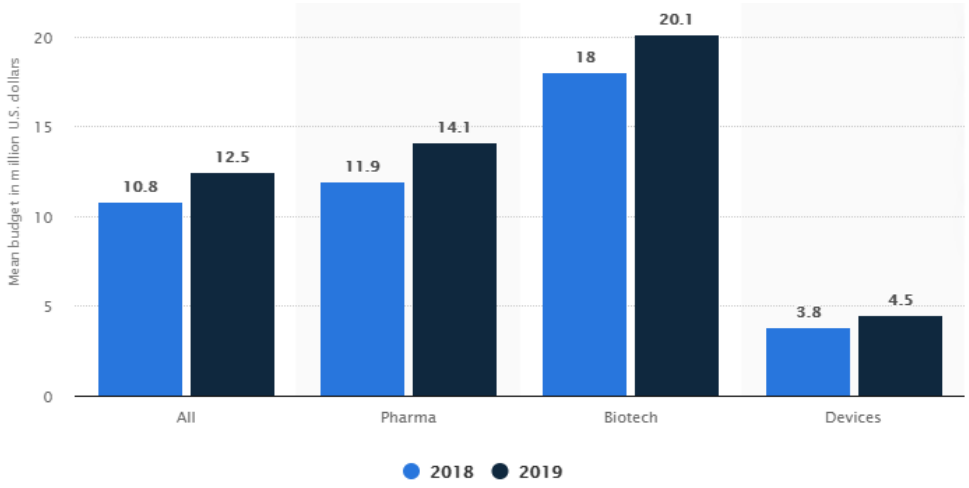
3.3. Marketing

Marketing is an essential element of the drug production in the pharmaceutical market. In most industries, the promoting and marketing of a product has an important role because it affects consumer behavior, not only by increasing the information available, but by affecting the prices, and thus the market outcome. In the pharmaceutical industry, given the product's nature, the role of marketing is even more prominent. Drugs are essential for life preservation and improvement. Therefore, when prescribing them, doctors ought to know every characteristic, every property and every side effect, in order to decide what to give to patients

with different characteristics (e.g. age, weight, health status) (Santerre & Neun 2012, p. 414). Besides the doctors, the patients, as consumers, ought to know the various characteristics of the products available for purchase, so as to ensure they make the optimal choice when following their doctor's prescriptions, or when they purchase something themselves.

The following figure depicts the budgets for various types of health care companies in the United States for 2018 and 2019:

Figure 5: **Mean marketing budgets of health care companies in the U.S. (US$ million) (2018 - 2019)**



Source: ***Statista, https://www.statista.com/statistics/275384/marketing-budgets-of-us-health-care-companies/#statisticContainer (Accessed 23/4/2020)***

Even though pharmaceutical companies do not spend as much as biotech companies in marketing, the average budgets are still considerable, increasing by $2.2 million per company, from $11.9 million to $14.1 million, between 2018 and 2019. However, the aggregate amount of marketing budget is considerably higher; according to Statista (2020), the pharmaceutical industry spent $6.5 billion, in total, on advertising in the United States in 2018. The top company in marketing investing, Pfizer, spent nearly $1.2 billion.

Without doubt, the aim of marketing and advertising of the pharmaceutical products is to promote them to doctors and patients. This promotion is achieved by a combination of information and persuasion, as Leffler and Hurwitz and Caves (as cited in Caves et al. 1991) point out. The information side of promotion emphasizes on detailing, while the persuasion side of promotion focuses on establishing a brand in the market, and thus earning the benefits of brand loyalty. Both information and persuasion have a significant effect on the pharmaceutical market's competition, the product's pricing, and, consequently, the welfare of the consumers and the society.

On the one hand, promotion through information and detailing includes frequent visitations to healthcare professionals by representatives of the pharmaceutical company, who provide detailed information on the new drug and its properties, through direct communication with the doctor. The information that becomes available to the doctor serves two purposes; not only does it increase the demand for the specific drug, it helps establishing a certain loyalty to the brand as well (Caves et al., 1991). Other ways of informing the professionals include advertising in medical journals and direct advertising, but they are considered complementary to detailing through visits. Leffler (as cited in Santerre & Neun 2012) finds out that marketing intensity is more significant for products that have recently entered the market, and that marketing contributes to earning higher market shares.

On the other hand, promotion through persuasion is more related to brand loyalty as a factor in the competition of the market, since consumers prefer specific products not by taking into consideration their benefits and disadvantages, but by habit. A pharmaceutical company owning a patent is expected to increase its marketing costs before the patent's expiration, in order to build trust between themselves and the patients, through proper persuasion. However, after the patent has expired and competition has increased, the interests shifts to information. Persuasion is not that important, because emphasis needs to be put into

assuring that trust will not be broken. Caves et al. (1991) have found out that generic companies cannot earn considerably high market shares, despite lower pricing, a situation that reflects the efficiency of brand loyalty through proper persuasion from the pharmaceutically innovative companies.

The two aspects of promotion, information and persuasion, have somewhat opposite effects on the society's total welfare, through their effect on competition; information encourages competition in the pharmaceutical market, while persuasion hinders it. (Santerre & Neun 2012, p.414). Given that both sides of marketing and promotion, in theoretical analysis, are highly important in the pharmaceutical industry, empirical evidence is needed to verify which prevails. In doing so, one can have a better understanding as to what is the final effect of marketing in the pharmaceutical market's competition, and thus in the total welfare.

In his work, Rizzo (1999) has analyzed the effect of marketing in the pharmaceutical competition through the price elasticity of demand. More specifically, since microeconomic theory suggests that promotion decreases the price elasticity of demand of a product and increases its price, while information has opposite effects on both factors, marketing is closely associated with public policies and legal procedures, like legislative restrictions on advertising and antitrust litigations (Rizzo, 1999).

Using data for antihypertensive drugs, the market of which contains mostly brand-name products, under protection by patent diplomas (Rizzo, 1999), the empirical analysis suggests that product promotion actually prevents competition in the pharmaceutical market, since it decreases the price elasticities and leads to higher price at the equilibrium (Rizzo, 1999). More specifically, the value and the role of detailing is questioned, since evidence suggests that many physicians are not that affected by it (Rizzo, 1999). Therefore, increasing promotion in general decreases the short-run price elasticities, and vice versa. It is worth

mentioning that long-run elasticities are high, in consistency with microeconomic theory regarding profit-maximizing.

Taking both theoretical and empirical analysis into consideration, it is evident that marketing is a useful tool for the pharmaceutical companies in many ways. However, despite certain positive aspects, like informing both doctors and patients for the pharmaceutical product's properties, promotion is used mainly as a means to increase the firm's power in the market, through the process of consumer persuasion. Policymakers ought to take into account the positive and negative properties of marketing and promotion, in order to apply the proper policies, so as to ensure that the society's welfare is not harmed.

4. Pharmaceutical Market Returns

In this part the returns of the pharmaceutical industry are evaluated. Restrictions in the competitive market, like patents, trademarks and high promotion costs, characterize the pharmaceutical market, which means that the established firms may have enough market power to limit production, increase prices and enjoy incredibly high profits.

First, the inflation rate for the prices of prescription drugs is compared to the general inflation in the US, in order to determine whether these products have relatively higher prices. The movement of prices needs to be analyzed, not only because it has direct consequences regarding the quantities being supplied and demanded in the market, but because it acts as a "signal" for the industry's behavior as a whole.

Second, the production of new pharmaceutical products falls under the microscope. More specifically, the new chemical entities that have been produced around the world for the past years could induce improvements in the quality of life, therefore the relationship between prices, quantities and consumer benefits in the short and long run needs to be analyzed.

Finally, using financial statistics, the profitability of the pharmaceutical sector is examined, in order to answer the questions regarding the high profitability of the firms and the sector as a whole.

4.1. Prices

A significantly important aspect of evaluating the returns of the pharmaceutical industry is the level of prices for drugs and other pharmaceutical products. A continuous inflation in the price of drugs could result in a decrease of the consumers' surplus, especially if their income does

not change (Santerre & Neun 2012, p. 421) therefore the price movement in the pharmaceutical market should be taken into consideration by the policy makers when public policies are to be applied in the market.

The analysis begins by comparing drug prices among certain developed countries, in order to determine if there are any outliers among them. The existence of outliers means that there are countries that have significantly higher drug prices than the average, and therefore it is necessary for public policies to account for that price levels, in order to maximize the society's welfare. Table 3 presents the descriptive statistics, by country, for average drug prices, across 12 countries:

Table 3: **Descriptive Statistics on Prescription Drug Prices for Select Countries (2018)**

Country	*Average*	*Min*	*Max*	*Pharmaceutical spending/capita*	*Drugs listed*
US	466.15	5.36	16597.86	12220.00	79
UK	105.45	0.08	2921.09	469.00	78
Japan	69.50	0.15	488.66	838.00	58
Canada (Ontario)	132.59	0.27	3557.82	832.00	47
Australia	113.57	0.67	3043.87	673.00	62
Portugal	82.97	0.32	682.02	403.00	37
France	104.51	0.42	2455.79	653.00	54
Netherlands	152.86	1.42	3742.87	396.00	61
Germany	165.01	0.46	4728.76	823.00	65
Denmark	182.29	0.90	4719.68	318.00	65
Sweden	143.91	0.54	3612.73	515.00	59
Switzerland	116.22	0.69	3745.85	963.00	72
Average	152.92	0.07	16597.86	675.25	79
Average (excluding US)	124.45	0.08	4728.76	625.73	59.9

Source: ***A Painful Pill to Swallow: U.S. vs. International Prescription Drug Prices (Accessed 2/5/2020)***

From the data depicted on the table, it appears that drug prices in the United States are considerably higher than the rest of the countries in the analysis. Regarding average prices and pharmaceutical spending per capita, the average is nearly 25% and 5% of the U.S. statistics, respectively. U.S. drug prices are outliers in all categories, therefore prices are

definitely higher, even if the association with the GDP per capita for each country is taken into account. A positive association would result in lower differences, something that does not happen in this case. (Ways & Means committee, 2019).

Given these differences, emphasis is placed on the United States. In the U.S., the changes in the price of prescription drugs are calculated using the CPI Prescription Drug Index (CPI-Rx) by the Bureau of Labor Statistics (BLS). The Council of Economic Advisers (2019) suggests that the CPI-Rx is the optimal way to measure those changes, since it contains a large number of prescription drugs, accounting for the lower-cost generic ones. Moreover, the CPI-Rx uses transaction prices, taking into account any price discounts that might occur. However, using the CPI-Rx, one cannot measure properly the improvement in the value of the consumer, with the entry of new goods, higher in quality. Also, since CPI-Rx uses average drug prices, individual products may have extreme increases (or decreases) in their prices that are omitted.

However, one cannot draw proper conclusions without comparing the movement of drug prices with prices in general. Using data on the CPI for all urban products, taken from the Federal Reserve Bank of St. Louis (FRED), comparison between the general price levels and the price levels of prescription drugs can not only depict the movement of drug prices, but how is that beneficial or not. Prices can be compared either at their original data value, using 1982-84 as a base period, or their 12-month percent change. The results are depicted below:

Figure 6a : **CPI-Rx & CPI-U, Original Data Value (Base period: 1982 - 84 = 100) (1984 - 2019)**

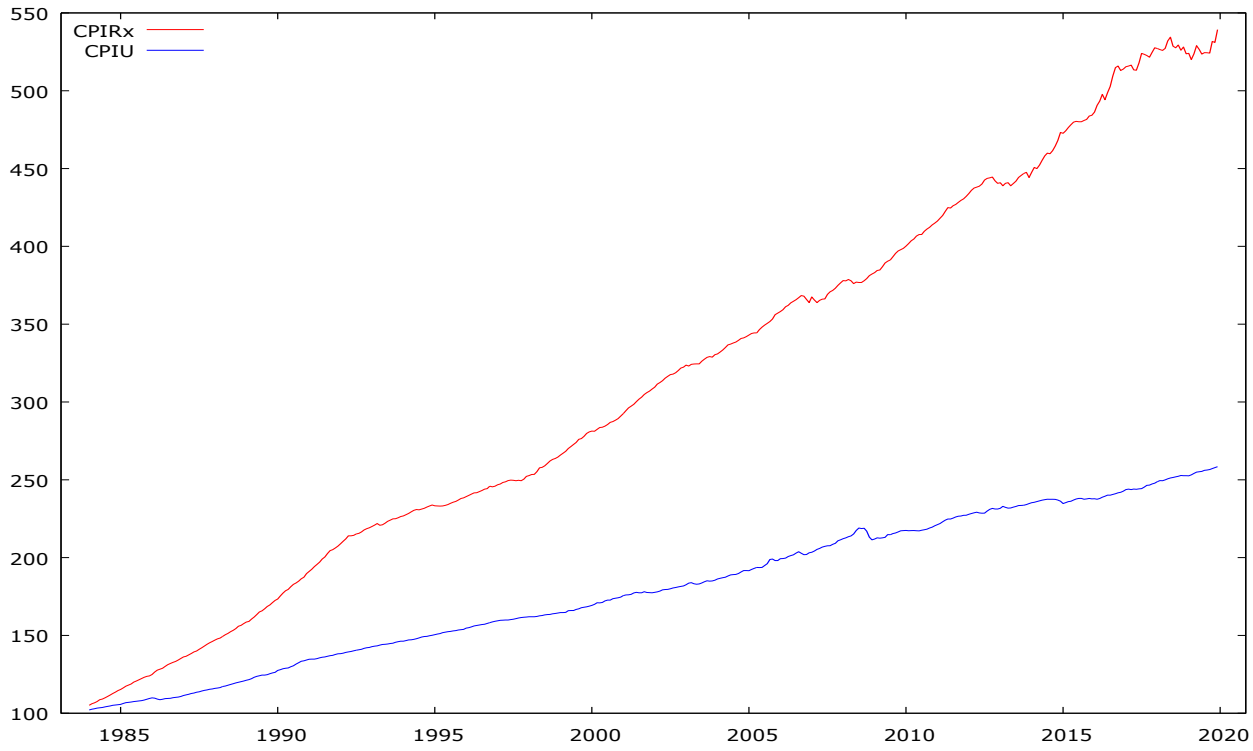
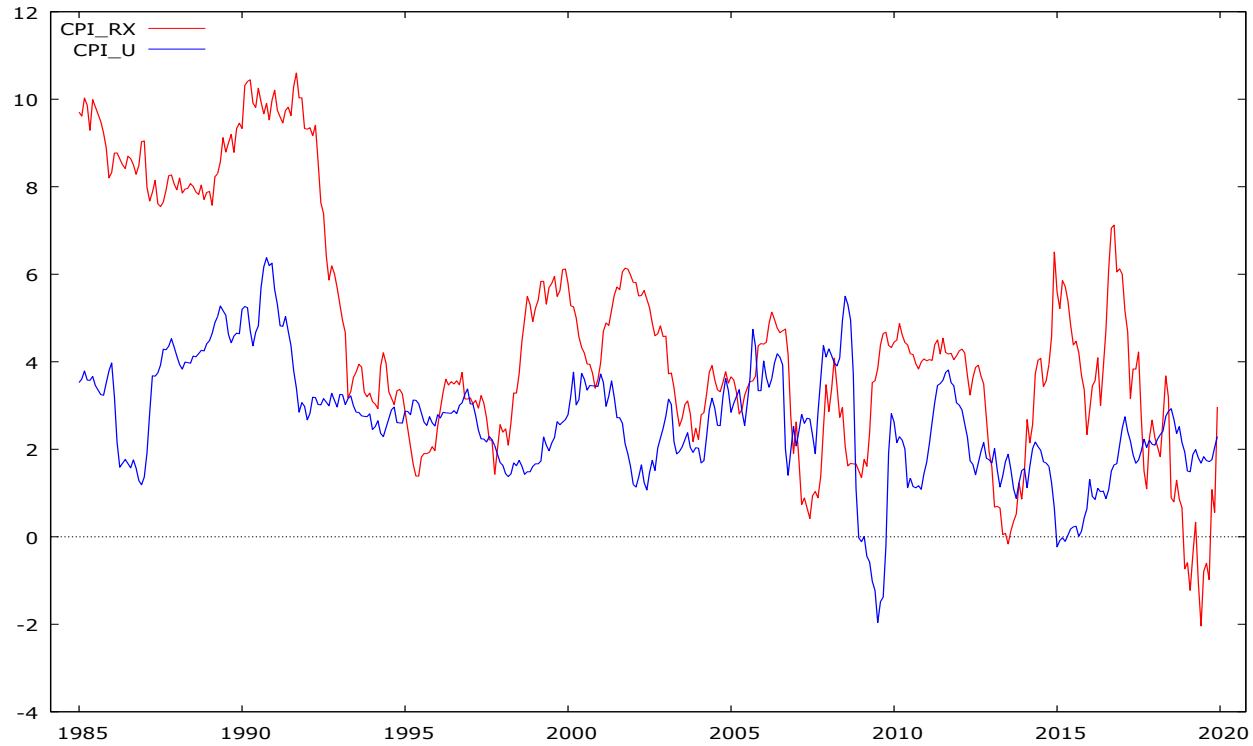


Figure 6b: **CPI-Rx & CPI-U, 12-month percent change (1984 - 2019)**



Upon analyzing those graphs, it appears that prescription drug prices have been, for the most part, relatively higher in comparison to general price levels, and increasing with a higher rate. These price movements could signal reductions in the consumers' surplus, and their continuous upwards trend should be a matter of public policy. However, in the last couple of years, drug prices are increasing more slowly than general prices, or even decreasing. This could be a positive sign towards increasing the consumer's welfare

Nevertheless, as mentioned before, the CPI-Rx, using average drug prices, does not account for any outlying movements in specific drugs. Moreover, the consumers' welfare is not properly estimated, since quality improvements in drugs are not taken into account. Scherer (1993) supports the existence of this issue:

> *Some new drugs, by improving the quality of life or making expensive surgery unnecessary, plainly yield enormous increments of consumer surplus. Except in the case of computers, the Bureau of Labor Statistics does not use hedonic methods to derive its manufactured product price indices, and as a result, its indices do not capture the gain in consumers' surplus contributed by new products. This leads one to suppose that "true" (i.e., hedonic) rates of price increase are overstated. (p. 103).*

In any case, the movement of the prescription drug prices needs to be constantly evaluated when the pharmaceutical industry is analyzed. Since drug prices are affected by many industry factors, like investment in R&D and marketing expenditures, their movement could signal the behavior of the pharmaceutical industry in total. However, overpricing could be an issue; excessive profit margins, resulting in excessive profits for the pharmaceutical firms at the expense of the consumers' welfare, need to be under constant supervision by the public policymakers.

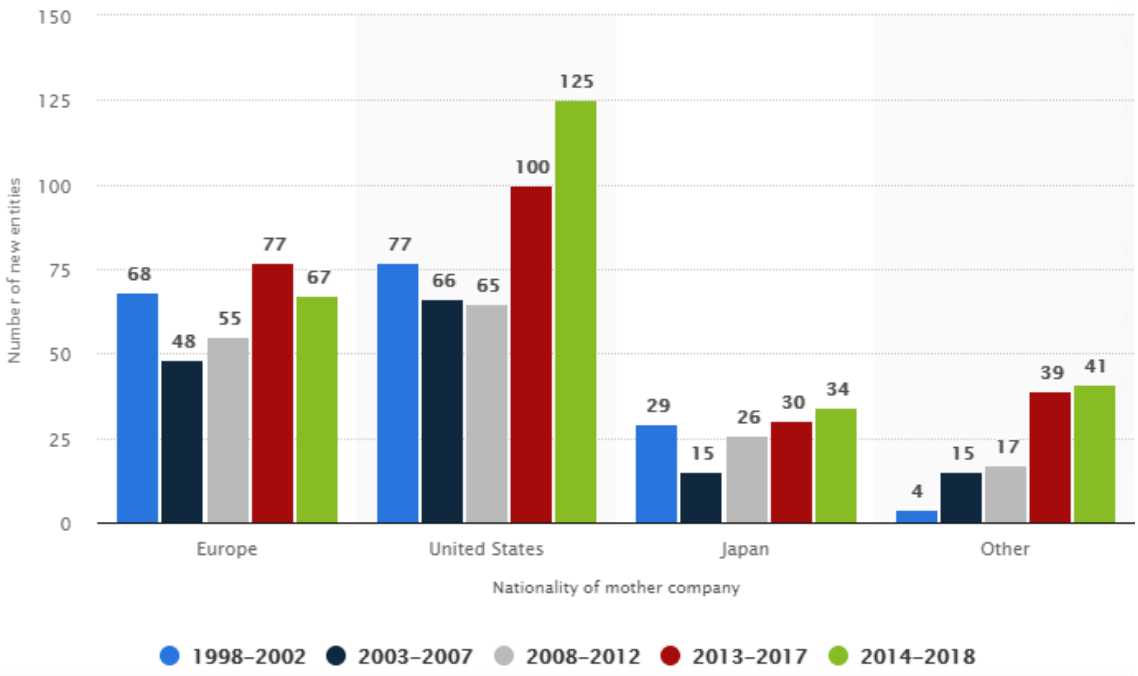
4.2. Production of New Pharmaceutical Products

Basic economic theory states that the society's welfare is increased when goods are produced until the marginal benefit of the society (MSB) is equal to the marginal cost (MSC). There is no reason to assume that this does not apply to pharmaceutical products. Therefore, the production of new drugs could signal the changes in the society's welfare, taking into account the pharmaceutical industry's structure and behavior, as well as the motives for producing efficient levels of pharmaceutical products (Santerre & Neun 2012, p.422). New Chemical Entities, or NCEs, are a suitable way of measuring pharmaceutical production. According to the Code of Federal Regulations (2016):

> *New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other NDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 C.F.R. §314.108)*

The following graph depicts how many new chemical (and biological) entities developed between 1998 and 2018, by nationality of the company producing them. Europe, the United States, Japan, and other countries are the four regions, while the time period is separated into 4 sub-periods (1998 - 2002, 2003 - 2007, 2008 - 2012, 2013 - 2017) plus a fifth, separate, to account for data for the last four years (2014 - 2018):

Figure 7: **Number of new chemical or biological entities by region of origin (1998 - 2018)**



Source: ***https://www.statista.com/statistics/275262/pharmaceutical-industry-new-entities-by-region/***

Two are the main observations when analyzing this graph. First of all, it is evident that the United States are the country with the most NCEs produced in every time period, a fact that confirms the leading role of this particular country in the pharmaceutical industry worldwide. However, despite a general increasing trend between the time periods, during the years of the financial crisis and its aftermath (2008 - 2012), as well as few years before it, the amount of new entities was lower than the beginning of the millennium, and considerably lower than the last 2 to 7 years. This could signal positive results for the consumer's welfare.

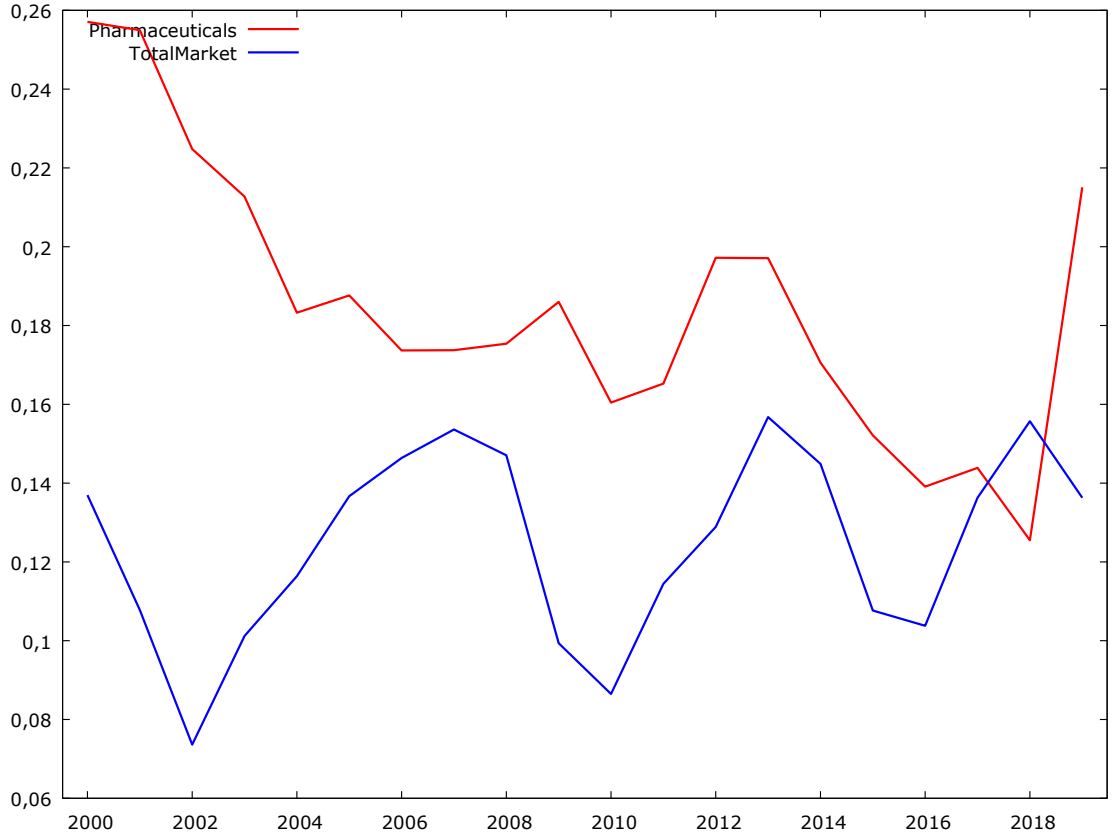
Studies have shown that new pharmaceutical products improve the quality of life, increase the life expectancy or even substitute for costly surgical procedures (Santerre & Neun 2012, p.422). Lichtenberg (2001), suggests that, in replacing older with newer drugs, mortality, morbidity, as well as total medical spending, actually decrease. Therefore, any analysis conducted on prescription drug spending, much of it being due to this replacement, should take into account the differences in quality.

The fact that the cost of new pharmaceutical products could, often, be offset by reducing the non-pharmaceutical costs is often referred to as the “new drug offset effect” (Santerre & Neun 2012, p.423). The offset effect of drugs should be measured when their price movement is analyzed, given that their production is based on research & development. As mentioned before, pharmaceutical R&D is closely related to expected returns and cash flow for a firm. Theoretically, therefore, the correlation between prices and new products is expected to be positive, a phenomenon that not only confirms the *law of supply*, but it raises questions as to whether increases in price can actually be beneficial for the consumers in the long run.

4.3 Profitability

When one performs an economic analysis on the pharmaceutical market, it is usually assumed that the so-called pharmaceutical “giants” make use of various aspects of the industry, like patents, first-mover advantages, and inelastic demand on certain products, in order to achieve excessively high profits. A robust way of measuring the profitability of a company or sector is the Return on Equity ratio (ROE), which is equal to the net income over the shareholders’ equity (Bodie, Kane, Marcus 2018, p. 544). In figure 5, the ROE of the pharmaceutical industry is compared to that of the market’s total:

Figure 8: **ROE of pharmaceutical sector and market in total (2000 - 2020)**



Source: ***Damodaran Online, http://people.stern.nyu.edu/adamodar/New_Home_Page/dataarchived.html***

Figure 8 shows that, despite the negative trend, the pharmaceutical ROE is always (with the exception of 2018) higher than the market ROE. Therefore, the profitability in the pharmaceutical industry is higher in comparison. However, it is worth mentioning that there could be mistakes in the estimation of the pharmaceutical ROE, if expenditures for R&D and marketing are not taken into account; the results could be lower. Even correcting for any accounting mistakes, pharmaceutical profits remain higher than the market average (Comanor, as cited in Santerre & Neun 2012, p.426).

Companies in the pharmaceutical industry usually claim that, given the high risks that come with investing in R&D, pharmaceutical returns should be high, because otherwise risk-averse investors would not put their money in the pharmaceutical industry (Santerre & Neun 2012, p.426). In order to properly measure the risk, however, one should not only take into account

the variation in the pharmaceutical returns as an industry, but the risks for individual firms as well. In their study, Grabowski and Vernon (1990) have found high skewness in the variation of returns, since only the top 30 drugs have covered the average R&D costs. An important conclusion of Grabowski and Vernon (1990) was that firms, in order to be able to afford the process of developing new drugs by covering their (large) fixed costs, must have a successful product in the market from time to time.

Even though the high returns in the pharmaceutical market can be explained by the high risks of R&D, a study by the Office of Technology Assessment (1993) has found evidence that shows higher returns on R&D than the levels required to reward investors. Therefore, the existence of high profitability in the pharmaceutical industry cannot be denied. The question asked though, is what can be done to ensure that the pharmaceutical companies do not make excessive profits by increasing their prices, because that would mean that the R&D budget is not allocated properly, affecting the consumers' welfare through the production of new drugs in the long run.

5. Government Intervention - Clawbacks

Taking into consideration all of the above, and given the fact that health is considered to be a basic right for everybody, it becomes apparent that the pharmaceutical industry needs to be under government regulation, so as to ensure that the quantities and prices in the market do not decrease the consumer's surplus and/or create high dead weight losses. The government's intervention in the pharmaceutical market takes many forms; through their health systems, each government ensures that the market operates optimally, by deciding which products will enter the market, as well as their prices (to a certain degree), and who is going to pay for them. The pharmaceutical companies control the products' supply, therefore they have certain ways of "responding" to government interventions.

5.1. Discounting policies - clawbacks

In the decision - making process of both the government and the pharmaceutical companies, discounting policies, taking the form of rebates and clawbacks, play a major role by preventing an overshooting of the government's budget on healthcare. Table 4 presents the situation regarding discounting policies in the European area, for 2017.

Table 4: **Rebates and clawbacks in European countries (2017)**

Country	Rebates & Clawbacks (€ millions)	Percentage contribution of industry to total expenditure
Germany	5559	13.30%
France	1637	6.00%
Italy	1401	7.40%
Greece	946	27.30%
Spain	500	3.10%
Romania	243	7.80%
Portugal	161	6.60%
Ireland	51	2.90%
Sweden	16	0.80%
Netherlands	0	0.00%
Average	1168	8.60%

Source: ***sfee.gr, Greece holds negative record of heaviest burden on pharmaceutical companies – three times the European average! (Accessed 20/6/2020)***

From the data depicted on the table, it appears that the discount policies are not the same for every country in Europe, with German pharmaceutical companies spending nearly 5.6 billion euros on rebates and clawbacks, while in relative terms, Greek pharmaceutical companies cover around 25-30% of the overall spending. The percentage contribution, on average, is 8.6%. Therefore, rebates and clawbacks are widely used in European countries. However, there is no systematic review of these policies for the states in the European Union (Carone, Schwierz & Xavier, 2012).

In this analysis, emphasis is placed on clawbacks, the refund that is claimed once the budget that the government has decided upon has been exceeded (Carone et al. 2012).

5.2. The model

A Cournot duopoly market is taken into consideration, where two firms $i = 1, 2$ produce a nearly identical pharmaceutical product. For simplicity reasons, the assumption that firm 1 produces an innovative product, while firm 2 produces a generic product, and thus their prices are differentiated, is omitted. However, the model could be rendered to include that scenario.

Without loss of generality, it is assumed that each firm's strategic variable is the level of marketing employed in order to increase their demand. However, since the marketing techniques are not only used to persuade, but to inform as well, it can be assumed that there are positive externalities created from each firm's marketing level to the quantity level of the other. The quantity equations are:

$$q_1 = am_1^2 + b_1 * m_1 * m_2 \quad (1)$$

$$q_2 = am_2^2 + b_2 * m_1 * m_2 \quad (2)$$

where $a > 0$ represents the size of the market, and $b_i \in (0, 1]$, $i = 1, 2$ represents the degree of externality created by each level of marketing. Moreover, since the products' price is set by the government, it can be assumed that $P = P_0$. Regarding costs, the function of both firms is linear.

$$C_i = c_i * m_i \quad (3)$$

The clawback mechanism is activated when the total revenue of all firms is greater than the clawback threshold (CB_{Max}). Therefore, if

$$TR_i = P_0 * q_i \quad (4)$$

is each firm's revenue function, the clawback function for each firm is:

$$CB_i = \begin{cases} 0, & \sum_1^i TR_i \leq CB_{Max} \\ MS_i\left(\sum_1^i TR_i - CB_{Max}\right), & \sum_1^i TR_i > CB_{Max} \end{cases} \quad (5)$$

with MS_i being the market share percentage for each firm

$$MS_i = \left({}^{q_i}/_{Q}\right) \tag{6}$$

Finally, each firm's profit function is:

$$\Pi_i = TR_i - C_i - CB_i \tag{7}$$

Substituting the equations (1) to (6) in the above, the result is:

$$\Pi_1 = \begin{cases} P_0(am_1^2 + b_1 m_1 m_2) - c_1 m_1, & TR_1 + TR_2 < CB_{Max} \\ P_0(am_1^2 + b_1 m_1 m_2) \\ -c_1 m_1 \\ -\left(\frac{am_1^2 + b_1 m_1 m_2}{am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2}\right)(P_0(am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2) - CB_{Max}), & TR_1 + TR_2 \geq CB_{Max} \end{cases} \tag{8}$$

$$\Pi_2 = \begin{cases} P_0(am_2^2 + b_2 m_1 m_2) - c_2 m_2, & TR_1 + TR_2 < CB_{Max} \\ P_0(am_2^2 + b_2 m_1 m_2) \\ -c_2 m_2 \\ -\left(\frac{am_2^2 + b_2 m_1 m_2}{am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2}\right)(P_0(am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2) - CB_{Max}), & TR_1 + TR_2 \geq CB_{Max} \end{cases} \tag{9}$$

If the sum of total revenues is not greater than the clawback threshold, the profit equations are:

$$\Pi_1 = P_0(am_1^2 + b_1 m_1 m_2) - c_1 m_1 \tag{8a}$$

$$\Pi_1 = P_0(am_1^2 + b_1 m_1 m_2) - c_1 m_1 - \left(\frac{am_1^2 + b_1 m_1 m_2}{am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2}\right)(P_0(am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_1 m_2) - CB_{Max}) \tag{8b}$$

$$\Pi_2 = P_0(am_2^2 + b_2 m_1 m_2) - c_2 m_2 \tag{9a}$$

$$\Pi_2 = P_0(am_1^2 + b_2 m_2 m_1) - c_2 m_2 - \left(\frac{am_2^2 + b_2 m_2 m_1}{am_1^2 + b_1 m_2 m_1 + am_2^2 + b_2 m_2 m_1}\right)(P_0(am_1^2 + b_1 m_1 m_2 + am_2^2 + b_2 m_2 m_1) - CB_{Max}) \tag{8b}$$

Since clawbacks are imposed by the government, the analysis begins using equations (9a) and (9b). If, as a result of the maximization process, the sum of total revenues is lower than the clawback threshold, equations (8a) and (9a) will be employed.

Given the complexity of the optimal marketing levels equations, it would not be easily feasible to calculate how each variable affects the final result using derivatives. Instead, the usage of arbitrary values for the market size, the degree of externality the marginal costs and the products' price is employed, in order for the behavior of marketing levels to be analyzed, when a clawback threshold is in effect.

5.3. Results

As mentioned before, at first some values are set arbitrarily, in order to determine the relationship between the clawback threshold and the marketing levels. The analysis begins under the hypothesis that all the other variables ($a, b_1, b_2, c_1, c_2, P_0$) are equal to 1, and thus equations (8b) and (9b) are, respectively:

$$\Pi_1 = m_1^2 + m_1 m_2 - m_1 - \left(\frac{m_1^2 + m_1 m_2}{m_1^2 + m_2^2 + 2m_1 m_2}\right)(m_1^2 + m_2^2 + 2m_1 m_2 - CB_{Max})$$

$$\Pi_2 = m_2^2 + m_1 m_2 - m_2 - \left(\frac{m_2^2 + m_2 m_1}{m_1^2 + m_2^2 + 2m_2 m_1}\right)(m_1^2 + m_2^2 + 2m_2 m_1 - CB_{Max})$$

The first order conditions of the profit maximization problems yield the following reaction functions:

$$m_1 = \frac{CB_{Max} m_2}{m_1 + m_2} - m_2 \quad (10a)$$

$$m_2 = \frac{CB_{Max} m_1}{m_1 + m_2} - m_1 \quad (10b)$$

Solving simultaneously the system of the reaction functions (10a) and (10b), the results are:

$$m_1 = 0.25 CB_{Max}$$

$$m_2 = 0.25 CB_{Max}$$

A very important conclusion can be drawn from the results; *the higher the clawback threshold is set, the higher are the marketing levels that the firms choose*. The second step of the analysis is to determine the movement of the profits for each firm, when the clawback threshold is increased or decreased. This can be done using arbitrary values for CB_{Max} and substituting on the equations above. The results are presented on Table 5:

Table 5: **The relationship between Clawback Threshold and Firm Profits**

$\boldsymbol{CB_{Max}}$	$\boldsymbol{m_1}$	$\boldsymbol{m_2}$	$\boldsymbol{TR_1}$	$\boldsymbol{TR_2}$	$\boldsymbol{TC_1}$	$\boldsymbol{TC_2}$	$\boldsymbol{\Pi_1}$	$\boldsymbol{\Pi_2}$
50	**12.5**	**12.5**	312.5	312.5	12.5	12.5	**12.5**	**12.5**
100	**25**	**25**	1250	1250	25	25	**25**	**25**
150	**37.5**	**37.5**	2812.5	2812.5	37.5	37.5	**37.5**	**37.5**
200	**50**	**50**	5000	5000	50	50	**50**	**50**
500	**125**	**125**	31250	31250	125	125	**125**	**125**
1000	**250**	**250**	125000	125000	250	250	**250**	**250**

The results show that pharmaceutical firms achieve higher profits if the clawback threshold is set higher, therefore the reduction of the threshold, imposed by the government, can act as a measure against over-profitability in the pharmaceutical sector.

A sensitivity analysis could also be conducted, by altering the parameters $a,\ b_i, c_i$ and P_0. The analysis is performed by altering the value of each parameter, *ceteris paribus*. Starting with the market share, the question is what will happen if a is doubled, for example.

The first order conditions of the profit maximization problems yield equations (11a) and (11b):

$$2(m_1^2 + m_1 m_2 + m_2^2) = \frac{CB_{Max} m_2 (m_1^2 + 4m_1 m_2 + m_2^2)}{m_1^2 + m1m2 + m_2^2} \quad (11a)$$

$$\frac{CB_{Max} m_1 (m_1^2 + 4m_1 m_2 + m_2^2)}{2(m_1^2 + m1m2 + m_2^2)^2} = 1 \quad (11b)$$

Solving simultaneously for m_1 and m_2 the results are:

$$m_1 = 0.333CB_{Max}$$

$$m_2 = 0.333CB_{Max}$$

Once again, there is a positive relationship between the clawback threshold and the marketing levels, and the more a is increased, then the higher the effect that CB_{Max} has. Without loss of generality, if the clawback threshold is set to 100, the firms' profits can be determined for different values of a. The results are presented on Table 6a:

Table 6a: **The relationship between Market Share and Firm Profits** ($\boldsymbol{CB_{Max} = 100}$)

$\boldsymbol{a}$	$\boldsymbol{m_1}$	$\boldsymbol{m_2}$	$\boldsymbol{TR_1}$	$\boldsymbol{TR_2}$	$\boldsymbol{TC_1}$	$\boldsymbol{TC_2}$	$\boldsymbol{\Pi_1}$	$\boldsymbol{\Pi_2}$
1	**25**	**25**	1250	1250	25	25	**25**	**25**
2	**33.33**	**33.33**	3332.67	3332.67	33.33	33.33	**16.67**	**16.67**
5	**41.67**	**41.67**	10418.33	10418.33	41.67	41.67	**8.33**	**8.33**
10	**50**	**50**	22722.73	22722.73	45.45	45.45	**4.55**	**4.55**

The same process is repeated for $CB_{Max} = 200$**:**

Table 6b: **The relationship between Market Share and Firm Profits** ($\boldsymbol{CB_{Max} = 200}$)

$\boldsymbol{a}$	$\boldsymbol{m_1}$	$\boldsymbol{m_2}$	$\boldsymbol{TR_1}$	$\boldsymbol{TR_2}$	$\boldsymbol{TC_1}$	$\boldsymbol{TC_2}$	$\boldsymbol{\Pi_1}$	$\boldsymbol{\Pi_2}$
1	**50**	**50**	5000	5000	50	50	**50**	**50**
2	**66.66**	**66.66**	3332.67	3332.67	66.66	66.66	**33.34**	**33.34**
5	**83.34**	**83.34**	10418.33	10418.33	83.34	83.34	**16.66**	**16.66**
10	**90.90**	**90.90**	90890.91	90890.91	90.9	90.9	**9.1**	**9.1**

The results of tables 6a and 6b lead to an important conclusion: *An increase in the market size would yield profits for the pharmaceutical firms only in the scenario of an at least relatively equal clawback threshold increase*. Profits decrease otherwise, because the total revenue greatly exceeds the clawback threshold.

The analysis continues by altering the degree of externality $b_i, i = 1, 2$. Since $b_i \in (0, 1]$, the sensitivity analysis covers the scenarios in which the degree of externality is decreased, *ceteris paribus*, and with $CB_{Max} = 100$. If, $b_i = 0.5$, for example, the first order conditions of the profit maximization problems yield equations (12a) and (12b):

$$2(m_1^2 + m_1 m_2 + m_2^2) = \frac{CB_{Max} m_2 (m_1^2 + 4m_1 m_2 + m_2^2)}{m_1^2 + m1m2 + m_2^2} \quad (12a)$$

$$\frac{CB_{Max} m_1 (m_1^2 + 4m_1 m_2 + m_2^2)}{2(m_1^2 + m1m2 + m_2^2)^2} = 1 \quad (12b)$$

Solving simultaneously for m_1 and m_2 the results are:

$$m_1 = 0.333 CB_{Max}$$

$$m_2 = 0.333 CB_{Max}$$

Once again, there is a positive relationship between the clawback threshold and the marketing levels, and the more b_i is decreased, then the higher the effect that CB_{Max} has. The firms' profits can be determined for different values of b_i, and the results are presented on Table 7:

Table 7: **The relationship between the degree of externality and Firm Profits** ($\boldsymbol{CB_{Max} = 100}$)

$\boldsymbol{b_i}$	$\boldsymbol{m_1}$	$\boldsymbol{m_2}$	$\boldsymbol{TR_1}$	$\boldsymbol{TR_2}$	$\boldsymbol{TC_1}$	$\boldsymbol{TC_2}$	$\boldsymbol{\Pi_1}$	$\boldsymbol{\Pi_2}$
1	**25**	**25**	1250	1250	25	25	**25**	**25**
0.75	**28.57**	**28.57**	1428.43	1428.43	28.57	28.57	**21.43**	**21.43**
0.5	**33.33**	**33.33**	1666.33	1666.33	33.33	33.33	**16.67**	**16.67**
0.25	**50**	**50**	2000	2000	40	40	**10**	**10**
0.0001	**49.95**	**49.95**	2497.50	2497.50	49.95	49.95	**0.05**	**0.05**

It becomes rather obvious that the lower the degree of externality between the 2 firms, the lower their profits, even though their marketing levels are higher. This makes sense, since

the externality is positive, and therefore its decrease has negative effects on the firms' revenue, through lower quantity levels.

Doubling the firms' marginal cost c_i and taking the first order conditions yields the following equations:

$$2(m_1 + m_2) == \frac{CB_{Max} m_2}{m_1 + m_2} \quad (13a)$$

$$\frac{CB_{Max} m_1}{(m_1 + m_2)^2} = 2 \quad (13b)$$

Solving simultaneously for m_1 and m_2 the results are:

$$m_1 = 0.125 CB_{Max}$$

$$m_2 = 0.125 CB_{Max}$$

Similar results can be yielded for different marginal costs. Table 8 depicts the results produced for different values of c_i.

Table 8: **The relationship between Marginal Costs and Firm Profits** ($\boldsymbol{CB_{Max} = 100}$)

$\boldsymbol{b_i}$	$\boldsymbol{m_1}$	$\boldsymbol{m_2}$	$\boldsymbol{TR_1}$	$\boldsymbol{TR_2}$	$\boldsymbol{TC_1}$	$\boldsymbol{TC_2}$	$\boldsymbol{\Pi_1}$	$\boldsymbol{\Pi_2}$
1	**25**	**25**	1250	1250	25	25	**25**	**25**
2	**12.5**	**12.5**	312.50	312.50	25	25	**25**	**25**
4	**33.33**	**33.33**	78.13	78.13	25	25	**25**	**25**
10	**2.5**	**2.5**	12.5	12.5	25	25	**25**	**25**

Interestingly enough, when the marginal costs are increased, the marketing levels decrease and the profits stay the same, with lower total revenues. This could be attributed to the fact that the firms want their total costs to remain at the same levels (and they do so), while at the same time, the decrease on the total revenues reduces the clawback margin, and thus the clawback refund.

Finally, increasing the price level, for example from $P_0 = 1$ to $P_0 = 2$. The first order conditions of the profit maximization problems yield the following reaction functions:

$$m_1 = \frac{CB_{Max} m_2}{m_1 + m_2} - m_2 \quad (14a)$$

$$m_2 = \frac{CB_{Max} m_1}{m_1 + m_2} - m_1 \quad (14b)$$

Equations (14a) and (14b) are identical to (10a) and (10b), respectively, and thus the results are:

$$m_1 = 0.25 CB_{Max}$$

$$m_2 = 0.25 CB_{Max}$$

Therefore, the price level does not affect the equilibrium of the model. This could be due to the fact that the price is set by the government, and therefore it is not decided by the firms.

In general, a very important conclusion from the model is that the existence of clawbacks in the pharmaceutical market does not allow for over-profitability from the side of the firms, however there is a positive correlation between the level of the clawback threshold and the profits made. Moreover, in order for a market size increase to be profitable for the companies, the clawback thresholds should increase with at least an equal rate, and, under the assumption of positive externalities from the marketing levels of each firm to one another's quantity levels, in the presence of clawbacks those externalities should be as high as possible.

6. Conclusions

The structure of the pharmaceutical market suggests a relative high concentration, not only on the supply side, but on the demand side as well. The industry is somewhat dominated by great pharmaceutical companies, a phenomenon that, combined with a high coverage of the pharmaceutical expenditure from the government side, could result in a budget overshooting and inability to pay for the patients' needs.

In order to determine if problems do exist in the market, its structure and functions have been analyzed. It appears that the existence of patent diplomas in the market results in first mover advantages for the companies that own them, giving them monopolistic power, a power that can be enhanced by the mergers and acquisitions occurring in the industry, not only between companies, but with pharmaceutical benefit managers as well. The consequences of these activities could be either positive or negative; it depends on their effect on the products' prices.

Moreover, the marketing practices of the market participants are of high importance, since they, too, have both positive and negative consequences, given that they can either inform or persuade the consumer, depending on the firm's goals. The expenditure on marketing levels could be a strategic variable for a pharmaceutical company, when the government's intervention in the market is present.

The pricing strategies, greatly affected by the aforementioned industry characteristics, usually constitute a game between the leader companies and the followers, as it has been pointed out in numerous researches. The fact that prescription drug prices have been, however, higher in comparison to general price levels, and increasing, creates the need for government intervention in the scenario that high prices, which signal monopolistic power as well, are not related to investments in pharmaceutical research & development. If the profits of the firms

increase with time, without any drug quality improvement or increases in product availability then the government spending does not contribute to the society's welfare.

In order for the government to regulate the profits, the use of clawbacks has been employed. As the model described above has shown, the existence of a clawback threshold limits the profitability of the marketing expenditure, given the product's price, when the market size, the degree of externality and the marginal costs are fixed. The sensitivity analysis conducted proves that when clawbacks tend to limit the market, firms want the externalities of their marketing levels to be as high as possible, but for a market size increase to be profitable, the clawback threshold has to be increased too. In summary, in the absence of government intervention, the pharmaceutical industry a market is characterized by high profitability for the firms participating, with the revenues created not resulting in better (and more) products as efficiently as possible, through R&D activity. Therefore, since the government is responsible for most of the budget for pharmaceutical expenditure, regulation is often needed, in order to ensure that the operation of the pharmaceutical market is optimal.

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