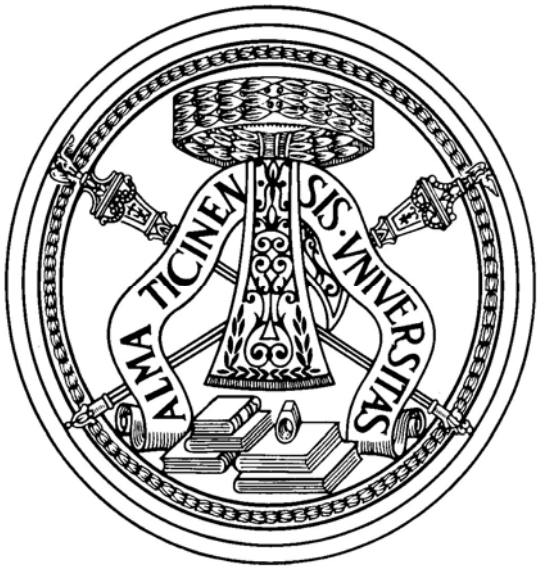

UNIVERSITY OF PAVIA

DEPARTMENT OF ECONOMICS AND MANAGEMENT

MASTER PROGRAMME IN ECONOMICS, FINANCE AND INTERNATIONAL INTEGRATION

THE GENERIC ENTRY INTO THE PHARMACEUTICAL MARKET: EVIDENCE FROM ANTITRUST CASES

Supervisor:

Prof. Alberto Cavaliere

Discussant:

Prof. Birgit Hagen

Student:

Floriana Bove

Matr:

431540

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“The only thing that stands between you and your dreams is the will to try and the belief that is actually possible”

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Chapter 3. The Economic Role of Patents and Patent Strategies

Chapter 4. AstraZeneca

Chapter 5. Reverse Payment-Settlements

Chapter 6. Servier

Chapter 7. Lundbeck

Chapter 8. Johnson&Johnson and Novartis

Introduction:

A generic drug, as described by the World Health Organization, it is an interchangeable product with the "original" drug or with the patented one, also called branded. This interchangeability could be seen both in terms of formulation, pharmaceutical equivalence, or in terms of utilization in the clinical practice, therapeutic equivalence. Following the expiry of the patent of a branded drug, other pharmaceutical firms can market a generic whose interchangeability has been documented.

Many government agencies have promoted the production and clinical use of generics in order to lower the cost of health expenditure incurred by public or private welfare systems. In order to ensure that generic drugs are of adequate quality and bioequivalent to the brand name drug, the regulatory authorities of different countries, in particular the Food and Drug Administration (FDA) in the US and European Medicines Agency (EMA) in the European Union issued guidelines for the development of generics.

Although these guidelines are very detailed, the marketing and usage of these drugs met the distrust of doctors and patients.

The scarce presence of generic drug in the European pharmaceutical market and the difficulties that generic producers found in competing originator drug producers are the starting point and crucial nodes of this thesis.

The first chapter will describe the pharmaceutical market, providing a picture of the functioning, market failures and principal rules governing this sector.

The focus of the second chapter will be the description of the generic drug market. It will study the wreaked benefits above the overall market and the difference in generic market shares between European countries. Then the governmental factors able to influence, both in the demand and in the supply side, these differences in market presence will be analyzed.

The third chapter aims to presenting the intricate and colossal word of intellectual property rights' protection, in particular with patents. The chapter stresses out the important role of innovation and how it is correlated with patents.

It will be shown that European Commission ensures fair competition in the pharmaceutical sector. Its role is of preventing unfair trading conditions, monitoring the behaviors of companies and enforcing the rules when it is necessary. In particular, when pharmaceutical companies are deterred from unfair competition, the social welfare and in particular citizens, are better off. In fact, new better products are developed, prices go down and health budgets are spared.

The Commission has in recent years investigated the attempts by originator companies to delay or hamper the introduction of generic medicines or new drugs that could compete with their products in the market. For this reason, it launched in 2008 a sector inquiry with the aim of discovering the reasons behind the scarce level of competition in the sector.

In the next chapters, we shall consider three real antitrust cases involving behaviors conducted by originator firms in their “battle against generic entry”.

Thus, the fourth chapter concerns evidence from the AstraZeneca case, where the Commission investigated the suspected and then confirmed abuse of the patent system

and the system for the authorization of medicines, with the aim of delaying competition to a blockbuster drug from generic and parallel imported pharmaceuticals.

The practices of the firm violated Article 102 TFEU. The aim of this thesis is also to consider general principles derived from the AstraZeneca study on assessing patent-filing strategies and discover where these principles are not generally applicable.

With the pharmaceutical sector inquiry the European Commission discovered other behaviors used by originator in order to deter generic entry: patent settlement agreements, called reverse payment or pay-for-delay settlements. This kind of agreement, are the opposite of typical settlement, they end with the patent holder that pays a value transfer to the alleged infringer.

This work will examine European Competition law work concerning these settlements. They have anti-competitive effects that can be seen in prices on brand drugs kept artificially high and generic drugs kept off the market.

In the fifth chapter is presented the Servier case, able to provide an example for the study of these anti-competitive settlements. Considering that the European jurisdiction relied above many US cases, it will make a comparison with the United State jurisdiction concerning the legality of reverse payment settlements.

The sixth chapter examines the Lundbeck case, another important milestone, in setting the basis for the judgment of anti-competitive behaviors.

Eventually, the seventh chapter will consider the Johnson&Johnson case, another example of reverse payment settlement.

Each chapter, constituting real antitrust cases, will be studied making references to Article 101 and 102 TFEU and will be indicated which parts of the two Article the scrutinized firm violated.

Chapter 1. The Pharmaceutical Market

The pharmaceutical market is highly dynamic, as it is characterized by innovation and high competition. Drugs have a bivalent nature. On one hand they are simple industrial products, while on the other hand they are essential goods for public health due to their therapeutic effects.

There are several elements that differentiate this market. The first lies in the fact that the price is regulated by the intervention of the government. The public control aims at ensuring control of collective health and at guaranteeing the quality of drugs.

Other peculiarities lie in the nature of drugs, the difficulty of assessing the quality of drugs, the role of innovation and patent protection, the fact that actors are characterized by different economic and social interests.

1.1 Actors in the Market

In order to better understand the functioning of the market, it is necessary to explain and to understand who are the relevant and pivotal economic actors in the pharmaceutical market.

On the demand side, there are three distinguished actors:

- Physicians; characterized by little price sensitivity
- The national health service
- Patients; they consume the drugs and are unable to evaluate the goodness of treatments and the difference between costs and benefits

On the supply-side, in most countries there are few big multinationals which can afford to both invest a lot of money in innovation and to exercise market power while satisfying the demand for goods.

The informational imbalance could lead to advantages for manufacturers, because they can provide distorted information in order to augment their own sales.

1.2 Market Failures

According to the Health Economics and Drug Series, no 005 (1997) there exist different market failures.

The first inefficiency is the informational imbalance, where the information is about:

- Drug efficacy; consumers and physicians are less informed than manufacturers about the efficacy and safety of drugs.
- Drug quality; only manufactures know what is the true quality of the products.
- Appropriateness of a drug; physicians and prescriber know more that consumers about the appropriateness of specific drug. Thus, the assessment of the appropriateness of a drug varies between involved parties.

The second market failure concerns the legal monopoly arising from the patent system and other factors. Due to their market power firms can charge markups on retail prices, as opposed to perfect competition case[1]. The presence of a legal monopoly necessary leads to an increase in price and governments try to limit these inefficiencies with regulation.

Market power is created through:

- Patent protection; encourages research and development

[1] In perfect competition the marginal price of production is equal to the selling price

- Brand loyalty; created through marketing and able to generate market power even after patent expire
- Market segmentation
- Control of key inputs; prevents effective competition
- Collusion between firms

The third failure is the non-internalization of externalities.

For example, immunization and treatment of contagious tuberculosis have benefits for people who consume the service but they also have positive benefits for the entire population.

According to Bennet, Quick, Velasquez (1997) if the consumption of services with externalities is left to the market, the level of immunization or treatment will be less than what is desirable from a social perspective. It can happen that both individual and collective health costs rise and public health will suffer. In order to avoid this problem, governments should subsidize the pharmaceutical market. By reducing the price for some consumers, it can increase consumption of a drug and boost demand. The appropriate level of subsidy will depend on how far the level of consumption falls short of the optimal level.

1.3 The Role of the Government

Given the presence of market failure, the government should control the supply and demand of pharmaceutical products in order to ensure public health, to control pharmaceutical expenditure and to promote innovation through R&D[2].

It should control the supply of pharmaceutical goods through:

[2] Research and Development

- The patent system
- Investment in R&D
- Legislation on distribution channels
- Rules on advertisement

The demand side is controlled through:

- Legislation on the classification of medicines
- Legislation on reimbursement
- Pricing mechanisms

According to Bennet, Quick, Velasquez (1997) governments should exert a minimum function:

- Policy making; developing national drug policies
- Drug regulation; licensing authorizations, registration of drugs, control manufacturing, post-marketing control
- Professional standards; education and standards for pharmacists and doctors, developing codes of conduct
- Access to drugs; guaranteeing universal access, supplying drugs through governments health services, financing essential drugs for the poor
- Rational use of drugs; developing standards, training health professionals and endorsing public and patient education

1.4 Limitation of Public Expenditures

In recent years all European countries registered an increase in the pharmaceutical expenditures and in order to limit these costs they developed and introduced regulations both in the demand and supply side of the pharmaceutical market.

1.4.1 Demand-Side Measures

Demand-side measures involve actions limiting the behavior of patients and doctors. The first important instrument is the patient co-payment system, followed by two other restrictive instruments like the limitation of budgets available to doctors and prescription guidelines at which every single doctor must adapt.

The patient Co-Payment System is a way through which the patient can interact with its healthcare system and can influence with its decisions the type of pharmaceutical products available on the market.

According to Perry (2006) all European countries with the exception of Ireland and Malta use the co-payment system but the contributions of patients is very limited.

There exist different methods through which patients co-operate in the payment of drugs.

They can pay a fixed fee per prescription, per item or according to pack size. They can contribute by paying a percentage of the price of the drugs. In this case, the drug is partially reimbursed as patients pay only the difference above the reference price. They can pay a fixed fee together with a percentage of the cost.

1.4.2 Supply-Side Measures

In each country there exist a number of listed drugs subjected to reimbursement. There is a strong control for prices of drugs with a maximum sale price by type of drug. A

generic drug, equally effective in term of therapy, could be introduced into the market at a lower price. The supply could be controlled through the reference price system.

The reference price system is a regulatory mechanism enforced by authorities which consists of establishing a maximum redemption price (reference price) to be paid by the investor, to all substitutes products and included in the same reference group. If the price of the drug is greater than the maximum redemption price for the group, the difference in payment is charged to the patient. This method helps governments to contain public expenditure, as it controls the reimbursement level of medicines

This is a regulated-price system in which there are set of drugs with the same or similar active ingredients called reference groups. The authorities have the duty to assign a reference price or reimbursement to each of these groups. National health authorities establish similarities between drugs on, chemical, pharmacological and therapeutic equivalence.

Many European governments have introduced reference pricing systems. According to Dylst, Vulto, Simoens (2012) " [i]t reduces medicine prices but not always below the reference price, increases the use of medicines priced at or below the reference price, generate savings in pharmaceutical expenditure that tend to be limited to the short term, and do not seem to adversely affect health outcomes" so "[i]t is a popular policy for governments to contain pharmaceutical expenditures and seems to be effective in the different European countries".

In Europe, according to a survey conducted by EGA[3] internal survey in 2006, 82 % of the thirty analyzed countries adopted a price regulated system.

Figure 1.1: European countries with or without reference pricing system

Reference pricing system	No Reference pricing system
Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Latvia, The Netherlands, Poland, Portugal, Spain, Turkey	Austria, Norway, Sweden, UK

Source: GaBi Journal

Sweden has adopted a reference pricing system in 1993 but abandoned it in 2002. Norway has a system called index pricing that is similar to reference price system.

A country can choose one or a combination of methods to establish reference price.

In 36 % of European countries prices are set below the originator price[4]; in 21 % prices are estimated on the basis of the average price of selected countries; in 19 % prices are determined according to the maximum price; in 12 % prices are settled according to the negotiable price and in 12 % of countries prices are settled according to other factors.

[3] The European Generic and Biosimilar Medicines Association
[4] This is the price of the firm that firstly produce the drug

Figure 1.2: Methods for setting reference prices in European countries in 2011

Reference price	Country
Based on the average price of medicines	Hungary, Croatia
Based on the average price of generics medicines	France
Based on the lowest priced medicines	Bulgaria, Czech Republic, Finland, Hungary, Italy, Latvia, Poland, Spain, Turkey
Based on the lowest priced generic medicines	Bulgaria, Denmark, France, Latvia
Based on the average of five lowest priced generic medicines	Portugal
Based on the percentage of originator medicine prices	Belgium
Based on the weighted average of all products in one group and calculated by regression analysis	Germany
Based on the weighted average price of medicines	The Netherlands

Source: GaBi Journal

The adoption of reference pricing system lead to different competition effects. In Lithuania there was a price reduction of all medicines, generics and branded. In Germany prices dropped by 10-26% in the first year following the introduction of the reference pricing system. In Slovenia and Spain this lowering did not occur.

1.5 Patents

According to Viscusi and Levy (1998, 1999) property rights in the form of patents and trademarks are more important in the pharmaceutical industry than in other sectors and the strategic firms' decisions are more dependent on the presence of adequate patent protection.

According to the definition of AIFA[5] the patent is a legal instrument which gives the exclusive right to exploit an invention in a given territory. The owner of the patent is therefore the only one that can produce, sell or use the invention. In the case of drugs their patent protection period is twenty years. The delay between the filling of the patent request and the marketing authorization could be long and can reduce the patent's life. It may take many years to receive regulatory approval for the marketing of a patented pharmaceutical, thus eating into the effective term of the patent monopoly and perhaps even rendering its exploitation uneconomic[6] and for this reason US in 1984 and EU in 1991 with France and Italy first, implemented the CPCs[7]. It is important to underline that after the expiry of the patent the product becomes of public domain.

There are two consequences arising from the presence of patents.

The first issue that comes from patenting the drug is that the price is fixed at a level above the marginal cost of production. This phenomenon leads to market inefficiency and the consequences of this inefficiency can be relevant. It could happen that the evaluation of sales cost for one medicine is unfavorable and direct towards the utilization of other cheap, but less effective drugs.

[5] Agenzia Italiana del Farmaco
[6] See EU Intellectual Property Law and Policy, Catherine Seville
[7] Complementary Protection Certificates

The second issue concerns the strategies that pharmaceutical firms adopt in order to delay the deadline of exclusive rights. Firms try to modify and to improve originating and patented products in order to allow a new patent deposit and to obtain a new patent coverage. Firms adopt the following strategies:

- Reformulation of the product, matching the same active ingredient with different and secondary chemical elements
- Conversion of the same product into new drug-intake methods
- Different calibration of power and release time, leading to an higher number of patients free to assume the drug and to an improvement in the side effects

However the complete study of the economic role of patents is carry out in chapter 3.

Chapter 2. Generics Market

The market for generic drugs is a relevant point. In the last decades it has gained importance in the European economy because there has been an increasing interest in improving public health.

The commercialization of generic drugs granted significant savings to heath systems, safeguarding the tightness of the budget for basic pharmaceutical expenditure.

Europe is the world's second largest market for generic drugs with a value of 69 billion euros in 2014. In Italy, for example, 90% of medicines consists of products that are no longer patent protected.

Growing pharmaceutical expenditure forced governments to develop pharmaceutical policies in order to improve health care improvements with the development of generic drugs markets ready to bring into the market-place different and cost-effective products.

The threat of countless firms that could enter the market, after the expiry of the patent lead to a radical and disruptive change into the market that previously counted one producer.

Generic manufacturers do not face higher research costs paid by the originator firms in order to innovate products. Hence, they can focus all their activities and resources on improving the efficiency of production processes thereby reducing their production costs and lowering their sales prices.

It is important to underline that generic drugs have the same quality, safety and therapeutic effects of branded ones.

Normally generics are placed side by side to branded drugs in the pharmacies, in this way the consumer could have complete information of its choice.

2.1 What is a Generic?

A generic drug is also known as an interchangeable multisource pharmaceutical product, the adjective interchangeable means that the product should be a perfect substitute for the original one.

There exist three different categories of generics according to the way through which these products are commercialized:

- Branded generic; has a proper and distinctive mark
- Semi-branded generic; commercialized with the name of the active principle followed by the name of the producer
- Pure generic; which is unbranded

Firms should market their medicines without definite brand but using the International Non-proprietary Name (INN) but this rules are generally neglected. According to the World Health Organization: "INN facilitates the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name".

In order to be sold into the market and to be considered generic, a generic drug has to fulfill the concept of bioequivalence to the originator drug. A generic product and an originator one are bioequivalent when their effects are similar after the administration of the same dose, they would not produce differences in terms of therapeutic effects or side effects so they have the same cost/benefit profile.

Bioequivalence means that the two drugs must exert in the same qualitative and quantitative effect on the patient. Thus, there must not be contaminants such as different crystallization[8] of one of the active components or the presence of chemical products formed during the processes. Indeed, if the generic drug differs in the chemical structure from the originator, there could be different absorption and different effects on the patient. In the worst scenario there could be an increase in the toxicity of the drug.

2.2 Market Entry

The generic drug can be placed on the market after the expiry of the patented version by firms competing with the originator one. The originator firm has to develop, launch and invest in research and development thereby incurring in a significant amount of expenses, which explains why the sales price is higher than the one charged by a generic firm. Indeed, generic firms usually do not have to invest in R&D, or at least faces very low costs of doing so.

2.2.1 Benefits of Generic Entry

There exist four principal benefits coming from the presence of generics into the market:

- Lower price
- Increased competition
- More innovation possibilities
- Creation of new firms

[8] Crystallization is a key component of almost all processes in the manufacturing of pharmaceuticals Whether for purification of intermediates, formation of the product, or prevention of crystallization in amorphous products, crystallization is essential in both processing and development. It can be natural or artificial process of formation of solid crystals precipitating from a solution melts or more rarely deposited directly from a gas.

As to the first, there are several studies which evaluate if the introduction of generics leads to a decrease in brand-name market prices.

Caves, Whinston and Hurwitz (1991) study the experience of 30 drugs that went off patent between 1976 and 1987. By running a egression, they find that initial entry of generics lead to reductions in brand-name price of about 2%. Entry by 20 generics results in a price decrease of 17%.

According to Grabowski and Vernon (1992) the generic producers can gain an important market share immediately after patent expiration by taking advantage of the difference in price between the originator drug and the generic one. Consequently, the incumbent firm lowers the price due to more competition in the market.

In his study about European markets, Hudson (1992) finds that in France and Germany the price of the incumbent firm is lowered after the entry of the generic competitors, while in the UK the prices remain stable.

Wiggins and Mannes (1994) show that market entry by generics results in significant reductions in the price of anti-infective products.

A study conducted by Frank and Salkever (1995) reveal the opposite pattern, and is for this reason called “paradox of generics”. They find out that increased competition from generics does not result in aggressive responses of price behaviors by brand-name producers. Indeed, they show that market entry of generics is not followed by brand-name price reduction.

Lower price allows the national health systems to reduce the co-payment of patients. As a matter of fact, the prices of generics are between 20 and 80% lower than the prices of branded drugs[9].

The second important consequence of the introduction of generics is the boosting in competition and higher innovation sources.

Looking at the case of the United States, there is a massive increase in investment and research thanks to the rapid approval authorization for generics. The US has the highest innovation rate and 60 % of market presence of generics.

In Italy, according to Farmindustria since 2002 the growth of the pharmaceutical R&D expenses was 35.9%.

2.3 Differences in Market Shares

Generally among countries there is consistent difference in the presence of generics. In particular, among European countries there is a huge difference in size for generic market shares and these differences are due to heterogeneous policy and regulatory frameworks.

According to Perry (2006) the differences in the presence of generics in the market depend on economical and historical backgrounds but also on the government's choices between a more interventionist approach to creating a robust environment for promoting generics and a less interventionist approach.

The largest generics markets are Canada, Denmark, the UK and the US where the sales of generics medicines exceed 40% of the total volume of pharmaceutical sales. The next

[9] Source: www.assogenerici.org

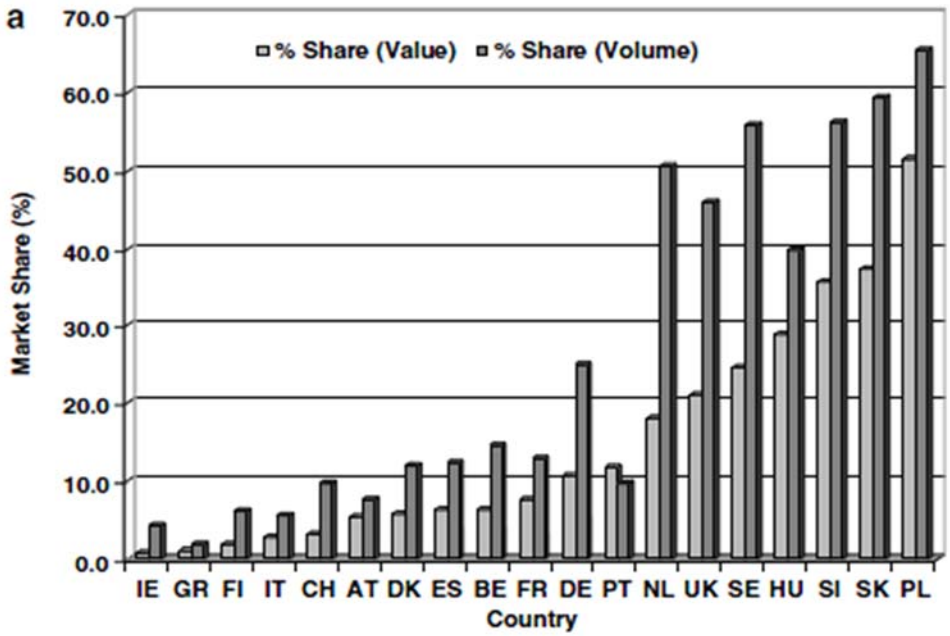
largest generic drug markets are Germany and the Netherlands. According to King and Kanavos (2002) Germany has achieved a high volume of generic sales, with an average price difference between generic and branded in the order of 30%. This difference amounts to 50% for Canada, 80% for the UK and 50-90% for the US.

In 2005 Austria, Belgium, Finland, France, Ireland, Italy, Portugal, Spain had a market share of less than 10%.

Denmark, Estonia, Netherlands, Slovak Republic, Slovenia, Sweden, Turkey and the United Kingdom have a market share that lies between 10% and 40%.

Croatia, Czech Republic, Germany, Latvia, Lithuania, Hungary and Poland have a market share greater than 40%. The following figure 2.1 shows the market shares in Europe in 2015 and outlines the increase of the generics presence in every European country.

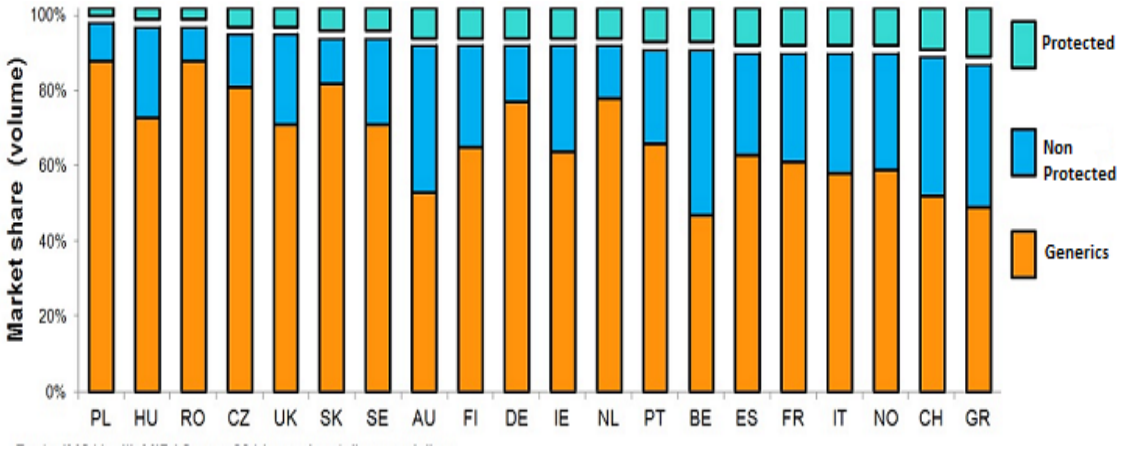
Figure 2.1: Generics Market Shares in Europe, 2005



Source: IMS health,MIDAS, 2014

From 2006 to 2014, the market share of generics in each EU country is augmented as it is readable in Figure 2.2. While the percentage of market share for protected brands and non-protected one is diminished.

Figure 2.2: Market Shares of Protected Brands, Non-protected and Generics, 2014



Source: IMS Health, MIDAS, 2014

It is interesting to notice that in Italy the generic market share increased by 10% in the period between 2009 and 2014, according to IMS Health.

2.4 Government Intervention

Every government develops its own policies in order to both satisfy the need of the population to benefit from a sustainable healthcare system and to ensure access to affordable medicines.

The penetration into the market for a general drug according to Simoens and De Coster (2006), depends on a number of variable factors every European country has to work on and to follow with active ad innovative policy actions and decisions.

Generally, there exist two factors to control pharmaceutical expenditures that are able to explain the penetration of generics into the market, namely: demand and supply-side factors.

Every European country has different methods of pharmaceutical price regulation, which explains the heterogeneity in the market presence of generics and pharmaceutical expenditures across countries.

2.4.1 Supply-Side Factors

According to Simoens and De Coster (2006) generic medicines enter the market following determination of price and reimbursement status by authorities. Each European country has national responsibility over pricing and reimbursement decisions. There could be a delay in entering the market because these two aspects require a significant amount of time. For this reason, the Transparency Directive 89/105/EEC specifies a 90-day limit for adopting a price and reimbursement decision. In practice, these limits are not respected like in the case of Italy and

Austria, or like in Denmark, where there is no formal pricing authorization. There is the need of such regulations because delays in the settlement of price and reimbursement approvals prevents the creation of a competitive European generic industry and impede the entry into the European market.

Figure 2.3: Type of Policy Adopted by Countries: Market Entry

Type of policy	Country of policy
Market entry	
Pricing and reimbursement approval process	Austria, Belgium, Denmark, France, Italy, Netherlands, Poland, Portugal, Spain

Source: Simoens, De Coster, 2006

Generally there are four main methods used to regulate pharmaceutical prices: Fixed pricing, profit controls, cost-effectiveness pricing and reference pricing.According to Mrazek (2002) all EU countries except Germany and the UK apply or have applied price fixing on inpatent drugs. There are multiple combination used to setting fixed prices. Fixing prices offers a better alternative to cost-based regulation, giving companies both an incentive to produce efficiently and the flexibility to price according to their changing market environment. Austria, Belgium, France and Italy fix prices by taking into account price comparisons between similar products within a country, or comparisons to identical or comparable products in other countries. Finland, Ireland, the Netherlands and Portugal compare basket prices across selected countries. Sweden compares prices not only with other EU countries but also requests data from Norway, Switzerland and the United States. Ireland uses UK wholesale

prices as reference. In Greece, prices cannot exceed those of comparator countries. Finland considers prices of comparable parallel imports.

Some countries apply a fixed form of pricing called price/volume agreements: France, Austria, Spain and Sweden. They set prices according to volume. Belgium implemented price/volume contracts for innovative products. Italy does not have a formal price/volume agreement though it considers the number of patients using the medicine and the sales level in price determination.

More EU countries are using economic evaluation alongside other methods for regulating pharmaceutical prices. France, Finland, Portugal, Sweden and the UK introduced guidelines for conducting economic evaluations of pharmaceuticals. In Finland, the reimbursement price dependent on the costs and benefits of a given therapy. According to Mrazek (2002) although there are no formal guidelines, economic evaluations may be required in other EU countries. Italy considers cost-benefit ratios in determining the price for reimbursement, and also requires pharmacoeconomic data from companies. In Belgium, a manufacturer must demonstrate that the total health care costs are lower than the competing products to justify the presence of a new product.

Since 1957 the UK has been operating a unique profit control scheme, called the Pharmaceutical Price Regulation Scheme. This method indirectly regulates the prices of branded pharmaceuticals sold to the National Health Service by setting profit limits. This is a rate-of-return scheme that lacks incentives for operational efficiency, because it increases costs and, consequently, prices.

Figure 2.4: Type of Policy Adopted by Countries: Pricing system

Pricing	
Free pricing of medicines	Germany, Netherlands, UK
Pricing regulation	Austria, Belgium, France, Italy, Portugal, Spain

Source: Simoens, De Coster, 2006

The third factor is the reference price that is used in all European countries with the exceptions of Austria and the UK. The reference price system gives best results in countries with a developed generic drugs segment, differences in price between drugs of the same group and a high level of medicines prices. In countries like Italy and Denmark where the reference price is equal to the cheapest generic drug there are low levels of reimbursement. In contrast, in the Netherlands, where the resale price equals the median price of all medicines in the group, and in Portugal, where the resale price is equal to the highest price of generic medicines, there are higher levels of reimbursement.

Figure 2.5: Type of Policy Adopted by Countries: Reference Pricing

Reference pricing	
Reference pricing system	Belgium, Denmark, France, Germany, Italy, Netherlands, Poland, Portugal, Spain
Low reference price	Denmark, Italy, Poland
High reference price	Portugal
Narrow reference groups	Denmark, France, Italy, Portugal

Source: Simoens, De Coster, 2006

Figure 2.6: Summary of Approaches to the Regulation of Pharmaceutical Prices in EU Countries

EU country	Free pricing	Fixed pricing	Cost-effectiveness pricing	Profit controls	Reference pricing	Applies to in-patent drugs	Applies to multi-sourced drugs[a]	Applies to OTC[b]
Austria		√				yes	yes	yes
Belgium		√				yes	no	no
Denmark	√		√			yes	no	yes
					√	no	yes	no
Finland		√	√			yes	yes	no
France		√	√			yes	yes	no
Germany	√					yes	no	no
					√	no	yes	yes
Greece		√				yes	yes	yes
Ireland		√	√			yes	yes	no
Italy		√	√			yes	no	no
Luxembourg		√				yes	yes	yes
Netherlands		√			√	yes	yes	no
Portugal		√	√			yes	yes	no
			√			yes	no	no
Spain		√				yes	yes	yes
					√	no	yes	no
Sweden		√	√			yes	yes	yes
					√	no	yes	no
United Kingdom			√	√		yes	no	no
		√				no	yes	no

[a]Multi-sourced drugs – brand name drugs that have generic equivalents.
[b]Over-the-counter pharmaceuticals.

Source: "Comparative approaches to Pharmaceutical Price Regulation in the European Union", 2002

2.4.2 Demand-Side Factors

While supply-side policies are related to market access, pricing and reimbursement of generic medicines, demand-side policies are related to incentives for physicians to prescribe, pharmacists to dispense and patients to ask for generics medicines.

Physicians play an important role in promoting the usage of generic medicines as they prescribe the latter. It is important that they have a sound knowledge about generic

medicines. In UK there is a high voluntary INN[10] prescribing due to their positive attitude towards generics. In contrast, according to Dylst, Vulto and Simoens (2013), in New Zeeland 52% of physicians were opposed to the introduction of generic substitution whereas 60% of Danish physicians were not satisfied with generic substitution two years after introduction. According to their study, physicians opted for restricting generic substitution in only 4-8% of the prescriptions.

In general the prescriptions of generics vary with several factors like physician demographics, patients' characteristics and drug classes. According to Shrank, Liberman, Fischer, Girdish, Brennan and Choudhry (2011) older physicians have significantly worse perceptions of generics. According to Tsiantou, Zavras, Kousoulakou, Geitona, Kyriopoulos (2009) some physicians declare that their decision to prescribe generics was influenced by the insurance coverage of their patients.

Governments have used financial incentives for physicians, in combination with other incentives to stimulate the prescribing of generics. UK, Ireland and Germany in order to stimulate generic prescribing used drug budgets (soft vs hard budgets, collective vs individual budgets, penalties vs reward). This method decreased the drug expenditures in the three countries and increased the use of generics in the UK and Ireland. Thus, France introduced the CAPI scheme, a voluntary pay for Performance scheme whereby physicians received additional payment for increasing their prescribing generic medicines versus patented medicines and achieving certain targets for specific drug classes (antibiotics, proton-pump inhibitors, statins, antihypertensive drugs and antidepressants). This scheme has got a positive influence on physicians' prescribing behaviors.

[10] International non-proprietary name

According to Dylst, Vulto and Simoens (2013) in New Zeeland the 70% of the pharmacists did not perceive any difference in safety between originator and generic medicines and only the 30% of the pharmacists had a perfect knowledge of generic medicines. Instead in France only the 42.5 % of the pharmacists encourage generic substitution. In countries like Italy and Spain, where the remuneration of pharmacists is set as a percentage of the drug's prices are financially penalized for dispensing generics. In order to solve the problem governments should replace the current price-dependent remuneration of pharmacists by a fee-for-performance payment. In this way pharmacists would then be rewarded like physicians, based on their knowledge and levels of service. The Netherlands, Slovenia and UK are adopting a fee-for-performance payment system and Belgium, Denmark, France, Greece and Portugal are moving toward a system based on a fee plus a percentage of the medicine's price. Italy and Poland use the sliding scales system, a method in which the percentage of remuneration increases as price rises. This kind of remuneration systems, however, are not very effective as one would expect and do not remove financial incentives behind the commercialization of originator drug.

Patients' preferences have been shown to influence the choice of physicians to prescribe and pharmacists to dispense an originator or generic drug. According to Hassali, Safie, Jamshed, Ibrahim, Awaisu (2009) patients have a positive perceptions of generic medicines but one third of them remains with negative perceptions. According to Hakonsen, Toverud (2012) patients generally are worried about the inferior quality of generic medicines, decreased effectiveness, equivalence compared with the originator and uncertainty due to changes in physical attributes. According to Shrank, Cox, Fischer, Mehta, Choudry (2009) the variables able to influence perceptions of generics

are education and wealth. Thus, age is not associated with a positive or negative perception. The patients with minor illnesses were more willing to use generics. According to Austvoll-Dahlgren, Aaserud, Vist (2008) governments expected that an increase of patients' financial responsibility for prescription medicines will result in a shift to cheaper, generic medicines. In France citizens have to pay basically nothing for drugs, thanks to private insurances that they have in order to cover all extra costs. Indeed, the use of generics drugs is very limited. Recently has been introduced a policy asserting that patients have to pay the health insurance proportion of the cost of a drug if they refuse generics substitution. Many governments opted to differentiate between the co-payments for generic and originator drugs. Portugal raised the reimbursement rate at 95% for the five last-expensive generics. In Belgium higher co-payment system are charged for drugs that have at least one generic alternative available in their therapeutic group.

In every EU country were adopted other different policies to improve knowledge and perceptions of generic medicines and facilitate the prescribing patterns. According to Dylst, Vulto and Simoens (2012) there are different policies adopted by each government.

The first adopted policies are the guidelines, audit and feedback on physicians' prescribing patterns. France drawn a list with all medicines for which generic alternatives are available. Denmark introduced clinical guidelines and individual feedback able to show that physicians prescribed less expensive drugs if these were recommended in the guidelines. Germany participated to Quality Control Programs giving the opportunity to physicians and pharmacists to exchange experiences. Belgium implemented and supported with the Belgium Federal Agency for Medicines and Health

Products and academic program. The Netherlands applied pharmacotherapeutic groups promoting the exchange of information between healthcare providers. Other countries used electronic prescribing systems: Portugal and the Netherlands. Moreover Portugal and France use media campaigns on television, radio, the internet and press to inform patients about generics.

However, there exists other methods used by governments in order to promote the usage of generics. Generic substitution allows pharmacists to dispense a generics containing the same active ingredient, dosage, form and strength as the originator medicine prescribed by the physician. Fourteen EU counties use generic substitution. In Finland, France, Germany, Norway, Spain and Sweden generic substitution is compulsory while in Czech Republic, Denmark, Hungary, Italy, Latvia, The Netherlands, Poland and Portugal is indicative. Pharmacists are obliged to inform patients of substitution in almost all countries and patients can refuse generic substitution at any time in all countries.

In figure 2.7 is presented a sum-up of the different policies adopted on the demand-side by European countries.

Figure 2.7: Different Policies Used by European Countries on the Demand-Side

Country	Physicians	Pharmacists	Patients
Austria	✓	×	×
Belgium	✓	✓	✓
Bulgaria	×	×	×
Denmark†	×	✓	✓
France†	✓	✓	✓
Germany†	✓	✓	✓
Greece	×	×	×
Ireland	×	×	×
Italy	✓	✓	×
The Netherlands†	✓	✓	✓
Poland†	×	✓	✓
Spain	✓	✓	×
Sweden†	✓	✓	✓
UK†	✓	✓	×

†Countries with a mature generic medicines market; other countries have developing generic medicines market.

Source: European Generic Medicines Association, 2011

Chapter 3. The Economic Role of Patents and Patent Strategies

Patents are indicators of invention and innovation and, as indicators, they have advantages and disadvantages. This chapter is going to describe these characteristics, their economic role and strategies with specific reference to the pharmaceutical sector.

Richard Levin (1987) and Wes Cohen (1997) conducted a survey in a large cross-section of U.S industries to identify which factors are most important and necessary in appropriating the benefits from innovations. They found out that patents are more important to pharmaceutical firms in appropriating the benefits from innovation compared with other high technology industries. According to Taylor (1973) and Silberston (1987), that conducted a survey on UK R&D managers, the pharmaceutical R&D expenditures would be reduced by 64 % in the absence of patent protection. Why patents have such importance in the process of appropriating the benefits from innovation, for the pharmaceutical firms?

According to Grabowski (2002) the answer is simple. Because it takes several hundred million dollars to discover, develop, and gain regulatory approval for a new drug. If there would not be patent protection, imitators could free ride and duplicate the compound for a small fraction of the originator's costs.

Generally, the patent system was designed in order to promote and diffuse innovation. The inventor and patent holder has the exclusive right over the commercial exploitation

of the invention for a limited period under certain conditions in return for publication of the invention.

The patent system could be perceived as a contract between the state and the individual. In fact, the State grants to the individual a legal and temporary monopoly on a certain invention against the disclosure of information which the inventor might otherwise keep secret.

According to Archibugi (1992) patents have several pros and cons. Firstly, patents are the outcome of those inventions which could have a relevant business impact. They can capture the competitive dimension of technological change. Secondly, inventors know that in order to obtain patent protection they need time and money. For this reason, applications are presented for those innovations which are expected to provide benefits able to compensate costs. Thirdly, there exist several information about patents and in particular patent statistics are available in large numbers and for a very long time series.

Fourthly, patents are broken down by technical fields, providing information not only on the rate of incentive activity, but also on its direction.

Thus, according to Archibugi (1992), patent also have several disadvantages. Firstly, firms protect their innovation with alternative methods notably industrial secrecy. For this, not all inventions are patented. Secondly, not all inventions are technically patentable[11]. Thirdly, the propensity to patent[12] varies across industries. In certain fields like the pharmaceutical one a large part of the inventions is codified in patent applications as we are going to study in chapter 4. Fourthly, firms have different

[11] For reasons that are not object of study in this thesis

[12] The number of patent registered for each unit of inventive and innovative activity

propensity to patent in each national market, according to their expectations for exploiting their inventions commercially. Fifthly, each national patent office has its own institutional characteristics. In fact, the attractiveness for applicants of any patent institution depends on the nature, costs, length and effectiveness of the protection accorded.

3.1 Patentability Criteria

In order to be patentable an invention must meet four requirements:

- Patentable subject matter: an invention satisfies this point if it is a machine, a manufactured product, a composition made from two or more substances or a process for manufacturing objects
- Utility: the invention must bring some benefits to the entire society
- Novelty: the invention must have something new
- Non-obviousness: the invention must differ from the "prior art[13]"

The maximum duration of a patent is twenty years from the date of the filing and in particular this feature will be analyzed in the study of AstraZeneca case, chapter 4.

Thus, the patent document is made of several claims. These claims are the minimal combination of elements able to qualify for protection. The applicant and the agents of

[13] It is constituted by all information that are available to the public in any form before a given date that might be relevant to a patent's claims of originality. If an invention has been described in the prior art, a patent on that invention is not valid.

the patent office choose claims[14]. Thus, any missing element saves the offending product from the infringement.

In order to be judged infringing the accused product must embody every element of at least one claim. A patent holder who believes that someone else is making, using or selling the invention can sue for patent infringement. This mechanism is commonly used by firms in order to deter entry of competitors as we are going to study in the last three chapters concerning reverse payment settlements. (Ch. 6 Servier, Ch.7 Lundbeck, Ch.8 Johnson&Johnson and Novartis) The defendant accused of patent infringement then has two possible defenses: invalidity and non-infringement. A non-infringement defense focuses on the monopoly that the inventor gets in exchange for that invention. On the other side, an invalidity defense focuses on whether he or she invented something novel and nonobvious and disclosed it to the world in compliance with the patent laws.

A non-infringement defense argues that even if a patent is valid, it does not cover what the accused infringer does.

The invalidity of patent groups five categories of defenses. The first group of defenses makes sure that patent monopolies only go to inventors who make full and timely disclosures to the patent office. The enablement requirement asserts that the patent application must describe the invention clearly enough that somebody can make use of it. This requirement is hardly respected because most patents are obscure and hard to read.

[14] The patent examiner

The second group of defenses applies when patent holders misuse their patents. Generally, the misuse of patents concerns an antitrust violation. A misuse defense is not permanent because patent holders can change their conducts.

The third group of defenses consist of judge-made exemptions in cases where the infringer's conduct is socially beneficial. The main users of this exemption are Universities because their projects usually bring some benefits to the society.

The fourth group of defenses is designed to keep patent owners from playing and loose with the federal court and Patent and Trademark Office.

The fifth group of defenses concern patents made by two inventors that receive separate patents for the same invention. These group of defenses differs from European and U.S law. In the former law priority is given to the first inventor that files an application, while in the latter priority is given to the first inventor which create or discover the product. For example, when the telephone was invented and patented on February 14, 1876 by Bell, another man called Elisha Gray arrived at the patent office two hours after Bell filed its application. In this case in the U.S, according to the current jurisdiction, the patent would be given to the first inventor of the object, while elsewhere to the first inventor to file an application and in this specific example to Bell.

3.2 Quality of Patents

The quality of patents is controlled by professional examiners: scientists or engineers. Generally, examiners must search for literature to make sure that the invention is actually new; must examine the application to make sure it meets the legal requirements for patentability; must ask the applicant to answer questions or amend the application to surrender overbroad claims.

3.3 Levers of Intellectual Property Law

Patents have the aim of protecting intellectual property. There exist two important policy levers of intellectual property law:

- the inventive step; able to govern which innovations are protectable
- the breadth; able to govern how different another product must be to avoid infringement

According to Scotchmer (2004) a right holder only gets protection by preventing rivals from marketing close substitutes. The right of rivals to market close substitutes is governed by breadth. The required inventive step matters when the patent holder will typically be better off if the substitutes are no patentable. For substitutes that are non-infringing the patent holder will be better off if the substitute is supplied by another patent holder than if it is supplied by competitors, since the prices is higher if there exist two oligopolists in the market.

For these reasons, the better place to be for the patent holder is where and when all infringing substitutes are non-patentable and when all non-infringing substitutes are patentable.

Moreover, many economists divided breadth into two spaces:

- product; defining how similar a product must be to infringe a patent
- technology; defining how costly is to find a substitute for the protected market

According to Scotchmer (2004) when we apply the product space definition of breadth, narrow patents are much less profitable that the broad patents.

According to the second interpretation of breadth is breadth itself able to govern the cost of inventing around the patent, and legally entering the protected market. The product sold by each entrant is a perfect substitute for the proprietary product, but since entry is costly, there will only be a limited number of entrant and the market will not be

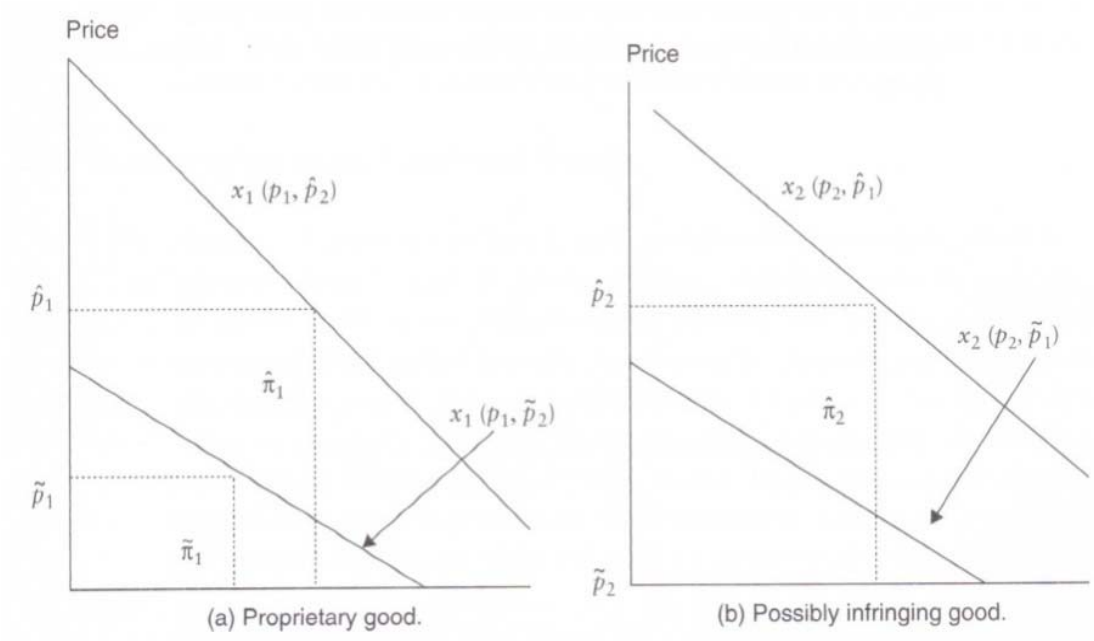
perfectly competitive. Entry will lead to a proprietary price lower than the monopoly price to an extent that depends on the cost of entry.

3.4 How a Patent Should be Modeled?

It is important to notice that a patent should provide a certain level of profit, called π thanks to which the firm can recoup the costs of patenting. (Scotchmer 2004). In order to generate this profit should patent be broad and short or narrow and long?

Here we introduce fig 3.1 that is not able to predict which of these regimes is better in absolute, but can show us two cases where it is possible to assert it.

Figure 3.1. Proprietary and possibly infringing goods



Source: Scotchmer, 2004, pp 105

It is possible to choose which patent suit better on the product basing on the elasticities of substitution[15] between the patented good in figure 3.1a and the possibly infringing good in figure 3.1b, and elasticities of substitution between those two goods together and all other goods.

With narrow protection demand will shift from market represented in figure 3.1a to market depicted in figure 3.1b or to other goods.

With broad protection, the switch from the demand of the first market to the demand of the second market is less evident, because consumers choose other goods. This happens because with broad protection both goods in figure 4.1 will have proprietary prices.

According to Scotchmer (2004) when the demand for the patented good is very inelastic, it is better for the product to have a broad and short patent. This occurs because, monopoly pricing becomes similar to a lump-sum tax[16] and lump-sum tax avoid distortions.

Another example of application of broad and short patent is when the two goods are not substitutes at all, but the potential infringement is by a different use of the same technology.

[15] It is the responsiveness of the buyers of a good or service to the price change in its substitutes. It is measured as the ration of proportionate change in the relative demand for two goods to the proportionate change in their relative prices.

[16] This tax is designed in a fixed amount of money assessed equally on all taxpaying entities regardless of their income level. Example of this taxes could be sales taxes, property taxes on cars and excise taxes. They are regressive taxes, since lower income people must apply a higher percentage of their income on the tax.

3.5 Patent Races

Sometimes it can occur that two or more companies try to gain the same targeted objective but only one firm is able to receive the intellectual property right.

Patent races can have different benefit on innovation:

- they can increase the profitability of innovation when inventors have different ideas for the solution of a problem
- they can accelerate progress

However, from the other side of the coin patent races show two defects:

- they do not aggregate information efficiently in the economy
- they do not necessarily lead to efficient investment decisions

These two inefficiencies usually occur because patent races do not promote investments by the firms with the best ideas. Moreover, in certain cases, firms have private information that are relevant for other firms. We can see an example from Scotchmer (2004) concerning the pharmaceutical market. If there are two firms that would like to invest in a vaccine, they mutually monitories the investments movements of the other one in order to better understand if the investment is profitable or not. Each firm want to know how optimistic the rival is. in order to understand and decided whether to stay out of the market or not. This example is able to show that sometimes firms could stay out of the market and the race, only because the other firm stays out. This example is able to show how firms can get locked in an equilibrium in which each stays out of the race solely because the other has stayed out. Only one equilibria is efficient and demonstrate that patent race need not aggregate and use information efficiently.

3.6 Cumulative Innovations

It is important to notice and describe that innovations can be cumulative. For example, especially in technological fields each innovator builds its innovation on prior developments and discoveries. In this case, the most important benefit of the innovation may be the boost it gives to later innovators. The incentive mechanism tries to guarantee right compensation for the contributions of earlier innovators, while ensuring that later innovators also have an incentive to invest.

As previously mentioned breadth and inventive step are the levers able to determine how profit is divided between successive inventors. According to Scotchmer (2004) if a second-generation product both infringes an earlier patent and receives its own patent, then each inventor has blocking rights on the second product.

There exist three types of cumulativeness. The first one is when a single innovation could lead to many second-generation innovations. For example a laser that can bused in surgical applications, spectroscopy etc.

The second one is when a second-generation product requires the input of many different first-generation products. For example bioengineered crop seed may require genes that code for traits such as sweetness or durability, genes that cause the inserted genes to express and research tools that facilitate insertion of the genes into the germplasm. (Scotchmer 2004).

The third case occurs when firms create successively better products, each improving the previous one. In this case arises the problem that competition between successive innovators could be so strict that firms take the most lucrative improvements.

The cumulativeness of research introduces two new worries in designing intellectual property rights. The main worry is how to compensate the first innovator for the foundation laid for later innovators. The second worry is that profit between successive innovators will be eliminated by competition between them. Thus, the innovator cannot cover costs because competition with the previous innovator forces the prices down.

In this kind of innovation in order that both generations of innovator are rewarded for their contribution the intellectual property rights should last longer that if the same innovator undertakes both basic research and its applications. Moreover, the incentives will work better if there is more flexibility in licensing.

In the cumulative context the policy levers of intellectual property operate differently. Here, breadth can be an important determinant of the life of the right. Breadth and patentability can lead to blocking rights, which creates a vehicle for dividing profit among sequential innovators. Disclosure accelerates progress, giving a boost to rivals. If there is a production function for knowledge, there is a role for incentive step in encouraging innovators to be more ambitious.

Otherwise, quality ladders present a different incentive problem. Here, there is no a distinction between a first-generation and a second-generation innovator; all innovators will eventually be in both positions. Infringement can force the consolidation of a limited number of sequential innovations in order to reduce competition and increase the flow of profit.

3.7 The economic role of licensing

Generally licensing is considered a pro-competitive practice because it allows right holders to share their intellectual property with others. Another important pro-

competitive aspect is that licenses are often needed to resolve blocking patents. These are cases where several patent holders can prevent a particular product or technology from being used.

For example, in cases involving exclusive licenses between competitors the agreements can be beneficial if they promote competition by encouraging the licensee to invest in technology, realizing economies of scale or allowing licensor and licensee to integrate complementary R&D, production or marketing efforts. However, these factors may not be sufficient if the exclusive license significantly reduces competition in a market. In fact, licensing can lead to anti-competitive acts. It can raise some issues for competition policy.

There exist licenses that are in every case under investigation, in particular: licenses that fix prices between firms, licenses that fix the price at which licenses can resell patented goods and provisions that keep the licensees from using or developing other technologies.

Licensing is a way through which it is possible to create rewards for innovation. In fact there exist several reasons according to which licensing is pro-competitive:

- It is possible to produce products efficiently
- Other producers can use intellectual property as inputs to innovations
- It is possible to resolve blocking rights or to enable development of complementary inventions.

Generally, a license granting the use of intellectual property, is made of fixed payments and royalties. The fixed amounts are paid per unit time and are not linked to sales, while royalties are based on units of a proprietary good sold or some other measure of use.

In particular the royalties helps the licensor to control the market price adding to the licensee's marginal cost of production. The fixed fee gives flexibility in sharing the profit.

3.8 Competition Policy in Innovation

The role of competition policy is to keep prices low and to promote efficiency through competition. However if the only goal was to keep price low, then competition policy and intellectual property would be in tension. In particular, competition policy have another aim in addition to the previous one. It ensures an healthy degree of competition in providing consumers with new products and cheaper production techniques. For example the role of competition policy in protecting consumers in U.S is described in the Antitrust Guidelines for Licensing Intellectual Property[17] of 1995. in these Guidelines intellectual property in not considered anticompetitive per se. In particular the Guidelines assert three main concepts:

- The agencies consider intellectual property as being essentially comparable to any other form of property
- The agencies do not assume that intellectual property generates market power in the antitrust context
- The agencies perceive that intellectual property rights licensing are generally precompetitive and allows firms to combine complementary factors of production

[17] These Guidelines state the antitrust enforcement policy of the U.S. They are issued by the U.S Department of Justice and the Federal Trade Commission on 6 April 1995, with respect to the licensing of intellectual property protected by patent, copyright and trade secret law.

Generally courts find harm to competition when a firm has market power in a well-defined market. In fact, the Guidelines in question extended the concept of market beyond production and sales of goods to technology markets and innovation markets.

3.9 Effects of Merger on Innovation

Generally two or more firms can merge into a unique firm. When these kind of alliances take place the antitrust could be against them. In particular because there exists two types of harm that may arise from alliances between innovative firms. Firstly these alliances could reduce competition to innovate and delay technical progress thanks to the hypothesis that competition leads to more R&D than cooperation. This occurs because competitive entry into the innovation market can increase the profitability of success or decrease the time to completion, even though it dissipates profit.

Secondly, alliances could reduce the number of substitute innovations and undermine competition ex post in a product market. However, concerning the first harm to the market, in the majority of cases the authorities apply rules of reasons in assessing whether an alliance could be harmful to the market. The rule of reason in the innovation context balances cost efficiencies that could arise from merger and other alliances against harm to consumers. In particular, cost efficiencies includes:

- avoiding duplication of effort
- delegating effort to the more efficient firms
- sharing technical information that could be hidden if firms compete
- sharing spillovers of the knowledge created

Concerning the harm to the market, merger or alliances could decrease competition in the ex post product market if the merging firms created a single product able to serve

the market where, without the merger, they would have produced competing products. For example in the pharmaceutical market, if a firm produced a non-infringing drug able to bring to the market a substitute at a lower price, it would be an error to allow an ex ante merger between the drug companies able to prevent the final competition in the market.

3.10 Patent Pools

In the previous paragraph we have discussed of how agreements and alliances are able to organize innovation market ex ante. In this paragraph we are going to depict how intellectual property rights are used ex post.

A patent pool is an agreement under which the owners of several proprietary technologies license them as a bundle. According to Merges (1996) in the patent pool there is no a guidance to follow for how members of patent pools share profit. According to Gilbert (2002) there is variance in the subsidiary rules about patents that can be licensed individually and if non-members can be licensees as well as members.

Patent pool is an advantage both for the right holders and for licensees in the case of proprietary technologies that are complements. In particular, if one technology requires the simultaneous use of another one or if the value of one technology increases with the utilization of the other one.

Instead, competition is in danger when pool includes non-infringing substitutes because the pool becomes a cartel in the technology market able to prevent the competition that the owners of rival technologies would otherwise face. In fact, it could happen that consumers can pay higher fees than if the intellectual property is licensed separately.

In patent pools incentives are determined by how the pool distributes profit, by whether non-member innovator can join the pool and on what terms, and how new technologies are received into the pool. According to Scotchmer (2004) if the pool provides for royalty-free cross-licensing within the pool but royalties must be paid by nonmembers, then all pool members benefit equally from a member's innovation. The incentive of a pool member to bear the cost of innovation can thus be diluted.

However, the perception for a nonmember of the pool is that pool can act as a barrier to entry, even in the case of complementary products.

Thus, patent pool could be seen as a solution to litigation and infringement because instead of fighting the two holders of a patent, could merge together and jointly exploit the technology.

3.11 Empirical Evidences of the Role of Patents for Generic Drugs

Especially in the U.S, were carried out several studies to better understand what happens to a drug after the loss of U.S patent exclusivity.

According to Aitken, Berndt, Bosworth, Cockburn, Franc, Kleinrock, Shapiro (2013) the extent and rate at which generic drugs capture market share in U.S retail drug markets as brands lose market exclusivity has increased sharply over the last decade. The authors conducted an analysis above six molecules[18] facing loss of US exclusivity (LOE) between June 2009 and May 2013. They were interested on prices and utilizations. They also found out that brands continue to raise prices after generic entry. However generic penetration rates are typically highest and most rapid for Third Party

[18] That were among the 50 prescribed molecules in May 2013.

payers[19] and slowest for Medicaid[20]. Cash costumers and seniors generally pay the highest prices for brands and generics, third party payers and those under 65 years pay the lowest price. In the end, the presence of an authorized generic during the 180-day exclusivity period, a part of the complex patent listing and certification process[21], has a significant impact on prices and volumes of prescriptions, but this is different from molecule to molecule.

In another study of Conti and Berndt (2014), the impact of loss U.S patent exclusivity on the prices and utilization of specialty drugs[22] was examined between 2001 and 2007. They observed the number of manufacturers entering specialty drugs following LOE and they noticed that the manufactures entering the production ranges between two and five molecules in the years following LOE. This observation is less that than observed historically for non-specialty drugs. They used pooled time series methods[23] in order to assess if the price of these drugs declines and the volume increases upon LOE. They found out a reduction of price after generic entry and in particular an average monthly

[19] An entity, other than the patient or the health care provider that reimburses and manages health care expenses.

Third-party payers include insurance companies, governmental agencies and employers.

[20] A program in the United States, jointly founded by the states and the federal government, that reimburses hospitals and physicians for providing care to qualifying people who cannot finance their own medical expenses.

[21] See chapter 5, paragraph 5.1.

[22] A drug that has unusually complex requirements for development, manufacturing, storage, transportation, administration and/or monitoring. Most drugs in this category are extraordinarily expensive.

[23] Regression econometrical model

price declines was larger among physician-administered drugs[24] (38-46.4%), compared to oral administration's drugs (25-26%). In addition, they discovered that the average prices for drugs produced by branded manufacturers rise and prices for drugs produced by generic manufacturers fall upon LOE; in particular for oral administration's drugs. Thus, according to the authors, in pooled models, volume appears to increase following generic entry, but this result appears to be largely driven by oral drugs.

3.12 The Role of European Commission: The Importance of the Patent System

The European Commission has got the role of ensuring fair competition in the pharmaceutical market. When the EU commission succeeds in restraining unfair competition through the enforcement of rules, new products are developed, prices lowered and health budgets spared. The Commission gives particular attention to the regulation of patents.

The aim of the Commission is that Member States, national health services and pharmaceutical companies respect free competition and free movement of goods and services rules within the market, because this leads to less pressure on national health budgets and less expensive healthcare for EU citizens.

In recent years the interest in the market for generic and its several difficulties in gaining market shares has been raising and the Commission started some investigations

[24] Drugs other than vaccines covered under section 1927(k)(2) of the Social Security Act that are typically furnished incident to a physician's services. These drugs are administrated by a medical professional in a physician's office or other outpatient clinical setting. They are incident to a physician's services that are separately billed to Medicaid. The reimbursement for physician-administered drugs is allowed only if the drug qualifies for rebate in accordance with 42 USC 1396r-8

concerning the attempts by originator companies to delay or impede the introduction of generic medicines or new one that could become a threat for their profits.

There exists several practices used by pharmaceutical companies aiming at restricting competition that are considered an violation of EU competition law: patent clusters, patent settlements aiming at promoting market exclusivity and other practices that lead to high prices and disincentive to innovation and therefore the exclusion of generics.

In March 2012, the EU commission, with the aim of developing and implement the pharmaceutical market, developed and updated the previous directives on transparency of pricing and reimbursement measures.

"The EU's so-called Transparency Directive (Council Directive 89/105/EEC) aims to ensure the transparency of measures established by EU countries to control the pricing and reimbursement of medicinal products. It defines a series of procedural requirements designed to verify that national pricing and reimbursement decisions do not create obstacles to the pharmaceutical trade within the EU's Internal Market" (Dg competition):

The decisions must be:

- made between 90 and 180 days;
- communicated to the applicant and contain reasons based on verifiable criteria
- open to juridical appeal at national level

In January 2010 the Commission applied the Unified patent package, granted by the European Patent Office, a specialized patent litigation system signed by 25 Member States in 2013. The unitary patent will co-exist with national patents and with classical European patents.

Starting from here the work will analyze the Astra-Zeneca story, indicted of abuse of patent system and system for the authorization of medicines with the aim of delaying competition for its blockbuster drug and parallel import of pharmaceutical. Moreover, it will study the cases of Servier; Johnson&Johnson and Novartis, and the Lundbeck, all responsible for dallying market entry of generic medicines.

Chapter 4. Astra Zeneca

In its Pharmaceutical Sector Inquiry of 2009, the European Commission found out defensive patent strategies that could be considered potential anti-competitive abuse in the sense of Article 102 TFEU. Such strategies include in particular patent filing that can delay generic market entry. The AstraZeneca case, with the judgment of the General Court in 2010, is considered a precedent for assessing the anti-competitive character of patent filings under EU competition law.

AstraZeneca firm was accused of having misused both the patent system and the procedure for obtaining marketing authorization for drugs. In addition, it was accused of a second abuse concerning the deregistration of marketing authorization for Losec capsules in several EU countries, combined with the withdrawal of such capsules form the market and the launch of Losec tablets.

The following section is going to depict all the aspects and characteristics of the case, with the presentation of the firm, its main businesses and product, Losec.

Thus, through the analysis of the Sector Inquiry Report it will be presented the evidence deriving from AstraZeneca principles on assessing patent filling strategies in the European market. On the other side will be presented the limitation of principles derived from AstraZeneca, applicable to general patent filing strategies. In conclusion, it will be shown the final decision carried out by the Commission to punish the anti-competitive behaviors of the firm

4.1 The Firm

The company was born in April 1999 through the merger between Swedish Astra AB and British Zeneca Group. It is a biopharmaceutical company focused on innovation, research, development and commercialization of medicines and vaccines.

Astra Zeneca produces goods for several areas:

- Oncology
- Gastroenterology
- Cardiovascular
- Infectious diseases
- Neuroscience
- Respiratory diseases
- Inflammatory diseases

Moreover, the company has developed numerous substances and other molecules that have a huge potential for the treatment of cancer (bicalutamide, anastrozole, fulvestrant, geftinib), gastrointestinal disorders (omeprazole, esoprazole), asthma (budesonide, formoterol), hypertension (candesartan), hypercholesterolemia (rosuvantin), the Acute Coronary Syndrome (ticagrelor), migraine (zomig) and schizophrenia (quetiapine).

Their blockbuster product is Losec which involves in treatments related to the acid-gastrointestinal diseases area. At its launch in Europe at the end of the 1980s, it was sold mainly in a capsule formulation but at the end of 1998, AstraZeneca withdraw the capsules in several European countries, including Sweden, Norway and Denmark and replaced them by tablets with the brand name Losec MUPS (Multi-Unit Pellet System).

4.2 Abuses

Two firms belonging to the same group, Generics and Scand Pharm, contended that Astra AB abused of its dominant position for omeprazole-based medicines, commercialized as Losec, in a number of national markets within the EEA[25]. This might have prevented the introduction of generic equivalent versions of omeprazole in Belgium, Denmark, Germany, the Netherlands, Norway, Sweden and the United Kingdom.

For the first time, the question arose of whether strategic use of procedures before patent office could be considered a violation of competition law.

The company was accused of having misused both the patent system and the procedures for obtaining the marketing authorization for drugs with the objective of delaying market entry of generics. In particular, the European Commission held that the firm violated Article 102 TFEU[26] by misinforming national patent office about the dates of the first marketing authorization of its blockbuster anti-ulcer drug: Losec. The violation concerned the structure of its application for national supplementary protection certificates under the EU SPC regulation rules.

The second abuse concerned the decision of AstraZeneca to remove the marketing authorizations for Losec capsules in Denmark, Norway and Sweden. It was combined with the withdrawal of such capsules from the market and the launch of Losec tablets, from 19 March 1988 until the end of 2000.

[25] European Economic Area

[26] Treaty on the functioning of the European Union

According to the Directive 65/65 on medicinal products, when AstraZeneca deregistered Losec capsules it created the conditions for the exclusion of generic companies. Generics could no longer rely on those authorizations to be granted marketing authorization essentially similar products.

AstraZeneca's acts resulted in:

- Excluding dominant firms' rivals, thus sheltering the incumbent's significant market power
- Harming consumer welfare, by increasing market prices, reducing market output, worsening product quality and variety and harming innovation

For these reasons the conduct of the firm violated Article 102 TFEU.

4.3 Article 102 TFEU Liability

The Article cannot provide a remedy against all forms of misuse of patent procedures. In order to incur Article 102 liability a firm must hold a dominant position in the relevant market. The European Court held that the concept of abuse is an objective concept referring to the behavior of an undertaking in a dominant position, which is able to influence the structure of a market.

According to Drexl (2011), the Court has derived from the concept of an objective abuse the notion of a special responsibility on behalf of the dominant undertaking not to

impair, by measures falling outside the scope of competition on the merits[27], the genuine undistorted competition on the internal market.

In other words, as long as the dominant firm works within the limits of competition on the merits, its behavior might not be abusive. The Court and the Commission gave to firms the possibility to exempt some behavior under Article 102 TFEU. They allowed for objective justifications, as a defense for the dominant firm.

In order to better understand the AstraZeneca case it is also important to understand the concept of market dominance existing in its background. Concerning the first abuse, the filling of SPC applications, the firm tried to maintain market dominance by extending the term of patent protection. With regard to the second abuse, AstraZeneca tried to perpetuate its dominant position by excluding price competition by generics, through a strategy of undermining these firms' capability of receiving marketing authorization more quickly and at lower costs.

4.4 Definition of Relevant Market

The Commission started investigations in order to assess the dominant position of the company concerning which drugs were used to treat cases of gastrointestinal illness. The substances used to treat these problems are the Acid reducers[28] (H2) and the Proton

[27] A dominant enterprise can lawfully engage in conduct that falls within the area circumscribed by that phrase, even if the consequence of that conduct is that rivals are forced to exit the market or their entry or expansion is discouraged.

[28]Acid reducers, drugs able to reduce the production of stomach acid; cimetidine, famotidine, nizatidine, ranitidine etc.

Pump Inhibitors[29] (PPI). The Commission checked if the H2 drugs and PPI active substances of drugs were competitors. Available proton pump inhibitors include omeprazole, lansoprazole, pantoprazole, rebeprazole and omeprazole, the substance contained in Losec.

The Commission analyzed trend of usage, demand and patient prescribing practice over the relevant period trying to demonstrate that there was a significant patient population for which only prescription of PPI was an appropriate treatment.

They found out that the treatment of more severe symptoms involved replacing H2 blockers by PPIs, which were a more powerful medicine. Moreover, the competitive constraints exercised by the two products groups were not reciprocal. In fact, PPIs exercised a constraint on H2 blockers but not vice versa. This asymmetric substitutability supported the finding that PPIs constituted a distinct market because:

- There was a significant patient population for which only prescription of PPIs provided appropriate treatments
- They had to refer to the fourth ATL level (Anatomical Therapeutic Chemical Classification System), departing from the normal starting point of the third ATC level (which refers to the therapeutic indicators)

The following table reports the average market shares and sales value on the PPIs market in the period 1991-2000.

[29] Proton pump inhibitors work by inhibiting a process called the hydrogen-potassium adenosine triphosphatase enzyme system, responsible of the production of the stomach's acid.

Figure 4.1. Market shares and sales value on the PPIs market

AVERAGE (1991-2000)	OMEPRAZOLO	LANSOPRAZOLE	PANTOPRAZOLE	REBEPRAZOLE
BELGIUM	89,73%	9,76%	4,31%	---------
DENMARK	88,08%	15,06%	3,36%	0,09%
GERMANY	75,03%	12,44%	20,56%	1,37%
THE NETHERLANDS	92,55%	6,33%	4,43%	1,00%
NORWAY	86,50%	15,97%	1,47%	2,45%
SWEDEN	93,34%	6,16%	1,17%	0,42%
THE UNITED KINGDOM	84,48%	19,20%	2,46%	2,36%

Source: Commission Guidance

As becomes evident from Figure 4.1, the omeprazole sales are much higher in each of the reported countries with respect to other drugs. This is why AstraZeneca gained huge market power.

4.5 First Abuse: The Acquisition of SPCs

In 1992, the Council issued Regulation 1768/92, also known as SPC[30] regulation, allowing patent holders to extend the length of patent protection to up to five years.

Generally, when a company files its application for patenting the active substance the period of 20 years of protection starts. De facto, this period is shorter than 20 years because it occurs time before the drug can be commercialized. Due to this gap between

[30] Supplementary Protection Certificate

patent authorization and the effective market entry of the drug presence the company wastes time to recoup its research and development investments. The regulation was introduced in order to offer complementary compensation for these investments.

According to Article 13(1) the SPC takes effect at the end of the lawful term of the basic patent and it lasts for:

"a period equal to the period which elapsed between the date on which the application for a basic patent was lodged and the date of the first authorization to place the product on the market in the Community reduce by a period of five years"

However, the period according to Article 13(2) can never be longer than five years.

The SPCs related to the patent owned by AstraZeneca acted as an exclusionary tool. It prolonged the firm's right to solely produce its invention and prevent generic drug companies from entering the relevant market. Moreover, it enforced the already significant market power of AstraZeneca.

In 1993 and 1994, AstraZeneca applied to several national patent offices, for SPC, active substance patents and a patent on omeprazole. The Commission argued that AstraZeneca gave misleading information in order to receive SPCs for a longer period than they were entitled to.

In order to balance the needs of the pharmaceutical industry and the needs of public health policy, every European state strikes a balance between the need to protect innovation and the need to ensure financial stability within the national health system. For this reason, in the AstraZeneca case, every EU member state obtained different dates for SPC protection, according to Article 19 of the SPC regulation. In all EU Countries, the patent could have gained SPC protection after 1 January 1985. Two

exceptions to this rules established that in Germany and Denmark 1 January 1985 was to be replaced by 1 January 1988 and in Belgium, Italy and Austria by 1 January 1982.

In several internal memoranda, AstraZeneca's patent department, pushed the product companies to sign documents, which would indicate the market authorization was first approved later than 1 January 1988 in Denmark and Germany.

Article 19 of the SPC regulation refers to the "first authorization to place on the market" and refers to the technical market authorization: obtaining the approval to place the product on the market. The firm, in order to gain more protection in Germany and Denmark, adopted a new interpretation of the wording in the Article 19 of the SPC regulation: as the date where it actually could be sold. This was the evidence used by the Commission to show that the firm did not have the right to obtain SPCs in Denmark and Germany.

4.6 Second Abuse: The Deregistration of Losec Capsules

The European Commission and the Court found out that AstraZeneca tried to withdraw the marketing authorizations in order to market a specific formulation of its patented drug Losec, in several countries where its patent was close to expiring. This conduct lead to an elimination of generic competition in the relevant market and prevented a price drop in arising from high competition. According to Directive 65/65/EEC the authorizations to market the specific formulation was necessary for the commercialization of generic and parallel imported medicines in the relevant market.

In this abuse the Court distinguished what is legal under the rules of medical law and what is to be considered illegal under competition law.

This is because in the majority of cases, according to General Court, abuses of dominant positions consist of behavior which is otherwise lawful under branches of law other than competition law. Hence, the conduct of AstraZeneca was lawful under competition law but this aspect did not save the firm conduct from competition law liability.

According to Drexl (2011), in order to assess whether the conducts of AstraZeneca were illegal under competition law it has to produce anti-competitive effects, in the sense of market foreclosure unless the conduct is objectively justified.

In order to assess if AstraZeneca's conduct had anti-competitive effects, the Court focused on three aspects:

- It refused the appeal of the firm to apply the essential facility doctrine [31]. The Court assumed that the standard had been developed in the context of exclusive rights. After the expiry of data exclusivity provided by directive 65/65 no such rights were accorded anymore to AstraZeneca, nor could the firm rely on property right in the data. According to Drexl (2011) the firm's abusive conduct was not a refusal to give access to the results of the pharmacological and toxicological tests and clinical trials contained in the file, since AstraZeneca cannot use its alleged property right to prevent the national authorities from relying on the data in question in the abridged procedure.
- It stated that there was sufficient evidence according to which the firm was aware of raising barriers to entry of regulatory nature
- It did not require, in contrast to US antitrust law, to provide evidence of consumer harm in addition to the foreclosure effect

[31] Specifies when the owner of an essential or bottleneck facility is mandated to provide access to that facility at a reasonable price

The Court argued that after the expiry of the exclusivity period, AstraZeneca was not able to claim a justification for delaying the market entry of generics in the light of its own incentives to innovate. The Court argued that AstraZeneca was not able to demonstrate a legitimate business rationale for deregistering Losec capsules. AstraZeneca argued that the deregistration was carried out in order to avoid the pharmavigilance[32] obligations of the holder of the marketing allowance. The Court was not convinced of this argumentation. If the intention of the firm was to avoid the obligation to report any adverse reactions that might appear to the holder of the marketing allowance, it would have deregistered Losec in Germany where the pharmavigilance was strictest. For this reason the Commission and the Court concluded the deregistration of Losec capsules in Denmark, Norway and Sweden was an abuse of dominant position. Moreover, the Court argued that the Commission committed an error in the failed extent of demonstrating that the deregistration in Denmark and Norway were capable of restricting parallel trade of Losec capsules to those two countries.

4.7 The EU Pharmaceutical Sector Inquiry Report

According to Drexl (2011) the AstraZeneca judgment provides a precedent for assessing strategies of pharmaceutical companies identified in the Sector Inquiry Report as potentially anticompetitive.

The Pharmaceutical Sector inquiry was launched in 2008, in the moment in which the Commission received indications that competition was not working optimally in the industry. According to the Commission, the strategies of originator firms to deliberately create artificial barriers to entry for generic products by misusing patent rights were

[32] The detection, assessment, monitoring and prevention of adverse effects of pharmaceutical products.

particularly relevant. According to the Commission AstraZeneca is an important example of misuses of the patent system

The Commission was given the power to conduct a sector inquiry and Article 17 of the Regulation 1/2003 describes this power[33]. In order to start a sector inquiry, the Commission should provide evidence of price rigidities or other factors able to distort or restrict competition within the market. A sector inquiry includes all firms of the pharmaceutical sector that could be potential violators or victims of competition law. It may also produce results that lead the Commission to start formal proceedings against individual firms. It is not supposed, however, to draw any legal conclusions on violations of competition law.

In its Pharma Sector Inquiry Report the Commission addresses a series of different potentially anti-competitive practices.

The first category of practices are those designed to reduce price competition by artificially delaying the entry of generic products into the market. The second category of practices, regards all those strategies carried out by originator companies and which have negative effects on the level of innovation.

The abuses carried out by AstraZeneca belong to the group of strategies concerning the delaying of market entry of generic product and thus belong to the first category.

Each of the two aforementioned categories has a subcategory which concerns patent-filing strategies. These strategies are used both to restrict price competition by blocking the market entry of generics and to obstruct R&D activities of other originator

[33] Council Regulation (EC) No 1/2003 of 16 December 2002 on the implementation of the rules on competition laid down in Article 101 and 102 of the Treaty, [2003]

companies. AstraZeneca is important for understanding patent-filing strategies in general. The latter aim at extending the duration and length of patent protection and at delaying the market entry of generic products. These strategies contribute to the creation of patent clusters and patent thickets that raise legal uncertainty for generic producers and make it more difficult for them to challenge invalid patents. Following Drexl (2011), these strategies are also identified as a sub-category of so-called defensive strategies which focus on excluding competitors, without pursuing innovative efforts. There could exist patent strategies affecting generic companies and patent strategies affecting other originator companies.

As to the former strategies, pharmaceutical companies try to achieve the exclusionary goals by applying for a number of secondary patents, like process or re-formulations, in addition to applying for the base patent in order to extend the exclusivity beyond the expiry of the protection period of the base patent. Moreover, pharmaceutical companies file patents for many forms of incremental innovation, creating patent clusters surrounding the base patent, like salt forms, metabolites, polymorphs and reformulations. The Commission found evidence that such "secondary patents" strategies are implemented by originator with the intention of blocking generics, raising legal uncertainty.

Concerning the latter strategies, the Commission found similar evidence regarding patent strategies aiming at obstructing R&D of originator companies. The Commission was able to depict those patent-filings of an originator company intended to block the development of a new competing product, rather than to protect an invention on its own. It could happen that a pharmaceutical firm, in order to preserve the freedom on the market, incurs in an overlap between the R&D investments efforts and its patents. The

Sector Inquiry Report provided a series of firms' reactions if they cannot avoid this overlap. The firm can:

- Completely abstain from further research in the field
- Try to invent around the already existing patents
- Contact the patent holder and enter in negotiations for a license
- Challenge the validity of the patent in legal proceedings

According to the Commission it is the lack of interest of the patent applicant at the time of the application in developing and bringing the invention to the market combined with the intention to prevent other originator companies from further developing a specific invention and bringing it to the market that raise competition law concern (Drexl, 2011).

In this context, the AstraZeneca case provides a case study to assess when patent filing strategies are anticompetitive.

4.8 Evidence from AstraZeneca Principles on Assessing Patent-Filing Strategies

The AstraZeneca judgment can be considered a landmark decision for assessing patent filing under competition law. There exist five principles arising from it that could be applicable in general to other strategies.

First, the AstraZeneca case confirms that the filing of a patent application can constitute an abuse in the sense of Article 102 TFEU. The mere fact that the applicant makes use of legally available proceedings does not immunize the applicant against competition law liability.

Secondly, patent filings may constitute an abuse in the sense of Article 102 TFEU, although the applicant may be fully entitled to the patent. According to Drexl (2011) the

principle according to which an abuse of market dominance is not excluded by the fact that the conduct is compliant with other fields of law was not limited by the Court to medical law but was formulated in a general way. Applying competition law to patent law-compliant filings is correct since, following the approach of the Commission, a patent examiner would not be able to detect the anti-competitive intent of exclusively using the patent for blocking purposes based on the application. This information is typically only being available in internal documents of the applicant company and can only be detected by using the investigative powers of a competition agency. In sum, the thinking that competition law cannot be applied to patent law compliant behavior would create an exemption of patent law from EU competition law that is contrary to the guarantee of undistorted competition in the internal market.

Thirdly, in order to asses if a patent filing is illegal under competition law one needs to consider whether the patent offices had discretion in making its decision or whether it was under a strict obligation to grant the patent. The AstraZeneca is a clear case of illegality, since the firm was not even entitled to the SPCs.

Fourthly, the case reports the established case law according to which Article 102 TFEU does not require a causal link between the existence of market dominance and the ability to harm competition. AstraZeneca was under the duty of not harming competition, because it was a dominant firm, irrespectively of whether the means of harming competition depend on the existence of market dominance or not.

Fifthly, the Commission has to select the relevant criterion for identifying those patent filings that cannot be considered competition on the merits. The AstraZeneca case does not provide guidance on this point. Concerning the first abuse, AstraZeneca was not

entitled to the SPCs and for this reason this conduct was obviously harming competition. Concerning the second abuse, Drexl (2011) point out that the issue was also whether such lawful use of procedures was to be considered anti-competitive behavior rather than competition on the merits. The General Court adopted a two-step approach in order to solve the problem. First, the competition agency identified the competitive harm consisting in delaying price competition by preventing generics from entering the market. Second, it established whether there was a business rationale that made the conduct legitimate.

4.9 Limitations of Principles Applicable to General Patent-Filing Strategies

According to Drexl (2011) this case is not able to provide answers to all issues concerning patent-filing strategies, and in particular to those strategies which concern the obstruction of R&D efforts of other originator companies.

First, AstraZeneca extended its market-dominant position through delaying the market entry of generic drugs and keeping lower prices on the market. This practice does not include the anticompetitive effects of eliminating incentives to invest in R&D, which arise from practices focused on excluding competitors without pursuing innovative efforts. It is important to underline that welfare loss due to a reduction of innovation may be more significant than the one caused by a mere reduction of price competition.

Second, the need to prove market dominance in the case of AstraZeneca was not important as it could be in other patent filing strategies. This is because the firm held patents at the time of its application for the SPCs and was already market dominant in the relevant market. Hence, the AstraZeneca analysis can only be applied successfully if

the applicant already holds a market dominant position and applies for blocking patents with the aim of excluding the market entry of originator firms.

Third, the patent filing concerning originator firms' incentives to innovate, are more complex. The AstraZeneca analysis provides the tools to distinguish between anti-competitive behavior and competition on the merits. The general abuses of patent filing and the two abuses of AstraZeneca require agencies to find a balance between price competition and innovation. The balancing of the two voices is useful to understand if the price reduction is justified by innovation. In the case of patent filing affecting other originator firms are required to balance the incentives to innovate of both the dominant firm and its competitors and AstraZeneca cannot provide a precedent for such a case.

Fourthly, AstraZeneca cannot provide a precedent for cases in which the patent applicant realized that the application is for a weak patent. AstraZeneca was under an obligation to inform the patent offices about the date of the grant of the marketing allowance, while a patent applicant is not under obligation to inform the patent office about this at the time of the application. Moreover, the patent offices did not have to question the correctness of the information provided by AstraZeneca when it had to assess whether the patent requirements were fulfilled. This underlines that the fact that secondary patents are invalid should not bring these patents into the competition law liability.

4.10 AstraZeneca Defense

AstraZeneca, tried to rely on the US case law in order to shoe that its behavior was legal. It is important to stress that even the US court would have forbidden the firm's behavior because it produced anticompetitive foreclosure. AstraZeneca tried to

demonstrate its innocence in the light of both the Noerr-Perrington doctrine and the Walker Process of US antitrust law.

4.11 Walker Process Doctrine

According to Hovenkamp (2008) the antitrust law Walker Process doctrine permits a patent infringement defendant to show that an improperly maintained infringement action constitutes unlawful monopolization or an unlawful attempt to monopolize. The infringement defendant must show both that the lawsuit is improper, which establishes the conduct portion of the violation and generally satisfies tort law requirements, and also that the structural prerequisites for the monopolization offense are present. The doctrine also applies to non-patent infringement actions and has been applied by the Supreme Court to copyright infringement actions.

4.12 The Noerr-Pennington Doctrine

This case law is line with the AstraZeneca case. The doctrine expressly escludes the application of antitrust liability in cases where a private party seeks governmental action by law that would restrain trade, extend the scope of a monopoly, or even create one. According to Maggiolino and Montagnani [2011] in reporting the Noerr doctrine the antitrust law cannot apply to those who enforce adjudicative procedures before courts and administrative agencies. This is the case even if their actions, IP-related actions included, plainly restrain competition or result in a monopoly.

An analysis of US case law shows that immunity does not extend to US administrative procedures, including IP-related procedure when:

- They do not consist in acts of petitioning

- They are fraudulent
- The two phase developed in PREI[34] applies

AstraZeneca reported argumentation in its defense before the Commission and the Court, showing that these three exceptional circumstances all apply to its behavior. According to the firm, its behavior could not be considered illegal.

Firstly, the firm attempted to elide antitrust liability by stating that Member States' patent office confirmed the two procedures that it was enforcing. In fact, when the EU institutions granted those SPCs, relied on the information that pharmaceutical companies supplied in their applications. When EU institutions considered the request to withdraw the market authorizations, they had to accept the request because the related regulation does not require them to ascertain the substantive legitimacy of a withdrawal request. According to the United State case law, when administrative agencies provide decisions on representations made by private parties the Noerr-Pennington doctrine does not apply, because agencies are not called to decide on merits. This means that when the agencies do not review the merits of a petition, their decisions do not grant immunity from antitrust laws, because these are not discretionary choices, but ministerial acts. According to Maggiolino and Montagnani [2011] in the AstraZeneca case the enforcement of the procedures did not require administrative authorities to

[34] Professional Real Estate Investors Inc., v. Columbia Pictures Industries, 508 U.S. 49 (1993), where the Supreme Court stated that an act of petitioning an adjudicatory authority is a sham when: it is objectively baseless. That is to say, when no reasonable litigant/claimant could have realistically expected success on the merits; and when it has been brought in order to interfere with the business relationships of a competitor

implement discretionary powers and the firm was fully responsible for the possible harmful effects that followed their enforcement.

Secondly in reaction to the accusation of having provided misleading information knowingly and deliberately in order to obtain the SPCs, AstraZeneca argued that the concept of abuse is an objective one.[35] This concept means that the abusive practice of the firm occurred regardless of whether it wanted to harm competition. The US Court developed an analysis similar to the European one. In particular, the Walker-Process doctrine said that a fraud occurs when the data submitted to an administrative agency are not only misrepresented, but also materially and willingly so. It must be shown that:

- The agency would not have acted absent the misrepresentation of a significant fact
- The firm acted with the intent to deceive the agency in question

Referring to the US case law, AstraZeneca asserted another argument in its defense. It said that there is no risk of anticompetitive foreclosure when the right obtained as a result of misleading representations has not been enforced yet. According to Maggiolino and Montagnani (2011) US case law exempts the mere procurement of fraudulent patents from violating antitrust law. This is because the Walker Process doctrine establishes that the application of Section 2, the functional equivalent of article 102 turns on the willing enforcement of an invalid patent. Therefore, although the existence of fraud bars the application of Noerr-Pennington immunity, US courts lack jurisdiction

[35] "The objective nature of the concept of abuse does not lead to the conclusion that the intention to resort to practices falling outside the scope of competition on the merits is in all events irrelevant, since that intention can still be taken into account to support the conclusion that the undertaking concerned abused a dominant position, even if that conclusion should primarily be based on an objective finding that the abusive conduct actually took place" Court.

if the patentee has done nothing but obtain the patent in a fraudulent manner. For these reasons to ascertain that the behavior of AstraZeneca was legal must be an error.

Fourthly, as far as the selective withdrawal of the market authorization for its patented drug is concerned, the EU Commission and Court showed that the practice of AstraZeneca lacked legal grounding. They asserted that the withdrawal of the market authorization had a strategic background. The strategy of the firm was to create an administrative barrier to the commercialization of general and parallel imported drugs in order to prevent competitors from entering the market. It is important to underline that the legal reasons why a firm can withdraw market authorization may be the protection of public health, the defense of the investments made by the firm and the protection of the economic viability of the pharmaceutical company producing the related drug. The US case law reasons in the same way about non-fraudulent administrative procedures and can be argued that a US court would find that AstraZeneca's behavior was unlawful.

4.13 The Fine

The Commission fined AstraZeneca € 60 million for abusing its dominant position, in relation to its best-selling anti-ulcer medicine Losec.

In order to assess the amount of the fine the commission followed several guidelines.

Under Article 15 of Regulation No 17: "The fine for each undertaking participating in the infringement cannot exceed 10% of its total turnover in the preceding business year […]"

It is crucial that the fine got a deterrent effect. The account must be evaluated and taken from the profit of AZ expected to draw from the abuse, even if the implementation of the strategy does not lead to an increment of profits.

The Commission also considered the duration of the single and continuous SPC abuse. In fact, it started on 1992 in Belgium, Denmark, Germany, the Netherlands and the United Kingdom and in 1994 in Sweden. It lasted until the end of 2000 in Belgium, the Netherlands and Norway, until the end of 1997 in Germany, until 1994 in Denmark and in the United Kingdom.

It also took into consideration the duration of the single and continuous second abuse.

The company tried to cooperate with the Commission in order to reduce the amount of the fine. To this end it said that it counted on legal advice in support of the interpretation of the SPC Regulation, deregistration, and helped the Commission during the investigation.

Taking into consideration all the evidences and proofs the Commissions decided that the amount of the fine should be fixed at 46,000,000 € for AstraZeneca AB and AstraZeneca Plc and 14,000,000 € for AstraZeneca AB.

AstraZeneca AB and AstraZeneca Plc brought an action before the General Court for annulment of the Commission's decision.

The General Court rejected most of the arguments put forward by AZ but reviewed the decisions of the Commission concerning the second abuse.

The General Court recognized the Commission's evidence arguing that the deregistration of the marketing authorizations for Losec capsules in Denmark, Sweden

and Norway delayed the entry of the market generic medicinal products in those countries and prevented the parallel imports of Losec in Sweden. The Commission did not prove that in Denmark and Norway there was a prevention of parallel imports.

For all these reasons the General Court reduced the amount of the fine imposed on AstraZeneca plc to 40,250,000 € and fixed the fine on AstraZeneca AB at 12,250,000 €.

In addition, AstraZeneca AB and AstraZeneca plc also lodged an appeal to the Court of Justice to have the judgment of the General Court set aside.

The Court of Justice rejected the arguments brought forward by the two companies concerning errors of law allegedly made by the General Court with respect to the assessment of two abuses and the determination of the amount of the fines.

4.14 Conclusions

Eventually, the behavior of AstraZeneca not only constituted an abuse falling within the scope of Art 102 TFEU but also within the case law that forbids the exercise of nationally-based IPRs[36] beyond their scope.

In practice, AstraZeneca's behaviors' harmed competition, lying under Art 102 TFEU, and directly hampered the single market, falling under Art 34-36 European Commission Treaty[37].

[36] Intellectual property rights

[37] Prohibit restriction on the freedom of movement of goods between member states. They prohibit restrictions on imports and exports, and equivalent measures between Member States

Chapter 5. Reverse Payment Settlements

After the pharmaceutical Sector Inquiry, the European Commission believes that patent settlements agreements such as those called reverse payments, concerning payments from the patents holder to the challenger could infringe EU competition law. However, the debate of such settlements is the subject of an argument, both in Europe and in the US. The European Commission started more investigations concerning these kinds of agreements looking at the US jurisdiction, where these kinds of agreement are considered presumptively unlawful.

The United States Court said that reverse patent settlements should be assessed to be unlawful or not under the rule of reason in the Actavis case[38]. The European Commission in the Lundbeck decision (See chapter 7) considers the reverse patent settlements per object restrictions of EU competition law and these agreements did not need to be analyzed. In the more recent case study concerning the Servier decision, the Commission in addition to demonstration that the reverse patent settlements were per object restrictions, also demonstrated that they had anticompetitive effects.

Moreover, the Commission analyzed the co-promotion agreement between Johnson & Johnson and Novartis, able to take the form of a reverse payment settlement.

[38] See Commission guidance concerning the Actavis Case

5.1 Legality of reverse payment settlements under the U.S antitrust law

In the US there is the Hatch-Waxman Act, enacted in 1984, which allows generic manufacturers to shorten the lengthy process required to approve a drug.

In order to launch a new drug onto the market, a firm needs the approval by the US Food and Drug Administration (FDA), filing a New Drug Application (NDA), with the FDA in order to prove that the drug is safe and effective for the intended use. A generic company can use a filing process called Abbreviated New Drug Application (ANDA) in order to market their product. In ANDA the company must demonstrate the bio-equivalence of the generic copy and it is not required to include safety and effectiveness data.

According to Clancy, Geradin and Lazerow (2014) when an originator files its NDA for a new drug, it must submit patents that cover the active ingredient of the drug, the composition or formulation of the drugs and/or the methods of using the drug. These patents are collected in The Orange Book, held by the FDA. Obviously, when a generic producer files its ANDA, it must obtain a certification for each patent listed in this book.

In the US, the Hatch-Waxman Act boosts challenges to drug patents, giving incentives to the first generic firm that files an ANDA, granting an exclusivity period of 180 days, during which the FDA will not approve subsequent ANDA applications to other generic companies.

The Act requires to filers of a certification to provide notice to each owner of the patent subject to the certification, as well as to the holder of the NDA for the reference listed drug. “Under the Act, if the patent holder files an infringement suit within forty-five

days after receiving notice of the certification, the FDA must stay the approval of the generic manufacturer's ANDA until the earlier of thirty months or a Court decision that the patent is invalid or not infringed" (Clancy, Geradin and Lazerow [2014]).

For this reason, the Act creates an incentive structure, the ANDA filers bears little financial risk thanks to the thirty-months stay allowing the parties to litigate before the generic drug goes to market. The generic will not be subject to damages. The originator could incur severe consequences. If its suit is successful, the financial loss is little, but if the generic firm wins, the originator loses a large part of the market. Many originator firms are risk adverse, especially in the case of small firms, because of the consequences of losing a Hatch-Waxman action.

5.2 Legality of reverse payment settlements under the EU antitrust law

Unlike the US, the EU does not have a regulation similar to the Hatch-Waxman Act, able to provide solutions to patent disputes between originators and generics.

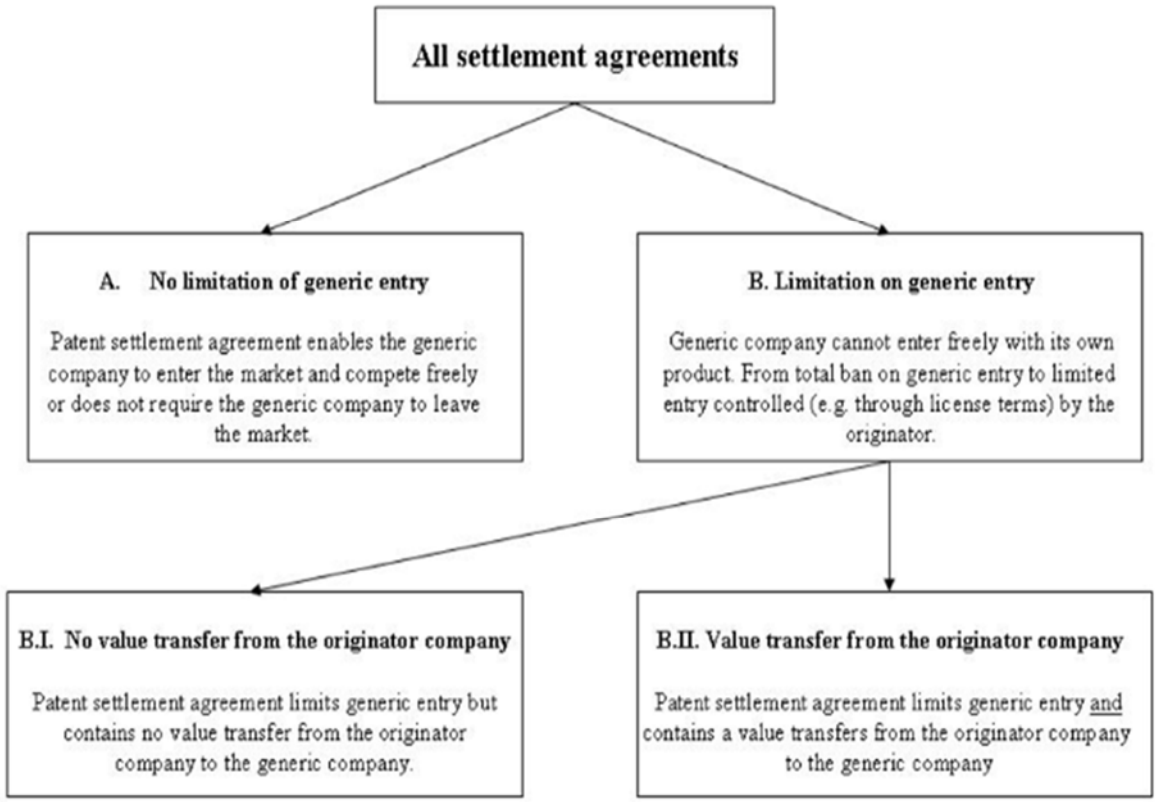
In fact, each individual EU Member State issues patents. Moreover, an originator seeking to enforce its patents and prevent a generic undertaking from entering the market, must bring litigation in the courts of each EU Member State. Each originator firm has huge problems in enforcing its patents to prevent generic entry. Moreover, the generic entry leads to a reduction in originator's price.

Due to these two features of the EU system, the originator companies have very strong incentives to conclude settlement agreements.

It is important to highlight that before 2008-2009 there was no guidance, or case-law available on the legality of reverse-payment patent settlements. In January 2008, the

Commission launched the Sector Inquiry focusing on relationships between generic and originator firms and depicted different kinds of settlement agreements.

Figure 5.1: All settlement agreements



Source: Commission Guidance

- Category A includes settlement agreements, which are no limitation of generic entry; in other words, the generic firm can enter the market and compete freely. Moreover, it is not forced out of the market.
- Category B includes settlement agreements which are limitation of generic entry; in other words, the generic firm cannot enter the market freely with its products
- Category B1 is a subcategory of category B and contains settlement agreements not involving a value transfer from the originator company; in other words, the patent

settlement agreement limits generics entry, but does not contain a value transfer from the originator to the generic

- Category B2 is the second subcategory of category B and contains settlement agreements including a value transfer from the originator company to the generic one, able to limit generic entry.

The Commission argued that settlement agreements concerning categories A and B.1 do not violate EU competition law. In the first case, because they do not restrict entry by the generic supplier and in the second case, because there is no value transfer to the generic supplier.

According to the Commission, it is important to define the concepts of limitation of generic entry and the value transfer, because settlement agreements involving these two aspects are the more problematic and are the ones ablest to violate European Competition Law.

5.2.1 Limitation of generic entry

The generic company's entry can be limited in several ways. Firstly, the settlement agreement contains a clause stating that the generic recognizes the validity of the originator's patent and abstains from entering the market until the patents have expired. The generic cannot enter the market with its own product, unless it has an agreement with the originator firm. The same reasoning could be applied for patent settlement agreements, where the generic becomes a distributor of a product of the originator or where it sources its supplies of the active ingredient from the originator company.

5.2.2 Value transfer

Even the value transfer from the originator to the generic can assume different forms.

The more intuitive one is a direct monetary transfer, in the mere form of cash settlement, in compensation for the generic company's legal cost in the patent dispute, or in the form of purchasing of an asset.

Moreover, the value transfer can take the form of:

- Distribution Agreements, where the generic company becomes a distributor of a product of the originator firm
- Side-Deals, where the originator grants a commercial benefit to the generic company
- Granting a Patent License to the generic company, where the commercial freedom of the generic is limited by the terms of the license agreement

According to Geradin, Ginsuburg, Safty [2011] the Commission indicated other settlement agreements that can generate problems:

- Settlement Agreements restricting entry by generic suppliers, where the restriction imposed on the generic suppliers exceed the scope of the relevant patents
- Settlement Agreements restricting entry by generic suppliers, where the patent holder knows that the underlying patent does not meet the patentability criteria; for example, where the patent was granted following the provision of incorrect, misleading, or incomplete information.

Finally, in 2014 the Commission added a guidance on patent settlements involving a license in the context of its Technology Transfer Guidelines. In particular it stated that this kind of settlement agreements are potentially problematic if the originator offers a value transfer in exchange for the generic's agreement to license terms that are more restrictive than would have been agreed absent the value transfer.

At the end of the Sector Inquiry, the Commission adopted two decisions against three firms incurred in reverse payment settlements with many generic undertakings. In the following work we are going to analyze settlements concerning:

- Servier
- Lundbeck
- Johnson&Johnson and Novartis

For each of the three cases the firms, their main business and products will be presented. Then, abuses and remedies that the Commission adopted in order to re-establish equilibrium in the market and the general rules derived from the single case will be analyzed, applicable to all forms of reverse payment settlements able to violate the competition rules.

Chapter 6. Servier

In Its decision, the Commission found that the firm held significant market power in the market for Perindopril. Servier's patents for the Perindopril molecule expired in 2003. Nonetheless, generic competitors continued to face a number of secondary patents, relating to processes and form that provide a more limited protection to Perindopril. There existed a limited number of technologies for the production of Perindopril that were not covered by Servier's patents, but in 2004 Servier acquired the most advanced one, forcing a number of generic projects to stop, therefore delaying their entry.

The Commission found that between 2005 and 2007, Servier settled the challenge every time a generic firm tried to enter the market. The generic firms agreed to not enter the market, in exchange for a large cash payment from Servier.

The Commission found that the restriction contained in this case was a restriction by object and its analysis contained two particular features.

Firstly, according to the case law there is no need to take into account the concrete effects of an agreement when it restricts competition by object. In addition, the commission stated that there is no need to take into account the restrictive effects of the agreement on competition.

Secondly, the Commission stated that the firm abused its dominant position on the Perindopril market, violating Article 102 TFEU. The Commission argued that Art 102 TFEU may apply to an agreement, together with Article 101 TFEU, only whether there is an additional element. The additional element consists of the fact that the patent

settlements concluded by Servier were “based on the fact that the firm used its market power in order to induce a number of closed generic threats to withdraw from competition with Servier, with their respective generic products”. (Commission guidance).

6.1 The firm

Servier is a privately owned French pharmaceutical company, founded in 1964, which specializes in medication for cardiological and rheumatological conditions, as well as for diabetes and clinical depression. It is the leading independent French pharmaceutical company and the second largest French pharmaceutical company worldwide. It accounts for 21400 employees in 146 countries, with more than 3000 employees working in Research and Development.

Thus, 42% of Servier’s medicines are produced in and shipped from France. The medicines contain active ingredients that are sourced mainly in France.

The parent company of the Servier group, Servier S.A.S has got numerous subsidiaries grouped into five names:

- Les Laboratories Servier
- Servier Monde
- Art et Techniques du Progrès
- Biofarma
- Servier International B.V

6.2 The product: Perindopril

Perindopril is the blockbuster[39] drug of Servier.

In the years 2007 and 2008, the annual sales of Perindopril exceeded USD 1 billion, making it the blockbuster drug because it accounted for approximately 30% of the firm's total turnover. Its average annual operating margins over the production and distribution of Perindopril in the period 2000-2008 exceeded 90-100% every year. All this made Perindopril a highly profitable product. Perindopril is an angiotensin converting enzyme (ACE) inhibitor[40] that is used for the treatment of cardiovascular diseases like high blood pressure, heart failure or stable coronary artery diseases. It makes blood flow more smoothly by preventing the production of certain natural chemicals that tighten the blood vessels.

6.3 Patents upon Perindopril

Perindopril was sold in many European countries: Austria, Belgium, Denmark, France, the United Kingdom, Italy, Luxemburg, the Netherlands, Sweden and Poland; States in which Perindopril's patent expired on 29 September of 2001, with the exception of Spain, Greece and Portugal. With the insertion of SPC certificates, there was an extension of the patents. Furthermore, SPC expiry dates differed from country to country[41].

[39] An extremely popular drug able to generate annual sales of at least EUR 1 billion

[40] It is a pharmaceutical drug used primarily for the treatment of hypertension and congestive heart failure. This group of drugs are able to decrease blood volume, blood pressure and lead to a decreased oxygen demand from the heart.

[41] As a result of different legislation in Member States, prior to the introduction of the European SPC rules

The following Figure 6.1 shows the expiry dates in the EU.

Figure 6.1. Expiry data in European member states

MEMBER STATE	PATENT EXPIRY	SPC EXPIRY
Austria	29/09/2001	22/06/2003
Belgium	29/09/2001	22/06/2003
Denmark	29/09/2001	22/06/2003
France	29/09/2001	22/03/2005
United Kingdom	29/09/2001	22/06/2003
Italy	29/09/2001	13/02/2009
Luxembourg	29/09/2001	22/06/2003
Netherlands	29/09/2001	22/06/2003
Sweden	29/09/2001	22/06/2003
Poland	29/09/2001	22/06/2003

Source: Commission Guidance.

The first marketing authorization for Perindopril was obtained in France on 22 June 1988 followed by the registrations in Belgium, Germany, Italy, the Netherlands, the UK, Denmark, Greece, Ireland and Portugal. Between 1989 and 2004, Servier launched all available and different dosages of Perindopril in France, the United Kingdom, the Netherlands and Poland. In Figure 6.2, the different launch dates of Perindopril-Erbumine, with the commercialization name of Coversyl are presented.

Figure 6.2: Coversyl launch dates

MEMBER STATE	COVERSYL 2 MG	COVERSYL 4 MG	COVERSYL 8 MG
France	01/01/1989	01/01/1989	23/04/2007
United Kingdom	01/03/1990	01/03/1990	07/11/2002
Netherlands	01/07/1989	01/07/1989	23/05/2003
Poland	----------	01/10/1992	01/02/2005

Sources: Commission guidance

6.4 Abuses

The commission started an ex-officio investigation on the 24 November 2008 and found out that between the end of the 1990s and the beginning of the 2000s, Servier used a variety of measures to prevent or delay generic entry after the expiry of the Perindopril compound patent.

Trying to strengthen its defense mechanism, Servier used various anti-competitive behaviors:

- Creation of a patent cluster, patent settlements and disputes
- Distribution agreements with friendly generic companies
- Acquisition of alternative technologies
- Publication of Perindopril monograph in the European Pharmacopoeia
- Selective switch to the arginine salt

However, according to the Commission after its Sector Inquiry, was the creation of patent settlements and disputes able to generate patent cluster, the most important violation of competition law able to prevent the entry of generics into the market.

6.4.1 Creation of Patent Cluster, Patent Settlements Agreements and Disputes

The company created a patent cluster around its production, because between 2000 and 2005, it obtained a number of process and crystalline form[42] patents. Between them, there were some patents with no innovative value to be added to the previous formulations or processes. In particular, the biggest protection able to prevent generic market entry was given to Servier by the 947 patent for "the alpha crystalline form[43]". Patent 947 filled in 2001, upon the crystalline form was used in order to extend the protection of the drug in the Member States that were EPO[44] members at the time of the filling until 2021.

Concerning patent settlements, in the period between 2005 and 2007, Servier concluded five patent settlement agreements with the biggest generics competitors: Niche/Unichem, Teva, Krka, Matrix and Lupin. These patent settlements were valid in all EU Member States for Niche/Unichem, Matrix, Krka and Lupin while Teva was excluded from the UK market. Moreover, from Krka and Lupin, the company obtained a transfer of certain patents[45] in addition to the patent settlements.

[42] The crystalline form is the solid form of matter compounding the drug

[43] It is a particular salt of Perindopril, the tert-bultylamine salt, that has got good characteristics of filtration, drying and ease of formulation.

[44] Member states of the European Patent Organization

[45] Documentation on the description of these patents is not available

In particular, Servier entered into two of the agreements with Matrix and Niche/Unichem on 8 February 2005. Both generic firms agreed not to enter the market of Perindopril before September 2008 and not to challenge any Servier patent. Moreover Niche/Unichem and Matrix cancelled, terminated and suspended all Perindopril transactions until the expiry of the process patents.

With reverse-payment agreements, Servier made significant payments, for an amount of e 120,000,000 to the generics in order to not be challenged in its patent and they not enter into the market for a number of years.

6.4.1.1 Agreements

Niche/Unichem and Matrix: Servier made two distinct agreements with the two generic companies. Both constituted an infringement from 8 February 2005 in all Member States except Italy and Croatia. In Latvia the infringement started on 1 July 2005. In Bulgaria and Romania on 1 January 2007, and Malta on 1 March 2007.

The end of the infringements was 15 September 2008, with the exception of the United Kingdom on 6 July 2007, and the Netherlands where the infringement ended on 12 December 2007.

Teva: made an agreement with Servier that started on 13 June 2006 and ended on 6 July 2007, covering the territory of the United Kingdom.

Krka: made three agreements, which constitute a single and continuous infringement in all European Member States with the exception of Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland Slovakia and Slovenia. The agreement started on 27 October 2006, with the exception of Bulgaria and Romania, where it started on 1 March 2007 and in Italy, where it started on 13 February 2009. It ended on 6 May 2009, except

in the United Kingdom, where it ended on 6 July 2007 and the Netherlands where it ended on 12 December 2007.

Lupin: made an agreement with Servier that covered all the EU Member States with the exception of Croatia. It started on 30 January 2007, but not in Malta where it started on 1 March 2007, and Italy where it started on 13 February 2009. The end of the infringement was 6 May 2009, with the exception of the United Kingdom where it ended on 6 July 2007, the Netherlands where it ended on 12 December 2007, and France on 16 September 2008.

6.4.1.2 Generics Involved

Krka is a pharmaceutical company of Slovenia, its main business consisting in the development, production, sale, marketing of human, animal health products, health resorts and tourist services.

Lupin Limited is the European company of the Indian-registered parent company. Its activities mainly involve the sales of APIs[46], the supply of finished products such as tablets, capsules etc., and the out-licensing of product marketing authorization dossiers throughout Europe.

Matrix is a public limited company based in India. It is involved in many areas, such as the supply of APIs to international generics companies; the manufacturing of APIs and intermediates for generic companies; the contract development and manufacture of finished dosage formulations and the manufacture and marketing of antiretroviral APIs and finished dosage formulations. Matrix Laboratories Limited and Mylan Inc. are the firms involved in the infringements.

[46] Active Pharmaceutical Ingredient: the part of any drug that is active

Niche/Unichem Limited is a pharmaceutical company based in the UK. It is involved in the launch and supply of generic pharmaceutical products for the entire European continent. Its principal business activities are patents, regulatory affairs, quality control, marketing and sales. Niche Generics Limited and Unichem Laboratories Limited are the two undertakings involved in the infringements.

Teva is a global pharmaceutical company based in Israel, able to produce and market generic drugs for all the major treatment categories. The undertakings concerning the infringements are Teva UK limited, Teva Pharmaceutical Europe B.V and Teva Pharmaceutical Industries Ltd.

Furthermore, there is another Swiss company called Azad involved in the case, which sold technology concerning the diverse creation of APIs, but to which the Commission does not address any kind of decision.

6.4.2 Distribution Agreements With Friendly Generics

Between 2003 and 2008, Servier used a number of warning letters, preliminary injunctions and court actions, in order to start patent disputes with its generic competitors. In these warning letters, Servier always referred to its thirty-five patents.

Between 2007 and 2008, Servier sent fifty-two warning letters to different generic companies. In particular, Teva received warning letters where Servier declared that its generic version could infringe thirty of Servier's patents, including the 947 patent. When the warning letters did not produce the blocking of generics production, Servier would launch injunctions.

Specifically, on 28 November 2008, Servier made an injunction against Teva Generics Belgium. It was granted until 17 December 2008, and repealed on 6 may 2009.

Servier made another injunction against Krka Hungary on 30 May 2006. This was rejected on 13 October 2006.

6.4.3 Acquisition of Alternatives Technologies

In the period between 2001 and 2009, the company acquired technologies developed by several firms regarding different non-patented methods of Perindopril production and all the supply sources of API used by generic companies.

The generic firm Teva, perceived that Servier was acquiring all the alternative supply sources. Teva declared:

"The position with Perindopril is very complicated in terms of patents- particularly process patents which affect API manufacturers. This is partly why everyone is late, once an API manufacturer has got round the process patent' Servier has bought the company, sourcing API has been very difficult". (Commission Guidance)

In 2004, Servier acquired from the Swiss company Azad, its know-how and patent applications in order to strengthen its defense mechanism on the Perindopril forms. Servier paid 13,374,243 EUR for these acquisitions. Therefore, Azad stopped all the activities concerning Perindopril and was no longer a potential source of API generic companies.

6.4.4 Publication of Perindopril Monograph in the European Pharmacopoeia

It is important to define another important strategy used by Servier concerning another field, not involved in the patents but aiming at reinforcing technical rules in order to deter generic entry.

The official standards published by the European Pharmacopoeia[47] provides legal and scientific basis for quality control during the development, production and marketing of medicines. In order to define the quality, composition and other issues concerning its own drug, every firm must report it on a monograph.

The Perindopril monograph was published in 2002 and became official and applicable in 2004, but in 2003 in order to obtain more protection, Servier published another monograph which became official in 2004.

One of the generics competitors, Krka, said that the high purity standards laid down in the perindopril monograph meant that the generics had to spend a lot of effort on the development of the drug and that the perindopril monograph in the European Pharmacopoeia is the second significant market barrier.

In fact, Servier raised the purity standard in order to produce the form of Perindopril, as already mentioned aiming at excluding generics.

6.4.5 Selective Switch to the Arginine Salt

The creation of a second-generation product in order to extend the lifecycle of Perindopril was the last, but not in importance and chronological order, abuse practiced by the firm. This strategy was based on the specificities of national substitution rules.

[47] Aims to provide common quality standards throughout Europe.

In fact Perindopril made of erbunine salt, is sold in dosages of 2, 4 or 8 mg while the one containing arginine, the second generation product, in dosages of 2.5, 5 and 10 mg thanks to their different molecular weights. The national substitution rules require pharmacists not to dispense a generic version of Perindopril, erbunine, if the prescription specified tablets with different dosages. It started in 2002 with the introduction of the arginine salt before the arrival of generic versions of erbunine. It is important to notice that the arginine salt did not add a therapeutic value.

Moreover, Servier obtained the patent for arginine salt on 14 July 2004 (expiry date on 17 February, 2023) and the introduction of Perindopril arginine started in 2006 in Poland. In 2008 it was sold in the majority of Member States; Bulgaria, Lithuania, Cyprus, Denmark, Finland, Czech Republic, Hungary, Ireland, Italy, Latvia, the Netherlands, Poland, Portugal, Romania, Slovenia and Slovakia.

According to Teva's point of view these were the biggest non-patent barriers able to exclude the generic entry of Perindopril into the market:

"In Ireland the product was formally launched in November 2008, Teva has achieved no sales, as Servier had moved the market to the arginine version" From Teva speech reported in the report of the Commission investigation.

6.5 Violation of the Treaty

According to the Commission, Servier held significant market power in the market for the Perindopril molecule, as no hypertensive medicines other than the generic versions could constitute competitive constraints.

This case implied the violation of Article 101[48] and 102 of the Treaty. In fact, the reverse payment settlements are considered anti-competitive conduct according to Article 101 of the Treaty, while the patent acquisition practices combined with the previous infringements are considered an abuse of dominant position and so regulated by Article 102 of the Treaty.

This case generated the first use of Articles 101 and 102 together in such circumstances. In particular, the acquisition of scarce competing technology is in breach of Article 102 TFEU. This, because in 2004, Servier as previously mentioned, acquired the most advanced competing technology from Azad in order to stop generic entry. As evidence, Servier recognized in its internal document that this acquisition sought to strengthen defense mechanisms and never used the technology for its own products.

Thus, pay for delay agreements are in breach of Article 101 TFEU, because they are violated under the Article.

6.6 The fines: Servier

In accordance with the Article 23(2) of Regulation No 1/2003 the Commission imposes fines not exceeding 10% of its total turnover in the preceding business year, taking into consideration the gravity and duration of the infringements.

For this reason, it is important to define the value of sales achieved by Servier during the years of infringements.

[48] Prohibits agreements between two or more independent market operators, who restrict competition. This provision covers both horizontal agreements (between actual or potential competitors operating at the same level of the supply chain) and vertical agreements (between firms operating at different levels. Only limited exceptions are provided for in the general prohibition.

For every infringement, the corresponding value of sales is reported in brackets.

"(a) for the infringement of Article 101 of the Treaty relating to the patent settlement with Niche/Unichem: EUR [400 – 500 million];

(b) for the infringement of Article 101 of the Treaty relating to the patent settlement with Matrix: EUR [400 – 500 million];

(c) for the infringement of Article 101 of the Treaty relating to the patent settlement with Teva: EUR [100 - 200 million];

(d) for the infringement of Article 101 of the Treaty relating to the patent settlement with Krka: EUR [400 - 500 million];

(e) for the infringement of Article 101 of the Treaty relating to the patent settlement with Lupin: EUR [500 - 600 million] and

(f) for the infringement of Article 102 of the Treaty relating to the patent settlements with Niche/Unichem, Matrix, Teva, Krka and Lupin, and the acquisition of API technology from Azad: EUR [300 - 400 million]"

(Commission argumentation).

Moreover, in order to evaluate the amount of the fine, the Commission takes into consideration the gravity and the duration of the infringement.

Concerning the gravity, the Commission considered the infringements constituted a market exclusion and an abuse of dominant position.

Thus, at the time of the practices Servier held a high market share in the relevant market and the infringement had also a wide geographic scope with Niche/Unichem, Matrix and Lupin agreements.

There was an implementation of all the patent settlements assessed under Article 101 and 102 of the Treaty and the acquisition of API technologies assessed under Article 102 of the Treaty.

The third important element to be considered in order to define the amount of the fine is the duration of the infringement.

The commission listed the duration in this way:

"(a) for the infringement of Article 101 of the Treaty relating to the patent settlement with Niche/Unichem: from 8 February 2005 to 15 September 2008;

(b) for the infringement of Article 101 of the Treaty relating to the patent settlement with Matrix: from 8 February 2005 to 15 September 2008;

(c) for the infringement of Article 101 of the Treaty relating to the patent settlement with Teva: from 13 June 2006 to 6 July 2007;

(d) for the infringement of Article 101 of the Treaty relating to the patent settlement with Krka: from 27 October 2006 to 6 May 2009;

(e) for the infringement of Article 101 of the Treaty relating to the patent settlement with Lupin: from 30 January 2007 to 6 May 2009;

(f) for the infringement of Article 102 of the Treaty relating to the patent settlements with Niche/Unichem, Matrix, Teva, Krka and Lupin,4064 and the acquisition of API technology from Azad: from 9 November 2004 to 6 May 2009." (Commission Guidance).

Table 2 shows the duration of each generic's infringement, concerning different European country.

In conclusion, the amount of the fine for Les Laboratories Seriver was 330,997,200 EUR, 135,841,600 EUR for Servier Laboratories Limited and 131,532,600 EUR for Biogaran.

Figure 6.3: Amount of the fine per infringement

Infringement	**Amount of the fine**
Niche/Unichem Art 101	Servier S.A.S.; Les Laboratoires Servier; Servier Laboratories Limited and Biogaran, jointly and severally: EUR 131 532 600
Matrix Art 101	Servier S.A.S. and Les Laboratoires Servier, jointly and severally: EUR 79 121 700
Teva Art 101	Servier S.A.S.; Servier Laboratories Limited and Les Laboratoires Servier, jointly and severally: EUR 4 309 000
Krka Art 101	Servier S.A.S. and Les Laboratoires Servier, jointly and severally: EUR 37 661 800
Lupin	Servier S.A.S. and Les Laboratoires Servier, jointly and severally: EUR 37 102 100
Article 102	Servier S.A.S. and Les Laboratoires Servier jointly and severally: EUR 41 270 000
Total	Servier S.A.S.: EUR 330 997 200 of which jointly and severally with: - Les Laboratoires Servier: EUR 330 997 200 - Servier Laboratories Limited: EUR 135 841 600

	- Biogaran: EUR 131 532 600

Source: Commission guidance

6.7 The fines: Generics

In the following Figure is presented the amount of fines for each of the five generic companies involved in the infringements.

Figure 6.4: Amount of fines for the generics

Undertaking	**Amount of Fine**
Niche/Unichem	13,968,773 EUR
Matrix	17,161,140 EUR for Matrix Laboratories Limited 8,045,914 EUR for Mylan Inc
Teva	15,569,395 EUR
Krka	10,000,000 EUR
Lupin	40,000,000 EUR

Source: Commission Guidance

6.8 Reactions to Fines

All the parties of the infringements presented different appeals, in order to obtain a reduction in fines and decisions.

Niche/United argued that it did not carry out any anti-competitive behavior but it acted in the position of a normally informed person that want to bring an end a specific litigation, because it foresaw that before the terms of Settlements Agreement with Servier, it could commercialize Perindopril.

Matrix said it was not by intention that it violated the Article 101 of the Treaty, because it entered into the Settlement Agreement with Servier in order to recoup the investments in the Perindopril project. It also claimed that before that moment, a reverse payment had never constituted an infringement of the so-cited Article.

In addition, Lupin asserted that it did not intentionally commit any infringement of Article 101, but the Commission rejected their argumentation for intent or negligence according to a case law of the Courts of the European Union:

“[a]n infringement of the competition rules to be regarded as having been committed intentionally, it is not necessary for an undertaking to have been aware that it was infringing those rules; it is sufficient that it could not have been unaware that its conduct was aimed at restricting competition " (Commission guidance).

Moreover, Servier argued that a patent settlement that was encouraged by public authorities and public policy, should not have sanctions even because to continue the litigation until the final decision would constitute a social loss.

Another excuse used both by Lupin and Servier referred to the degree of novelty of the case. In order to assert that Servier was aware that the agreements aimed at excluding competitors the Commission considers the Decision state for the AstraZeneca case [See Chapter 4]:

"… concerning the novelty of the two abuses of a dominant position, it must be stated that those abuses, as the General Court pointed out at paragraph 900 of the judgment under appeal, had the deliberate aim of keeping competitors away from the market. It is therefore common ground that even though the Commission and the Courts of the European Union had not yet had the opportunity to rule specifically on conduct such as that which characterized those abuses, AZ was aware of the highly anti-competitive

nature of its conduct and should have expected it to be incompatible with competition rules under European Union law". (Commission guidance).

Chapter 7. Lundbeck

At the end of the sector inquiry the Commission adopted another important decision against reverse payment settlement and in particular the one carried out by Lundbeck.
In June 2013, the Commission issued its decision, holding that settlements relating to Lundbeck's drug Citalopram violated EU competition law.
Lundbeck is a pharmaceutical company, based in Denmark and born in 1915, specializing in the development, research, manufacturing, marketing, selling and distribution of pharmaceuticals in the area of disorders of the central nervous system including depression, schizophrenia, epilepsy, insomnia, Alzheimer's, Parkinson's and Huntington's disease.

The operation employed around 5000 people worldwide and is one of the most important actors in the area of medicines for central nervous system disorders.

It is composed of a number of companies around the world, all owned by H.Lundbeck A/S. Denmark.

7.1 Citalopram

The main activity of Lundbeck concerned the selling of Citalopram, commercialized as a medicine with the names cipramil and seropram or as API. It is marketed in tablets of 10, 20 and 40 mg and as oral, liquid 40mg formulation.

Lundbeck filed the first patent on Citalopram in 1977, in Denmark. The patent covered the pharmaceutical compound of the molecule and two processes to produce it.

Between 1977 and 1985, many of the Western European countries were covered with the product or process patents with the exception of Austria, Denmark, Finland, the Netherlands, Norway and Sweden where the patents could only be granted for processes and not for the pharmaceutical compound. The expiration of patents allowed the market entry of generics on January 1999.

In other European countries like Greece, Italy, Luxemburg and Portugal, Lundbeck held neither the process patent, nor the product one.

In Figure 7.1 the expiration data both for process and product's compound in the EU Member States are reported.

Figure 7.1. Patent expiry[49]: process and compound

Member States	**Process Expiry Data**	**Product Compound Expiry Data**
Germany	-	30 January 1999
Spain	February 1998	February 1998
Sweden	December 2001	-
Belgium	-	January 2002
Denmark	January 2002	-
Finland	January 2002	-
France	-	January 2002
Ireland	-	January 2002
The Netherlands	January 2002	-

[49]It must be underlined that all these periods include the extended protection offered by SPCs

Norway	January 2002	-
The United Kingdom	-	January 2002
Austria	-	April 2003

In 1985, Lundbeck made an application for a new patent protection, in order to grant protection to a new process for purifying Citalopram. In fact from 1986 to 2003, the firm used a new process to manufacture its product, which was able to grant more efficiency and to bring the production onto an industrial scale. This patent expired in 2005.

Subsequently, in many European countries, the company patent protected a new successor product called Escitalopram, with the exceptions of the Denmark, Finland, Greece, Norway, Portugal and Spain. The patent protection for Escitalopram expires in most European countries in June 2014[50].

However, Lundbeck obtained its first marketing authorization in the EEA in Denmark in January 1989. Citalopram was introduced in the EEA markets only in 1994-1996. Citalopram become immediately the best-sold product.

"CIPRAMIL, although still in the introductory phase, is by far the most important Lundbeck product, accounting for 65% of the antidepressant business and 22% of total turnover in 1993. CIPRAMIL is marketed with great success in Denmark, Finland, Switzerland, Greece, Luxembourg, Austria, Belgium and Sweden. It is expected that half of Lundbeck's turnover in 1997 will come from the sales of CIPRAMIL and that its sales will have grown with about 800% by the year 2000." (Commission Guidance).

[50] Periods including SPCs

In 2002, the sales of Citalopram (accounting for 400-600 million of EUR) represented 80-90% of the firm's total sales in the EEA.

Concerning Escitalopram the successor product, the first marketing authorization was granted in December 2001 in Sweden. By the end of 2002 Escitalopram obtained marketing authorizations in Finland, Germany, Italy, Portugal and Spain and was marketed in the EEA under the brand names: Cipralez, Seroplex and Sipralexa.

It is important to define all the strategic movements that the company made on the patent protections and its production, in order to understand the anti-competitive behaviors against generic firms.

Lundbeck held patents covering both the citalopram molecule and the process by which the molecule was manufactured. As the 2002 patent expiry date for the citalopram molecule approached, several companies were preparing to enter the market with generic versions of the drug. The firm decided to open patent disputes against generic companies, asserting that they were infringing Lundbeck manufacturing process patents.

7.2 Agreements

In order to set the disputes with the generic companies, in 2002 Lundbeck decided to pay an amount of money to generic firms, able to satisfy the "price" of remaining out of the market.

Lundbeck also agreed to purchase the generic companies' stocks of the drug, in order to destroy them and offered them guaranteed profits in a distribution agreement.

In particular, in the period between January 2002 and June 2006 Lundbeck started disputes in 85 cases against generics Cipla and Matrix, in several EEA countries:

Belgium, Denmark, Finland, Germany, Netherlands, Norway, Spain, Sweden and the United Kingdom. Below are reported the words of the firm, where it reveals its anti-competitive policies:

“It is like a poker game: we have been dealt a mediocre hand – no aces, a couple of queens and some small uneven cards, but we have a large pile of $$$ at our side and we call it – "the Art of playing a losing hand slowly."

Lundbeck made six agreements from 2002 to 2003 with consistent transfers of money, all reported in the following Figure, with four generics firms: Merck, Arrow, Alpharma, Ranbaxy.

Figure 7.2: Agreements with generics

Generic Firms	**Period**	**Value Transerred**
Merck	For the UK: 24 January 2002 - 1 November 2003 For all the EEA: 22 October 2002- 22 October 2003	For the UK: 19,4 million EUR For all EEA: 12 million EUR
Arrow	For the UK: 24 January 2002- 20 October 2003 For Denmark: 3 June 2002- 1 April 2003	For the UK: 10.4 million EUR For Denmark 684000 EUR
Alpharma	For the EEA: 22 February 2002- 30 June 2003	11.7 million EUR
Ranbaxy	For the EEA: 16 June 2002- 31 December 2003	12.7 million EUR

Looking at Figure 7.2, we can check that Lundbeck's main focus was the UK market, thanks to its importance and sensitivity for generics presence.

Thanks to all the agreements concluded with the firms reported in Figure 7.2, the undertaking was able to obtain a significant market share in many of the EEA countries with its blockbuster product.

In the following table the market share of Lundbeck's Citalopram in the EEA Member States is reported, making a comparison between 2002 and 2003. It is useful to notice the difference in market share. In fact, after settlement agreements occurred in 2002, in countries such as Austria, Ireland and Italy, the market share increased. Only in countries such as Sweden and Finland, did the market share lower.

Figure 7.3: Lundbeck's market share in EEA countries

Member State	**2002**	**2003**
Austria	25-35	30-40
Belgium	20-30	20-30
Denmark	20-30	20-30
Finland	35-45	35-45
France	10-20	10-20
Germany	0-10	0-10
Greece	15-25	15-25
Ireland	15-25	20-30
Italy	15-25	20-30

Luxemburg	15-25	15-25
Netherlands	0-10	0-10
Norway	20-30	20-30
Portugal	0-10	0-10
Spain	10-20	10-20
Sweden	20-30	5-15
United kingdom	10-20	10-20

Let us now analyze in details each reverse payment settlement.

7.2.1 Agreement between Lundbeck and Merck

The agreement between Lundbeck and Merck was a single and continuous infringement able to cover the entire EEA with the two agreements covering first the UK territory and then the other EEA Member States.

Concerning the agreement covering the UK territory, Merck committed:

- Not to launch Citalopram based on Natco[51]'s API;
- Not to license its UK marketing authorizations for Natco Citalopram products to any other generics supplier
- To purchase exclusively from Lundbeck drugs.

All the commitments written above, according to the Commission were a limitation of competition under Art 101 TFEU because they prevented the introduction of a generic

[51] Pharmaceutical company, specialized in the production of APIs and in the production of generics

product into the market. There was such a big transfer of value able to prevent Merck from becoming an independent firm in the market.

Even the agreement between Lundbeck and Merck, regarding the EEA[52] restricted competition by object according to Article 101 TFEU because precluded the possibility of entry with generic Citalopram into the market.

In this agreement, Merck accepted to commit itself:

- Not to launch Citalopram products based on Natco's API and based on API from other API producers
- To use all reasonable efforts to ensure that Natco ceased to supply Citalopram product in EU Territory

7.2.2 Agreements between Lundbeck and Arrow

The agreements between Lundbeck and Arrow constituted a single and continuous infringement that covered with two distinct agreements, the British market firstly and then the Danish one.

The agreement covering the UK territory constituted an infringement of Art 101 of TFEU, because Arrow committed to several actions that limited its freedom of action to enter the Citalopram market in the UK.

The generic firm committed:

- not to import or to sell the Citalopram able to infringe the proprietary rights of Lundbeck

[52] With the exception of the UK

- not to make, to sell or to import any other Citalopram coming from Tiefenbacher, Matrix II and Cipla II[53]
- to deposit and eliminate the Citalopram tablet purchased from Tiefenbacher

According to all commitments, Arrow could not compete anymore with Lundbeck in the market of Citalopram and the strategy of the latter clearly aimed at delaying generic entry into UK market and constituted a restriction of competition by object, infringing Article 101 of the Treaty.

Concerning the agreement covering Denmark, Arrow committed:

- not to import or to sell products containing Citalopram that Lundbeck alleged to infringe its patents[54] and in particular the tablets that Arrow had in stock and the one that they could buy from Tiefenbacher or other API suppliers
- not to dispose of its license and marketing authorization. In particular Lundbeck and Arrow agreed on the fact that Arrow's marketing authorization for Tiefenbacher would not be used to sell Tiefenbacher Citalopram
- to deliver its current stock of Citalopram tablets to Lundbeck.

Taking into consideration the fact that Lundbeck transferred a lot of money to Arrow and the fact that all these commitments represented anti-competitive behaviors the Commission stated that they could be considered restrictions of competition within the meaning of Article 101 TFEU.

[53] These three firms are all generic producers that provided the generic form of Citalopram to Arrow before the settlement agreement with Lundbeck

[54] Because they produced with a production process covered by Lundbeck's patent

7.2.3 Agreement between Lundbeck and Alpharma

With this agreement, concerning all the EEA Member States, Alpharma committed to several behaviors:

- not to sell pharmaceutical products containing Citalopram coming from other API suppliers[55] and not to sell those products produced with processes protected by any patents of Lundbeck.

  In particular, the commitment referred to the Cipla Citalopram that the company had in stock, to the Citalopram coming from Tiefenbacher that Alpharma would have received, to any Citalopram from other API suppliers that Lundbeck considered infringing its patents and any Citalopram produced by Cipla or Matrix that were considered infringing.

- to voluntarily submit to interim injunctions in case of violation of the path[56]

  The facts that Lundbeck transferred a very significant amount of money to Alpharma in exchange for these commitments and the fact that these behaviors aimed at restricting competition in the market of Citalopram, the agreement between the two firms is considered an infringement of Art 101 of the Treaty.

7.2.4 Agreement between Lundbeck and Ranbaxy

In this agreement, Ranbaxy accepted several commitments that limited its freedom of action to enter into Citalopram market in the EEA.

[55] Different from Lundbeck itself

[56] Alpharma, in case of violation, must submit to voluntary restraining order

- to desist from any manufacture or sale of Citalopram based on any production method used by Ranbaxy during the term of the agreement with Lundbeck
- to voluntarily submit to interim injunctions, in other words if the firm tried to sell Citalopram API or medicines in the EEA, based on its production processes, it must cooperate with Lundbeck in order to give an interim injunction against such sales.

The agreement restricted competition in the markets covered by the agreement, and gave rise to the transferring of a huge amount of money that restricted competition in an anti-competitive way, infringing Article 101 of the Treaty.

7.3 Violation of Article 101 TFEU

The Commission considered every agreement between Lundbeck and generics presumptively illegal.

In particular, in its decision the Commission declared:

"When, in a patent dispute a settlement is reached without inducement on the basis of each party's assessment of the probability of a patent being held valid and infringed by a court, such a patent settlement will normally not infringe Article 101 of the Treaty if the agreed limitations on the behavior of the generic undertaking do not go beyond the right granted by patent law. By contrast "when an agreement is concluded in which the generic undertaking accepts to exit or not to enter the market for a certain period of time… but instead the originator undertaking pays a considerable sum of money to the generic undertaking, then such an agreement, whether referred to as a patent settlement or not, merits the full scrutiny of competition law" (Commission Guidance)

According to Clancy, Gerardin and Lazerow [2014] the Commission based its conclusion on the following allegations:

- Lundbeck and generics were at least potential competitors at the moment when the agreements were concluded
- Lundbeck transferred significant value to the generics manufacturers through the agreements
- The existence of a link between the value transfer and the generic commitments not to compete with Lundbeck in the EEA for a certain period

An important aspect of this decision that differs from the US Supreme Court in the Actavis decision, the Commission considered that the settlements between Lundbeck and the generic were presumptively illegal or in other words anti-competitive by object and did not access if the agreements had any anti-competitive effects.

The Commission based its conclusion on the following findings:

- Lundbeck and generics were potential competitors at the moment where the agreements were concluded
- The generic committed to limit, for the duration of the agreement, their independent effort to enter one or several market with their generic products
- The agreements provided for a transfer of value from Lundbeck, which reduced incentives of the generics to pursue their efforts to enter the market.

7.4 Other Anticompetitive Strategies

In addition to the analyzed settlement agreements, Lundbeck operated a series of other anti-competitive behaviors against generics, in order to extend the exclusion of

competitors in the market of Citalopram. The following section briefly discusses these behaviors.

7.4.1 Patenting Process to Manufacture Citalopram

In order to strengthen its defense, between 2000 and 2002, the company made applications for 14 new patents for the process and compound of Citalopram. Lundbeck filled patent applications in order to make the production of generic Citalopram harder.

In the specific case, Lundbeck used the crystallization patent as an instrument to prevent the entry of other generics firm and sent warning letters to many of them: Natco, Max, Herero, Cipla, Ranbaxy-Vorin, Dai-ichi, Sun and RPG Life Science. In all the warning letters, the company advised that there was the possibility of infringing its crystallization patent and informed generic companies to pay attention to this topic. The company said that its crystallization patent protected a method through which the process of production was more efficient than the processes of its rivals and for this reason, the competitors would like to use it, even if the original patent had not already expired.

7.4.2 Intervening in Marketing Authorization Procedures for Generic Citalopram

Starting from the initial point that generics must use different production methods for the production and from the issue that generic Citalopram should differ from the reference one, Lundbeck set out general actions to be taken towards marketing authorization in all EEA contracting parties, in particular in Austria and Netherlands[57]. With several of these actions, the company tried to delay the national licenses in all European countries for several months.

[57] The firm applied this strategy in these two countries because thought that was the proper one

For example, in 2001, Lundbeck argued that the firm Natco produced generic Citalopram with API that contained some impurities and for this reason the company was not in line with relevant guidelines. Subsequently Natco was forced to delay the market entry of its generic Citalopram, incurring financial losses.

7.4.3 Eliminating the Competition of API Producers

The intention of Lundbeck was to prevent the supply of API from generic competitors. One relevant example is the tentative of accordance with Norpharma an Italian firm. In 1999, the company bought three patent applications from the Italian one, that prevented generic companies from entering European markets with generic Citalopram, because it had been produced thanks to Norpharma processes.

Furthermore, in October 2000, Lundbeck purchased the Italian firm VIS and withdrew the possibility for Tiefenbacher (firm that collaborated with VIS in order to create generic Citalopram) to compete and supply all the country where Lunbeck did not have patent protections, where only the originated processes where protected and where the compound patent protection was expired. Greece, Italy, Luxemburg, Portugal, Austria, Denmark, Finland, the Netherlands, Norway, Sweden, Germany and Spain. Following this acquisition, Tiefenbacher enter into the market after nine months, having obtained a marketing authorization in September 2001, sourcing API from other companies called Cipla and Matrix.

The generic company called Merck also was in collaboration with VIS's production of generic Citalopram and after the acquisition from Lundbeck, Merck sourced from the producer Natco. The marketing authorization was also postponed by around nine months in this case.

In October 2002, Lundbeck acquired more bonds and shares in the firm called CF Pharma, a company able to produce generic Citalopram, eliminating and preventing the selling into EEA markets.

7.5 Remedies and Fines

The Commission imposed a EUR 93.8 million fine on Lundbeck and a total fine of EUR 52.2 million on the four generic undertakings involved.

In accordance with Article 7(1) of Regulation (EC) No 1/2003 the commission stated that the four agreements should have stopped and according to Article 32(2) of Regulation (EC) No 1/2003 the commission imposed fines on the firms involved in anti-competitive actions that infringed Article 101 of the Treaty and Article 53 of the EEA Agreement.

In the following Figure the amount of the fine for each of the infringements is reported.

Figure 7.4. Lundbeck fines

Infringement	**Fine**
Merck	H.Lundbeck A/S 19,893,000 EUR Of which Lundbeck Limited 5,306,000 EUR
Arrow	H.Lundbeck A/S 12,951,000 EUR
Alpharma	H.Lundbeck A/S 31,986,000 EUR
Ranbaxy	H.Lundbeck A/S 28,954,000 EUR
Total	H.Lundbeck A/S93766000 Of which for Lundbeck 5,306,000 EUR

Figure 7.5: Generics fines

Undertaking	Fine
Merck	Merck 21,411.000 EUR Of which jointly and severally with Generics(UK) 7,766,000 EUR Total amount: 21,411,000 EUR
Arrow	Arrow Group ApS: 9,975,000 EUR Of which jointly and severally with Arrow Generics Limited 9,360,000 EUR Of which jointly and severally with Resolution Chemicals Limited 823,735 EUR Total amount: 9,975,000 EUR
Alpharma	Zoetis Products LLC and Xelia Pharmaceuticals ApS jointly and severally 10,530,000 EUR Of which jointly and severally with A.L. Industrier AS 43,216 EUR Total amount 10,530,000 EUR
Ranbaxy	Ranbaxy Laboratories Limited and Ranbaxy (UK) Limited, jointly and severally 10,323,000 EUR Total amount 10,323,000 EUR

According to Clancy, Gerardin and Lazerow [2014], Lundbeck and all of the generic suppliers appealed the Commission's decision to the EU General Court. The issues raised on appeal include:

- Whether Lundbeck and the generic parties were potential competitors

- Whether reverse-payment patent settlements constitute a restriction of competition by object
- Whether the settlement agreements restricted competition in the market beyond the scope of Lundbeck's patent right
- Whether the Commission is correct that patents have exclusionary powers only once they have been confirmed in litigation and that a duty existed for the applicant to litigate or exhaust all other options before concluding the Settlement Agreements

However the judging of EU General Court is still pending, until 2017.

8. Johnson&Johnson & Novartis

In December 2013 the Commission considered the co-promotion agreement concluded between Janseen-Cilag, a Johnson&Johnson subsidiary and its generic competitor Sandoz, a Novartis subsidiary, violating Article 101 of TFEU.

The agreement concerned the Dutch market for Fentanyl in the form of transdermal patches. In July 2005, Janssen-Cilag B.V, entered into the co-promotion agreement with Hexal B.V/Sandoz B.V, which was the most advanced generic competitor of J&J in the Netherlands. This remained in force until December 2006, when a third party was about to launch a generic Fentanyl patch.

The Commission discovered that the agreement was not used in order to facilitate co-promotion, but to keep the price of Fentanyl artificially high in the Netherlands, allowing the parties to share the monopoly profits.

8.1 Fentanyl

Fentanyl is the generic of a synthetic opioid that is 80 to 100 times stronger than morphine and used to treat chronic pain conditions of cancer-associated pain, low back pain and osteo-arthritis.

Fentanyl could be sold through two different kinds of transdermal patches: the depot patch and the matrix one. The depot patch is fixed on the skin of the patient and contains a gel, mixed with the Fentanyl doses that regularly releases the dosage. The matrix type, also called second generation product, differs from the former patch because Fentanyl is contained in the adhesive matrix and not in the gel-reservoir. J&J

held the idea that the matrix patch is more efficient and provides additional benefits to patients. It is important to underline that in Netherlands, the market analyzed in this case, the depot and matrix patches are substitutable.

Johnson & Johnson sold Fentanyl patches with the name: Durogestic.

Durogestic, the blockbuster drug of the firm is able to provide millions of revenues: in 2011 it provided 575 million EUR in the EU and 1.6 billion worldwide.

Durogestic in the form of depot patch obtained the first marketing authorization in the EEA in March 1994 in the UK and in other Member States included the Netherlands in 1995. For this reason in July 2005, the patent protection expired in many EEA countries with the exception of Spain, Germany, France, UK and Italy.

Moreover, there is another exclusivity to be taken into consideration: the data exclusivity that in many of Member States expired on 4 March 2000 and in the case of Netherlands, depot patch lost exclusivity on 4 March 2004.

After the expiry of patents and exclusivity above depot patches in many EEA members, Johnson & Johnson decided to launch a new version of the patch, the second generation product, matrix patch. In 2002, three patent applications for matrix patches were filed and between August 2004, as in the Netherlands, and January 2010, the firm launched the matrix product substituting the depot one. J&J launched the 12.5 mg dosage for the Netherlands.

8.2 Johnson&Johnson

The company is an American based pharmaceutical, medical device and consumer packaged goods firm involved in many business areas. The company has its

headquarters in New Jersey and counts for 250 subsidiary companies operating in 57 different countries.

The active subsidiary of J&J in the Netherlands and involved in this case is Janssen-Cilag B.V that researches, develops and markets medicinal drugs and pharmaceutical products for patients, doctors and hospitals.

8.3 Novartis AG and Other Generics

Novartis is a Swiss-based pharmaceutical company, involved in the production of originator products and generic ones. Novartis owned the totality of shares of Sandoz B.V, which is a pharmaceutical company able to offer healthcare products, vaccines, generics in the Netherlands and through which it operated in the market of Netherlands. Another company through which Novartis operated in the Dutch market was Hexal B.V.

Novartis and Sandoz marketed the depot patch product with the brand name: Fentanyl-Hexal TTS, and obtained their marketing authorization in July 2004. The Novartis and Sandoz depot path was launched in June 2005 in Sweden and after the expiry of J&J patent on the depot patch was introduced in July 2005 in Germany, the UK, Poland, Finland, Hungary and in August 2005 in Ireland.

In the Netherlands market, Novartis and Sandoz obtained the marketing authorization in March 2005 but they never entered into this market because of the co-promotion agreement established with J&J, which impeded their entry from 11 July 2005, to 15 December 2006.

However, the two companies developed two different and proper Fentanyl matrix patches:

- Fentanyl Hexal MAT derived from depot Durogestic of J&J, which firstly entered the market in Germany in December 2005 and then in other Member States
- Fentanyl Hexal VS, derived from the matric Durogestic of J&J which entered the market in Germany in November 2008 and then in other Member States

In the Netherlands, the company launched the matrix patch only after the expiry of the co-promotion agreement in January 2007 but they were able to sell their own Fentanyl matrix patch after the expiry of a supply agreement made with J&J in January 2009.

8.4 Other generics

In addition to Novartis/Sandoz, many generic firms were competing in the market for generic Fentanyl.

The first according to the time of entry into the market was Ratiopharm, which is the first company that tried to enter the generic Fentanyl patch (matrix) market in Netherlands on 1 February 2006, but unfortunately on 15 March 2006 the firm had to leave the market following the decision of the Court, appealed by Janssen-Cilag B.V. Ratiopharm re-entered the market from 9 June 2006 to 28 July 2006 but was excluded thanks to the appeal of J&J. The firm obtained a permanent market authorization in the Dutch market on February 2007.

In January 2007, Johnson & Johnson launched its own generic Fentanyl matrix patch with the name Fentanyl Matrix J-C.

In June 2007, a firm called Nycomed entered the generic market of matrix patches but earned very low profits.

In January 2009, Actavis sold its transdermal Fentanyl patches in the generic market.

8.5 Co-Promotion Agreement

This agreement of one year's duration started on 11 July 2005 and terminated on 15 December 2006. It was concluded between Janssen-Cilag B.V and Hexal B.V/ Sandoz B.V and concerned several duties for both the parties.

The duties of Hexal B.V/Sandoz B.V mainly consisted of the fact that they could not sell the product:

"all sales of the Product in the Territory shall be made by Janssen-Cilag on such terms and conditions as Janssen-Cilag in its absolute discretion may from time to time determine" and "unless otherwise agreed in writing, Company [Hexal B.V./Sandoz B.V.] shall not be entitled to receive payments on Janssen-Cilag's behalf in respect of sales of the Product."

The duties of Jansseen-Cilad B.V mainly consisted in the payment of the total amount of 3.7 million in monthly rates to Hexal B.V/Sandoz B.V. (308,333 EUR per month). Furthermore, the company had to obtain all the licenses necessary for the sales of the product into the Netherlands, be respectful on the normative for any change in the laws and regulations of nature, method of manufacture, packaging, labelling or sale of the product. In other words, the duties of Jansseen-Cilad B.V merely consist of the obligation to comply with the applicable laws and the more restrictive one concerning the payment in rates.

The Commission observed that the amount paid to Sandoz considerably exceeded what Sandoz expected to make at the time of the conclusion of the agreement if it had launched its own Fentanyl patches in the Netherlands. Moreover, Sandoz's co-promotional activities pursuant to the agreement were poorly defined and not meaningful. Therefore, the co-promotion agreement was thus a fig-leaf for a pay for delay arrangement.

The agreement involved the possibility for third parties to cooperate with them, when they entered the Dutch market of Fentanyl matrix. They allowed the possibility for duplex registration, which is the possibility to register products for which the marketing authorization files is identical to that of an already registered product.

8.6 Supply Agreement

The supply agreements involved Janssen-Cilag B.V and Sandoz/Hexal Pharma Netherland, and had a duration of two years, starting from 1 January 2007.

Through this agreement, Janssen-Cilag B.V granted to Sandoz/Hexal Pharma and to third parties a non-exclusive right to purchase, promote and sell the Fentanyl patches in the Netherlands under the generic companies' respective brand.

This agreement allowed Hexal B.V/Sandoz B.V to introduce their generic versions once an independent generic player was present in the market. As in the case occurring after the introduction of the marketing authorization of Ratiopharm on 1 January 2007, Janssen-Cilag B.V decided to launch its generic version of Fentanyl matrix patches on the same date.

Consequently, Hexal B.V/Sandoz B.V entered the market with matrix Fentanyl supplied by Janssen-Cilag B.V. However Janssen-Cilag B.V accused Hexal B.V/Sandoz B.V to have entered the market one month earlier with respect to the introduction of their Fentanyl and for this reason the agreement terminated on 1 January 2009.

8.6.1 Consequences of the Agreement

This co-promotion and supply agreement, brought several consequences to Janssen-Cilag B.V, due to the fact that the generic entry into the market was limited:

- No reduction in price for Janssen-Cilag B.V. Fentanyl patch in Netherlands, that led to a positive price effect, estimated at 5.9 million EUR
- Did not have to pay an additional discount to pharmacies, saving 4.2 million EUR
- Supplied 90% of the Dutch market
- The generic partner that marketed Fentanyl patches held the 25% of the Dutch market
- It maintained profitable prices
- The net trade sales of Fentanyl patches in 2008 were 8.4 million EUR higher

At the end of the practices, Janssen-Cilag B.V. saved 14.7 million EUR by paying an amount of 5 million EUR to Hexal/Sandoz B.V.

8.7 Infringement of Article 101 TFEU

As in the Lundbeck decision, the Commission considered co-promotion agreement a restriction of competition by object, because “it contained a transfer of considerable value from the originator J&J, to a close potential generic competitor, Novartis/Sandoz, with the objective that the latter would not enter the Dutch market with generic Fentanyl patches.

These practices between parties were considered a restriction by object, of competition and had a huge impact on trade between Member States, because the co-promotion agreement had the object of restricting competition within the internal market, with a transfer of value from J&J to Novartis and Sandoz in order to keep the latter, with its own generic Fentanyl patches out of the Dutch market. Restriction by object means that by its nature, the agreement infringed Article 101 TFEU.

In particular the Commission demonstrated that J&J and Novartis/Sandoz were potential competitors when they concluded the agreement. The Co-promotion agreement included a non-entry mechanism, where for the duration of the agreement, strong incentives were provided for Novartis/Sandoz not to enter the Dutch market because if the latter was to enter the market, it would have lost considerable monthly payments. Moreover, the Commission demonstrated that the parties acted in full knowledge of the effects of the agreement:

- Novartis/Sandoz exclusion from the market
- J&J maximization of its profits for sales of the originator product
- J&J sharing of the extra-profit with Novartis/Sandoz

The Commission reached its conclusions on the basis that:

- No other co-promotion partners were considered
- Sandoz did not take part in any meaningful promotional activity
- The payments received by Sandoz exceeded those which it might have expected to receive had it launched its own generic Fentanyl

8.8 Remedies and Fines

In accordance with Article 7 of regulation (EC) No 1/2003 when the commission found that there was an infringement of Art 101 TFEU, it did not ask J&J and Novartis/Sandoz to bring such infringement to an end, because it had just ended when they investigated the case, but they expressly confirmed the addressees' obligations not to enter into new agreements that have the same object or effect on the market and parties.

As already mentioned, the agreement consisted of a voluntary violation of the Treaty and in accordance with Article 23(3) of regulation (EC) No 1/2003 the amount of the fine should be evaluated based on a variable and an additional amount. The variable amount comes from a proportion of the value of sales to which the infringement directly or indirectly relates, multiplied by the number participation to the agreement, while the additional amount is calculated as a proportion of the value of sales of the goods to which the infringement directly or indirectly relates in the last year of the infringement.

Concerning J&J, the annual average value of sales on which the Commission relied is 23,339,250 EUR and the duration of the infringement lasted one year and five months. For these reasons, the final amount of the fine for Johnson & Johnson and Janssen-Cilag B.V was 10,798,000 EUR.

In the case of Novartis/Sandoz the evaluation of the fine was based on the value transferred to Novartis/Sandoz by J&J matching profits that the latter could have made at the launch of its own Fentanyl patch. The infringement had the same duration as for J&J, one year and five months, for these reasons, the final amount of the fine for Novartis AG and Sandoz B.V was 5,493,000 EUR.

Both the fines were to be paid in euro within three months of the date of notification of the Commission's Decision.

Conclusions

In this work I presented some of the main causes that are responsible for the scarce presence of generic drugs in the pharmaceutical market. In order to achieve robust answers I studied four antitrust cases. I searched the causes of the limited competition faced from originator drug producers and I understood that thanks to their illegal and anticompetitive behaviors they are able to delay and/or prevent generic entry into this market. Generally their behaviors are directed towards patents and technologies, drastically limiting the innovations in the market. In particular the main resulting anticompetitive practices are:

- Reverse payment settlements ("pay for delay"): agreements involving a payment from the patent holder (originator) to the generic one. The former convinces the latter to stay out of the market simply by paying an higher amount than the expected generic revenue.
- Patents: acquisition, extension and manipulation. Originators illegally try to extend the lifecycle of patents in order to delay their expiration; this happens through Supplementary Protection Certificates. In some cases they acquire patented processes or products from generics, depriving them of the possibility of producing with their own technologies.
- Acquisition of alternative technologies: the originator firm strategically acquires technologies which are developed by other firms, regarding different non-patented methods of its drug production and acquires all the supply sources of Active Principle Ingredients used by generic companies

- Selective switch to another salt: originator firms change the production's method of their drug simply by modifying its formulation. In order to make more difficult the reproduction of the original drug the originator changes the salt used to create it. In this way generic producers will face higher barriers to entry
- Intervention in marketing authorization: originator firms intervene in marketing authorization in order to have access to new markets or to change the formulation of their products. Generally firms withdraw the marketing authorization in order to market a specific formulation of their patented drug in several countries, where patent was close to expiring.

All the over-cited behaviors are able to exclude any kind of competition in the market and in spite of having the same intentions, I found out that they are applied with different methodologies.

For these reasons, it is important that European Commission tries to monitor and to regulate all the aspects of the market and it is also important that every government develops demand and supply-side measures directed towards the encouragement of generics usage. In fact, the Commission has investigated the pharmaceutical market through a sector inquiry launched in 2008 and has updated the Transparency Directive which governs the transparency of pricing and reimbursement measures.

The increased use of generics would provide clinical benefits and substantial savings for the public and the National Health Service. In addition, generics entry leads to reduction in prices, increased competition, more innovation and creation of new pharmaceutical companies.

I would stress that from 2013 to 2018 generics drug are expected to account for 52% of global pharmaceutical spending growth, compared to 35% for branded ones. In 2017 we are going to see a growth in sales for generics at an annual rate of 10.6% thanks to:

- Major support from governments
- Major monitor from European Commission
- Expiration of patent protection for several branded drugs
- Generics raising power
- Industry consolidation

The entire economy would be better-off with the major presence of generic drugs within the system.

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