

A case study of AstraZeneca’s omeprazole/esomeprazole chiral switch strategy

Federico J Piñeiro¹, Pharm, MPH; Fernández Argüelles Rogelio Alberto², Pharm, PhD

Objective: To describe the chiral switch, an evergreening strategy used by AstraZeneca to position enantiopure esomeprazole as the new proton pump inhibitor market leader, displacing its predecessor omeprazole.

Methods: A four-stage systematic review which included: a preliminary review, bibliographic review using databases, classification of the body of literature, and content analysis.

Results: Using different legal and commercial strategies, such as patent thickets and aggressive publicity campaigns, AstraZeneca transferred consumer loyalty from their successful omeprazole to esomeprazole, its new and more expensive patent protected product which has the same therapeutic value as its predecessor. This chiral switch allowed AstraZeneca to maintain monopoly prices, which increased the financial burden experienced by consumers and payors and may have also had a negative impact on access to the medication.

Conclusions: This case study exemplifies how the current patent system, including patent thickets, can be used to enhance the profits of pharmaceutical companies while stalling innovation and placing undue financial burdens on the consumer.

Keywords: AstraZeneca, Big Pharma, biosimilars, chiral switch, esomeprazole, generics

Introduction

The 20th century witnessed extraordinary medical advances that have eradicated or controlled epidemics across the world and have lessened the impact of life-threatening diseases. Undeniably, the widespread use of pharmaceuticals has contributed to the sustained increase in life expectancy observed throughout this period. The pharmaceutical industry’s investments in research and development (R & D) have resulted in major contributions to our therapeutic arsenal. However, since Arnold Relman published “The new medical-industrial complex” [1], significant changes in the business model adopted by the major pharmaceutical companies (from now on “Big Pharma companies”) have been observed [2].

Under the new paradigm, these companies, which trade in the stock market and must respond to the interests of the stockholders, no longer prioritize the development of drugs that would add high therapeutic value, but rather those that would maxi-

mize their profits [3]. To achieve this goal, in the context of the emergence of generic drugs in the late 1980s and 1990s, Big Pharma started focusing on maintaining the high prices facilitated by monopolies and worked on extending the commercial exclusivity of brand-name drugs. In other words, the industry maximized profits by using incentives intended to reward innovation to instead maximize their profits. These are outlined in Table 1 and include the protection of intellectual property through patents and data exclusivity.

The term ‘evergreening’ refers to the use of legal, commercial and technological strategies to extend due-to-expire patents of successful products [6-8]. Big Pharma companies have used evergreening to prolong their legal monopoly, enabling the patent owner to maintain high prices and avoid losing the commercial benefits that would likely result from the commercialization of generic versions of their branded products [9, 10].

Table 1: Historic highlights of intellectual property protection of pharmaceuticals

Date	Description
Prior to 1994	Few high-income countries allowed patents for pharmaceuticals; more than 50 countries prohibited patents for new drugs for public health reasons [4].
December 1994	Creation of World Trade Organization and the signature of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) – all signatories of the TRIPS had provided strong protection of intellectual property rights. Pharmaceuticals are treated as any other commodity. From that moment on, patents would be enforced on a global scale and the tensions between protecting intellectual property and ensuring universal access to affordable drugs would become evident, especially in developing countries.
November 2002	Doha Declaration established that public health interests would trump intellectual property rights, enabling the use of the flexibilities contemplated in the TRIPS Agreement, including compulsory licences. However, few countries have been able to use these flexibilities due, among other things, to limited manufacturing capacity; insufficient technical knowledge and/or bilateral commercial pressures from countries that host major Big Pharma companies [5].

Source: Own elaboration based on Allard Soto (2015) & South Centre (2004).

Author for correspondence: Federico J Piñeiro, Pharm, MPH, 309 Thames, 1414, Buenos Aires, Argentina

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To shield the power of their monopoly, Big Pharma companies use evergreening and other strategies, such as taking advantage of aspects of legislation, to delay the entry of generics. For example, in the United States (US), the Hatch-Waxman act, extends the market exclusivity period of a new drug by six months when clinical trials are carried out in a paediatric population [11, 12], even if that drug does not treat a medical condition that occurs in paediatric patients.

Moreover, many Big Pharma companies have been increasingly developing drugs that are very similar to their original products (the so-called “me-too or follow-on drugs”). These are then launched just before the expiration of the patent on their original drug. When these drugs are released into the market, they are intensively promoted as being more advantageous than predecessors [7, 12, 13]. These new drugs can be developed using different shunting maneuvers, see Table 2, including the following: commercializing the active enantiomer of a drug already on the market (this “chiral switch” strategy is described in detail below), modifying the formulation of the active pharmaceutical ingredient (API), using the active metabolite of a previously commercialized product, and combining more than one API in the same presentation.

Most drugs that contain a chiral centre are marketed as racemic mixtures, that is, a combination of the two possible enantiomers. Usually, these two “halves” have similar clinical activity and adverse effects; however, sometimes a pure enantiomer –also called enantiopure– may offer some therapeutic advantages. The market launch of an enantiopure product just before the patent expiration of its racemic predecessor has been described as a “chiral switch” strategy, and often the new product does not offer any clinical advantages to justify the change [13, 14].

A relevant example of a chiral switch is the case of AstraZeneca’s omeprazole/esomeprazole. In 2000, omeprazole the lead proton-pump inhibitor (PPI), was the world’s bestseller, with annual US sales of \$6 billion a year, under the brand name Prilosec [15]. However, by 2010, enantiopure esomeprazole (sold as Nexium) became AstraZeneca’s bestseller with US sales of US\$5.63 billion, compensating for the plummeting of omeprazole [16]. According to Coherent Market Insights, in 2020 the

estimated value of the global PPI market was US\$2.9 billion US, and it was expected that its compound annual growth rate (CAGR) would be 4.30% during 2020-2027. The success in launching esomeprazole allowed AstraZeneca to maintain its leadership in the PPI market.

The objective of this article is to describe the omeprazole/esomeprazole chiral switch used by AstraZeneca as a case study that exemplifies the behaviours of the pharmaceutical industry. More specifically, we will analyse the published literature on the clinical evidence of esomeprazole’s therapeutic value and how AstraZeneca took advantage of regulations and pricing mechanisms to position enantiopure esomeprazole into a dominant market position.

Methodology

A qualitative systematic review was carried out in four stages. Initially, in the exploratory stage, the pre-existing knowledge and the theoretical framework were outlined. Subsequently, a literature search was carried out, using the digital databases: Scientific Electronic Library Online (SciELO), Scopus, Virtual Health Library (VHL), *Sistema de Información Esencial en Terapéutica y Salud* (SIETES) and PubMed. The goal was to generate a representative body of literature covering a wide geographic range and incorporating different approaches and opinions.

All searches, except SIETES, were done in English, using the terms: ‘blockbuster’, ‘pharmaceutical industry’, ‘esomeprazole’, ‘omeprazole’, ‘big pharma’, ‘patents’ and ‘evergreening’. In SIETES, due to the modality of this database, the search was carried out using the following Spanish keywords: ‘esomeprazol’, ‘patentes’, ‘enantiómeros’ and ‘industria farmacéutica’. Table 3 includes more details on the bibliographic search and the absolute number of articles identified through each search engine. Only peer-reviewed, scientific articles written in English, Spanish or Portuguese were included.

The references of all the included articles were reviewed to identify additional references and other technical reports suggested by experts were incorporated into the analysis. After removing duplicate articles and those that did not meet the inclusion criteria, 32 of the 167 articles that had been identified were selected for analysis.

Table 2: Evergreening strategies used in the development of new drugs

Strategic options	Description	Example
Chiral switch	Chiral drugs that have already been marketed as racemic mixture are replaced with a purified single-enantiomer version	Omeprazole/esomeprazole
Different methods of delivering drugs	Provision of the same drug, e.g. in extended release form or changing the pharmaceutical form	Fluoxetine/once-daily dosage form of fluoxetine
Fixed-dose combination	Two or more drugs contained in a single dosage form, such as a capsule or tablet	Efavirenz + tenofovir + emtricitabine
Different dosages	Approval of a drug with a different dosage	Donepezil 5 mg or 10 mg/donepezil 23 mg
Metabolite or analogue	Development of an active metabolite of a drug that is already on the market	Loratadine/desloratadine

Source: Adapted from Kakkar (2015) & Song & Han (2016).

Table 3: Number of articles found, per database or search engine used

Database	Term 1	Logic operator	Term 2	Logic operator	Term 3	Search field	Filter 1 (year of publication)	Filter 2 (article type)	Number of items
Scielo	blockbuster	and	evergreening			abstract	2001–2018		0
Scielo	evergreening	and	“pharmaceutical industry**”	or	“drug industry**”	abstract	2001–2018		1
Scielo	patent*	and	omeprazol	or	esomeprazol	abstract	2001–2018		0
Scielo	“chiral switch”	and	omeprazol	or	esomeprazol	abstract	2001–2018		0
Scielo	“big pharma”	and	omeprazol	or	esomeprazol	abstract	2001–2018		0
Scopus	blockbuster	and	evergreening			article title, abstract, keywords	2001–2018	article	7
Scopus	evergreening	and	“pharmaceutical industry**”	or	“drug industry**”	article title, abstract, keywords	2001–2018	article	24
Scopus	patent*	and	omeprazol	or	esomeprazol	article title, abstract, keywords	2001–2018	article	2
Scopus	“chiral switch”	and	omeprazol	or	esomeprazol	article title, abstract, keywords	2001–2018	article	0
Scopus	“big pharma”	and	omeprazol	or	esomeprazol	article title, abstract, keywords	2001–2018	article	0
PubMed	blockbuster	and	evergreening			title/abstract	2001–2018		6
PubMed	evergreening	and	pharmaceutical industry (MT)	or	drug industry (MT)	title/abstract	2001–2018		21
PubMed	patents (MT)	and	omeprazol (MT)		esomeprazol (MT)	mesh terms	2001–2018		0
PubMed	“chiral switch”	and	omeprazol (MT)	or	esomeprazol (MT)	title/abstract	2001–2018		3
PubMed	patent*	and	omeprazol	or	esomeprazol	title/abstract	2001–2018		13
PubMed	“big pharma”	and	omeprazol (MT)	or	esomeprazol (MT)	title/abstract	2001–2018		0
Sietes	esomeprazol	y	patentes			palabras clave	2001–2018		10
Sietes	omeprazol	y	patentes			palabras clave	2001–2018		12
Sietes	enantiomeros	y	patentes			palabras clave	2001–2018		6
Sietes	enantiomeros	y	industria farmacéutica			palabras clave	2001–2018		6
Sietes	enantiomeros	y	esomeprazol			palabras clave	2001–2018		8
VHL	blockbuster	and	evergreening			title/abstract/subject	2001–2018	article	5
VHL	“drug industry**”	and	omeprazol	or	esomeprazol	title/abstract/subject	2001–2018	article	4
VHL	evergreening	and	“drug industry**”	or	“pharmaceutical industry**”	title/abstract/subject	2001–2018	article	21
VHL	patent*	and	omeprazol	or	esomeprazol	title/abstract/subject	2001–2018	article	14
VHL	evergreening	and	omeprazol	or	esomeprazol	title/abstract/subject	2001–2018	article	2
VHL	“chiral switch”	and	omeprazol	or	esomeprazol	title/abstract/subject	2001–2018	article	2
VHL	“big pharma”	and	omeprazol	or	esomeprazol	title/abstract/subject	2001–2018	article	0
Total									167

The asterisk (*) is a truncation symbol used to retrieve all terms derived from a common root.
MT: Mesh Term.
Source: Own elaboration.

In the third stage, the body of articles were classified using content analysis techniques, particularly thematic analysis [17].

Results

Thirty-two articles were included in the final analysis and these

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were mostly written by researchers from Europe, the US and Australia. The information contained in the articles was classified into three different categories: clinical, regulatory and commercial.

Clinical aspects

Esomeprazole, the S-isomer of omeprazole, was launched in the US market by AstraZeneca, under the name Nexium® in 2001, a few months before the expiration of patent of omeprazole (Prilosec®). The loss of the omeprazole patent threatened the financial position of the company as it was their global best-seller [1, 15].

Given that omeprazole and esomeprazole have the same chemical structure and do not present pharmacodynamic differences, the company justified the development of the enantiopure exclusively on pharmacokinetic differences, particularly a difference in the affinity for CYP2C19, an enzyme belonging to the large hepatic enzyme complex of cytochrome P450, whose basic function is to transform its substrates into more polar and soluble molecules, thus facilitating their excretion. This would result in esomeprazole remaining active for a longer period than omeprazole [6].

In terms of published evidence, several studies [14, 18-20] have shown that the pivotal clinical trials of esomeprazole compared its efficacy against omeprazole at non-equipotent doses, and some trials used placebo as a comparator. Likewise, not all the results were favourable for the new enantiomer, and two articles [14, 18] unveiled the presence of publication bias. While the articles that showed the advantages of the new drug were published in the same year as its market approval, the studies that did not show a significant difference between the two drugs were published five years after approval when the new drug had already established itself as the best option to treat heartburn.

Regulatory aspects

Given the commercial importance of omeprazole, AstraZeneca deployed a wide variety of regulatory strategies to maintain its monopoly, as discussed in the following paragraphs.

Secondary patents: there are two types of patents; primary patents, which protect new chemical or biological compounds intended for therapeutic use in humans; and secondary patents, which protect non-essential aspects of the new molecule, such as small chemical variants, different crystalline conformations of the original compound, methods of use, new formulations, new dosage forms [8, 21].

A 2010 analysis of the Food and Drug Administration (FDA) website found that, in the US, omeprazole was protected by a total of 40 patents [22], constituting a 'patent thicket'. Another example of such a thicket is highlighted in an article on the Australian market [23] which asserts that, in addition to the original patent for omeprazole, there were 61 additional patents, two of which clearly appear to have prevented generics from entering the market. Initially, an enteric-coated formulation, developed to delay the absorption of the active principle, precluded the commercialization of generics between 1999 and 2006, a period during

which a new patent was introduced for the enantiomer esomeprazole [23, 24]. Taking the exclusivity period granted for the new product into account, the effective market monopoly of these two drugs (omeprazole and esomeprazole) in Australia exceeds 29 years [23].

Litigation for patent usurpation: Patent thickets are often used by Big Pharma to enable them to sue generic companies that attempt to enter the market; the greater the number of patents, the easier it is for Big Pharma to claim that one of them has been violated. The litigation process allows Big Pharma companies to extend their commercial exclusivity by the period noted in the legislation. For example, in the US, FDA-approved drugs and all their patents are included in the so-called 'Orange-Book', and when a generic manufacturer wants to market a generic of a brand-name drug it must submit an abbreviated new drug application (ANDA) to FDA. In addition, to ensure that no patent is being infringed, the generic manufacturer must certify one of the following:

- i) the drug has not been patented
- ii) the patent has already expired
- iii) the generic will not enter the market until the patent expires
- iv) the patent is invalid or will not be infringed by the generic.

If the fourth option is chosen (called 'paragraph IV certification'), a notice must be sent immediately to the patent holder, who will have 45 days to take the case to court on the basis that the generic infringes a patent listed in the Orange Book. If the branded drug producer decides to litigate, the generic approval will automatically be delayed for 30 months or until the dispute is resolved or the patent expires, whichever occurs first [18].

Generic manufacturers, who are generally smaller and have fewer financial resources, are often discouraged by the high costs of the legal process. They face the dilemma of having to choose between entering the legal dispute, assuming the costs and the risk of an unfavourable resolution, or simply postpone their market entry until being absolutely sure that both primary and secondary patents have expired.

Paediatric clinical trials: Using federal regulations, AstraZeneca conducted paediatric clinical trials with omeprazole in the US, obtaining an additional six months of market exclusivity [1, 18].

Switching prescription drugs to over-the-counter (OTC): According to Kakkar (2015), AstraZeneca imposed a 'double switch' in the US: the chiral switch of Nexium, and the subsequent switch of Prilosec from prescription to OTC, shortly afterwards. Another article reports the use of the same strategy in Sweden, where, in 1999, the company also requested the change of omeprazole from a prescription to an OTC drug [25].

Commercial aspects

Several authors agree that AstraZeneca's chiral switch was accompanied by an aggressive publicity campaign to encourage loyal consumers of the original racemic mixture to use the new patent-protected enantiopure product [26, 27]. In the US alone, it invested US\$500 million, in direct advertising to the consumer, medical samples and discounts offered to hospitals when using

the new drug [18, 28]. The US advertising campaign appears to have been successful as, shown in Figure 1, shortly after launching Nexium, its sales exceeded those of its predecessor.

Another article analysed the PPI market in Australia and highlighted that in 2003, of all prescriptions for the omeprazole/esomeprazole binomial, only 18% were for the new drug, while omeprazole retained the remaining 82%. By 2014, this proportion was inverted, and esomeprazole accounted for 77%, while omeprazole only held 23% [23].

A 2013 study [6] of the US market calculated the price difference between an equipotent dose of these two drugs for six-weeks of treatment and found that patients using esomeprazole spent US\$ 111 more than those using omeprazole. It is estimated in just a year, AstraZeneca generated an additional US\$1.5 million from this chiral switch. Another article claims that 40% of patients in the US had switched to the new drug in 2003, and that that change represented company earnings of US\$3 billion during that year, and at least US\$5 billion in 2004 [29]. In 2009, in England, the National Health Service (NHS) spent £42 million on esomeprazole at the primary healthcare level, despite the fact that it offers no clinical advantages and is 11 times more expensive than other available PPIs [30]. Similarly, an article that studied the costs associated with eight 'follow-on drugs' in Geneva, Switzerland found that the most prescribed was esomeprazole (55% of the total), which represented an additional cost of €5.2 million over the cost of using generic omeprazole during the period studied (2000–2008) [31].

In 2003 in Australia, shortly after its approval, the price of esomeprazole was 118% that of omeprazole. This continued to increase and, in 2014, it had become 200% more expensive [23], see Figure 2.

Discussion

The results show the success of the strategies used by AstraZeneca to switch consumer loyalty from the successful omeprazole to the new esomeprazole, which allowed the company to maintain high monopoly prices. This case study also highlights the inability of the current intellectual property protection system to guarantee universal access to pharmaceuticals at affordable prices. This failure is reflected in the three interrelated issues that are discussed below.

Patent thickets

The patent system was designed so that, after a period of exclusivity, competing companies could develop and market the same product, engendering competition and leading to lower prices, while the period of intellectual property protection would serve as an incentive for Big Pharma to continue to invest in R & D [32]. However, in the case of pharmaceutical products, the reality is usually quite far from this theoretical model.

Patent authorities often award patents for trivial changes, and Big Pharma companies are using this to their advantage and often succeed in avoiding the commercial losses that would ensue from the presence of competing generics. In some European countries, the price of generics could be as low as 2% to 4% of the originator's price before patent expiration [33], therefore

most innovative companies stand to lose a large share of their markets with the introduction of generics and therefore use a combination of strategies to maintain profits. In relation to this, a recent article points out that in the US, the popular etanercept is still under patent protection 37 years after its first patent was issued and 17 years after the main patent expired [32]. These patent thickets enable companies to maintain their market exclusivity, set high prices, and even expand their market share.

In the last two decades, the patent thicket practice has become widespread. Feldman (2018) shows that according to FDA's records, between 2005 and 2015, 78% of the new patents were not issued for newly developed chemical compounds, but for changes made to some characteristics and/or manufacturing processes of drugs that were already in the market. Moreover, in the US, the ratio between secondary patents and primary patents has recently reached 7 to 1 [33]. These low-quality patents have been questioned in various countries because they might not meet patentability requirements (novelty, non-obviousness and industrial applicability), and have led to an increase in the litigation of intellectual property infringements [34]. The trick consists of protecting the original products with multiple patents to increase the possibilities that the release of a generic version might infringe a patent, lead to litigation and delay the presence of competing products.

This would not be a serious problem if it were not closely related to the fact that the low level of required inventiveness to grant patents, discourages real innovation while maintaining monopoly prices.

In the case of AstraZeneca's chiral switch, the company wanted to maintain its leadership in the PPI market, so is not surprising that it was willing to use anti-competitive tactics, for which it has subsequently had to pay fines and defend its patents in court [15, 35].

Lack of innovation

If companies can extend their commercial monopolies without the need to strive for true innovation, it is not surprising that most newly commercialized drugs offer few additional benefits over older medicines. The increasing interest in enantiopure drugs seems to come in response to this way of thinking. Using data from the independent French publication *Prescrire* as a reference, of the 92 new products and indications that were approved in 2016, only 15 (or 16%) represented a possible therapeutic advance. This data does not appear to be exclusive to 2016 as the number of true innovative products has not changed much in the last 10 years [36].

Big Pharma's R & D is focused on resolving problems that affect a large number of patients who can pay for drugs [1]. So, the lack of innovation is even more pronounced for diseases that affect fewer people and these become neglected. Only 4% of the drugs approved by FDA and the European Medicines Agency (EMA) between 2000 and 2011 were intended for the treatment of such pathologies [37]. Given that most of these neglected diseases are concentrated in developing countries [38], it is reasonable to think that the responses that Big Pharma is offering to these countries is even less satisfactory.

High prices

Although patients' access to drugs depends on various factors, price is undoubtedly a key factor and high prices are a major public concern that threaten the medium-term viability of the health systems.

It should be noted that, according to the innovative pharmaceutical industry, prices do not only reflect the cost of raw materials, manufacturing and advertising of the approved product, but also the investment in R & D of products that have failed. However, the lack of transparency in Big Pharma's expenditures precludes observers from verifying if the prices are linked to reasonable expenditures on each of these components [39]. Critics have suggested that these industries engage in other behaviours that lead to excessive pricing, such as: providing high returns to investors, offering attractive compensation packages for high executives, paying fines due to regulatory violations, extensive lobbying activities, and being involved in mergers and acquisitions above market value [40-42].

Published data shows that governments, health insurers and patients in the US, Europe and Australia increased their expenditures on PPIs after esomeprazole became available in those countries.

Moir's results (2016) appear to support the use of 'shadow pricing', a concept proposed by Angell [1], referring to the fact that companies usually set the price of a new drug in a range very similar to that of its predecessor (or in some cases, lower), in order to favour the transition to the new drug. Subsequently, once various generic drugs have entered the market, competition usually reduces the price of the original drug, increasing the price gap with the successor that is still under patent.

The problem with high prices is that many populations are left behind and without access to life-saving drugs. It is widely demonstrated in the literature [43, 44] that commercialization of generics promotes competition and lowers prices. In the case presented, an aggressive marketing campaign and patent thickets allowed a monopoly to be extended, which was detrimental to patients' interests.

Together, these strategies have many consequences for patients, insurance companies and healthcare institutions. This article has attempted to shed light on the problem and to encourage the implementation of independent cost-effectiveness studies. The comparison of all available therapeutic options could lead to better treatment choices, better health outcomes and the improved use of available resources.

Strengths and limitations

This article's main strength is that it has systematically and qualitatively evaluated the published literature surrounding AstraZeneca's chiral switch omeprazole/esomeprazole. It has also systematically scrutinized the strategies used by AstraZeneca to extend its commercial monopoly in different countries.

The article also has some limitations, being a qualitative systematic review, the use of search terms and the selection of articles is always affected by the subjective decision of the authors. Therefore, although the choice of databases and search terms

was aimed at generating a representative body of literature, some relevant articles may have been omitted. Furthermore, the inclusion of additional chiral switch case studies could yield additional information on how new enantiopure substances have entered the market, in some cases such products may have provided clinical benefits to patients.

Conclusion

AstraZeneca's omeprazole/esomeprazole chiral switch evergreening strategy was used to extend the commercial exclusivity of their blockbuster drug product. They introduced the enantiopure esomeprazole to the market as a new product, although it had no clinical advantages over its predecessor, omeprazole. As mentioned previously, this case was chosen due to the size of the PPI market and because it exemplifies the way in which the company deployed different strategies to prolong commercial exclusivity and increase its profits. This led to an increase in drug spending, both for individuals and for the public health systems.

Our continued reliance on Big Pharma companies for drug R & D and production has resulted in markets flooded with products with little or no utility, that often do not respond to the actual needs of the population.

This study has outlined three major problems that have resulted from the failure of the patent system and how they are closely related. The case of omeprazole/esomeprazole is paradigmatic; it shows that Big Pharma's main goal is no longer the development of drugs with therapeutic value, but one of pseudo-innovation to maintain commercial monopolies for extended periods. This business model aims at maximizing profitability and not at preventing or curing diseases. Unless changes are promoted in the institutions responsible for guaranteeing intellectual property protections in the different countries, the granting of low-quality patents will continue to result in prolonging monopolies and discouraging true therapeutic innovation.

The study highlights that the current patent system is inefficient and does not work to benefit patients. It is therefore imperative to strengthen knowledge and competence at all levels of the healthcare systems to enhance the use of the most cost-effective medical options. It is also important to promote mechanisms to orient the R & D of the pharmaceutical sector towards medicines that respond to the health needs of the population and not to the interests of Big Pharma. Alternative models are being proposed, including public R & D, innovation prizes, and governmental investments in new products that are later sold by private companies with a reasonable profit margin. It is important to invest in exploring these and other alternative paths, to improve access to medicines in all regions of the world and prevent access to medicines being a privilege only for the few.

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Summary paragraph: I believe the information contained in this article may be relevant for prescribers, patients and the community in general. All of them will benefit from learning about the strategies used by the pharmaceutical industry that lead to increased prices for prescription drugs.

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Authors

Federico J Piñeiro¹, Pharm, MPH

Fernández Argüelles Rogelio Alberto², Pharm, PhD

¹Instituto de Salud Colectiva, Universidad Nacional de Lanús, 309 Thames, 1414, Buenos Aires, Argentina

²Universidad Autónoma de Nayarit, 56 Shangay, Colonia Insurgentes, 63183 Tepic. Nayarit, México

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