Product hopping and pre-emptive cannibalization in Pharmaceuticals

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Abstract

This paper looks at the impact of a new drug on the revenues and sales of the incumbent products. Using information at firm level on all the anti-ulcers sold in Italy between 2001 and 2003, we study the nature of the competition among products in an environment where prices are strongly regulated. Our analysis points to three main findings. First, the new entry did not have a significant market expansion effect. Second, substitution from the old to the new chemical is mainly between products of the same firm. Third, studying the revenues and quantities lost by the incumbents before and after the new entry, we show that cannibalization accounts for more than 82% of the overall market for the new products. We conclude that the drug is an example of strategic cannibalization, where the new product replace the old one in order to escape future competition.

1 Introduction

It is well known that innovation in pharmaceuticals is a long and expensive process. Patent protection artificially creates the appropriate economic incentives for the necessary investments in research (Sherer, 2007). Once patent protection expires, the chemical is considered off-patent and generic drugs (drugs commercialized with the name of the chemical) can enter the

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market. From a societal point of view, generic competition is beneficial, although in general the moment of patent expiry is a traumatic event for the patent-holding incumbent.

The theoretical literature identifies different strategies that can be put in place with the purpose of limiting imitation. Lobbying for supplementary protection certificates, patent infringement litigation and the accumulation of patents for different formulations are probably the most commonly used (Lamote et al., 2009). Another approach often discussed in the economic literature (Frank and Salkever, 1992; 1997) and acknowledged as a ‘new form of competition’ by the OECD (2009) is for patent-holders to ‘join the enemy’, i.e. introduce their own generic version of the same drug, with the purpose of capturing part of the after-expiry elastic demand. In general, however, the impact of generic competition is rather important and difficult to contain.

In the present paper, we focus on a different, and potentially effective, strategy sometimes implemented in order to limit the impact of imitation and generic competition. In this context, the patent-holder introduces a minimal or insignificant improvement over the existing chemical and tries to patent a new product with similar characteristics in proximity of the patent expiry of the old one. If the strategy is successful, a relevant share of the sales and revenues of the old chemical shifts to the new one, pre-empting the market for the incoming generic competition. Since this approach requires patenting a close substitute and cannibalizing your own product in order pre-empt mature markets, we define it as ‘pre-emptive cannibalization’. The same strategy is known as ‘product hopping’ in the legal literature (Lamote et al., 2009, OECD, 2009) A good overview of several products suspected of this practice is given in Cheng (2008).

Since, to be awarded, a patent must be, among other things, ‘non-obvious’, a logical way to challenge pre-empting patenting from a legal stand is to question the concept of ‘obviousness’ (Metzke, 2010). Although this approach tackles directly the issue at stake, it is mainly a question for the Courts and for the Law literature to define a general and precise concept of obviousness in pharmaceutical patenting. Product hopping has however been challenged also in the antitrust law. In the Walgreen vs AstraZeneca case, five small drug sellers accused AstraZeneca of a violation of the Sherman Act.

\[1\] Throughout the paper we will refer to ‘cannibalization’ as the process through which a firm replaces its own product with a new one. Instead, we use business stealing to indicate the process of earning market shares at the expenses of other firms.
Plaintiffs allege that AstraZeneca deliberately switched the market from its prescription heartburn drug Prilosec [Omeprazole], just as Prilosec's patent was about to expire, to both its newly FDA-approved equivalent Nexium [Esomeprazole], which had a patent that would not expire for several years, and to its newly FDA-approved over-the-counter (OTC) Prilosec (Walgreen Co v. AstraZeneca Pharms, 534 F. Supp. 2d 146, DDC 2008)

In 2008, however, the U.S. District Court for the District of Columbia dismissed the complaints.

Theoretical and empirical economics can contribute to the debate in different ways. For example, by defining what strategies are most effective in preventing profit losses and what are the welfare effects attached to them. On the other hand, by looking at post marketing data, it might be possible to find evidence that could be more or less consistent with alleged strategic behaviors.

The main purpose of the present paper is to investigate the relation between claims and empirical evidence and, where possible, to provide a robust consistency check of alleged product hopping behaviors. For the purpose, we examine the post-entry effects of the launch of a new drug on sales and market shares of the existing products. We analyse the case of Proton Pomp Inhibitors (PPIs) in Italy in the period January 2001-December 2003. In April 2002 a New Chemical Entity (NCE) was introduced: Esomeprazole. This new chemical was launched by the same company (C) holding the patent of the leading chemical in the market (Omeprazole), whose patent was about to expire within two years.\(^2\)

The main idea here is that for product hopping to be a concern for authorities, two conditions must be met. First, the product must be chemically a close substitute (in fact, a ‘hop’) of the existing one. Practically, this implies that it should not address needs that were left unmet by the old product. Hence, no market enlargement should be observed. Second, the new product must substitute the old one, since it was mainly developed with this purpose. Empirically these conditions require us addressing two simple but important questions. Did the launch of the NCE have significant market expansion?

\(^2\)Note that this are exactly the same products considered in the cited Walgreen vs AstraZeneca. The choice is deliberate. First, it makes sense to perform the analysis on actual and important cases. Second, a previous version of this paper existed before the judicial case was decided.
effects? How did the new entry affect the equilibrium among the incumbent products? Addressing the two questions, we show that the new product did not cause any significant increase in the overall market for PPIs. More important, we show that there was an almost one to one substitution between the old and the new chemical from the same company.

Note that this approach could theoretically provide also a consistency check between doctors’ prescribing behaviour and scientific evidence. For example, the medical evidence could tell us how good a drug is compared to the existing products. These results could then be compared with what doctors actually prescribe.

The paper is organized as follows. First, we formalize the issue by presenting a simple description of how the demand system might be affected by both patent expiry and the entry of a similar NCE. The purpose of this Section will only be to introduce the topic highlighting the strategic variables that can actually play a role in the success of the strategy of pre-emptive cannibalization. In Section 3, we provide motivation to the study by linking the research question with both the economic and the medical literature. After presenting the data, in the analysis of Section 5 we will test the impact of the new drug, Esomeprazole, on the overall size of the relevant market. The graphical and econometric inspection will show that the new product has not significantly enlarged the market for Anti-Ulcer drugs. In Section 6 we develop a specific empirical test to understand whether the substitution patterns reflect the pre-entry market shares. In Section 7, we quantify these patterns, in terms of quantity and revenues’ losses. With this information, we then provide an estimation of the pre-emptive cannibalization in the period of observation. Finally, in Section 8 we discuss how these results can be interpreted.

2 A simple framework

A formal description of the relation between new and old products and patients/doctors preferences and perceptions might help the reader and provide a more solid basis to better understand why and how product hopping can represent a valid strategy for an incumbent firm. In this Section we thus provide a simple formalized framework of a demand system relevant for the case under study. However, it should be noted that here we do not look for equilibria or optimal pricing strategies, for several reasons. First, although
interesting and certainly doable, these issues go beyond the objectives of this empirical paper. Second, since cannibalization is mainly about demand shifting, many intuitive insights can be drawn just by looking at the demand system. Third, since we borrow heavily on previously existing models for the pharmaceutical sector, namely Brekke et al. (2007), Miraldo (2009) and Ghislandi (2011), we refer to these papers for punctual solutions.

Imagine an incumbent drug producer selling drug A. A fixed number of M patients need the drug.\footnote{Although potentially we could make the market size depend on product level variables such as prices, in order to keep the analysis as simple as possible we exogenously set M.} The drug is distributed at a certain cost $c_A$ for the patients. This is not the price received by the firm, but rather the price directly paid by patients. Obviously $c_A$ is positively related to $p_A$, however different regulatory and insurance systems might imply different levels of costs even for the same price. For example, patients might be required to co-pay for the drug. Alternatively, patients might have to pay a fixed fee or even nothing. For our purposes it is not much relevant how $c_A$ is determined. What matters is that, as long as A is covered by patent protection, M people will buy the drug at the stated unit cost.

Once patent expires, the active compound used by A can be replicated by generic firms. As a first step, abstract from any horizontal differentiation issue. In this context, patients might choose between two products that are chemically equivalent but that can be perceived as qualitatively different. Following Ghislandi (2011), one effective way to model this situation is to use a quasi-linear utility function where the utility from the health gains is $V(H)$ and is the same for everyone. Each patient $i$, however, trusts generic products less than the incumbent, hence expecting a health benefit of $\alpha_i V(H)$, where $0 \leq \alpha \leq 1$. The overall utility function for patient $i$ buying a generic version of drug A is then:

$$U(i, G) = \alpha_i V(H) - c_G$$

while if the branded product is chosen, the utility is:

$$U(i, A) = V(H) - c_A$$

where $c$ is the cost to the patient, always positively related to the real price. Hence, the demand for the two products will depend on the distribution of the beliefs across patients. A bimodal distribution, for example, pictures the case of a divided market where brand loyal consumers are not particularly price-sensitive, a situation where the well-know generic paradox might arise.
Frank and Salkever, 1992; 1997). Whatever the distribution, the overall demand for the generics is given by all the patients with a value of $\alpha$ higher than the threshold $\tau \equiv 1 - \frac{c_A - c_G}{V(H)}$. Hence, once patent expires, the branded product has to share the market with other producers.

What if the incumbent expects low levels of brand-loyalty, for example because other cheaper brand substitutes are available anyway in the market? Is there a strategy it can implement in order to reduce the market shares loss following patent expiry? As underlined in the Introduction, different strategies are available. Here we focus on product hopping, which consists in the launch of a new chemical very similar to the existing one with the purpose of pre-empt the market for generic drugs.

Brekke et al. (2007) and Miraldo (2009) offer a nice simple setting to model this situation by over-imposing to the vertical differentiation presented above a horizontally differentiated demand function (Hotelling type). Specifically, imagine that the M patients are uniformly distributed on the line segment $S = [0, 1]$, where the location of an arbitrary patient $i$ is $x_i$ and is associated with the patient "proximity" to a drug characteristics. As usual in these models, a mismatch cost of $t$ measures the utility loss per unit of distance between the position of patient and the actual drug. The same firm can offer product A and a new product B, placed at the two opposite side of the $S$ interval. While product B is patent protected, product A is subject to the previously described competition by generics producers.

In this context the utility functions from buying product $j = 0, 1$ are defined as:

$$U(i, j) = V(H) - c_j - t|x_i - j|$$

while the utility from buying the generic version of drug A is (remember that A is placed at 0 in the horizontal line):

$$U(i, G) = \alpha_i V(H) - c_G - tx_i$$

Notice the choice of a patient $i$ between the branded or a generic version of the same chemical does not change. Patients will choose G in comparison with A if and only if $\alpha_i > \tau$. On the other hand, they can also choose between B and G and between A and B.

Specifically, it is easy to show that for those with $\alpha_i > \tau$, G is preferred to B if:

$$x_i < \tilde{x}_G \equiv \frac{1}{2} + \frac{V(H)(\alpha_i - 1) + c_B - c_G}{2t}$$
and that, among those with $\alpha_i \leq \tau$, A is preferred to B if:

$$x_i < \tilde{x}_A \equiv \frac{1}{2} + \frac{c_B - c_A}{2t}$$  \hspace{1cm} (6)

The overall demand is then pictured in Figure 1.\footnote{In the picture it is assumed that $V(H) > \frac{c_G - c_A}{(\alpha - 1)}$ so that $x_A < \tilde{x}_G$.}

If B did not exist (no product hopping), all the area above $\tau$ would go to the generic product G.\footnote{Here we assume that all consumers gain a positive utility from consuming one version of the drug. Formally, we assume that $t < V(H) - c_A$.} Product hopping is then associated to a gain in the overall share of the market equal to the area CDEF. At the same time, the area $\tilde{x}_A NA1$ represents the gain in demand from the brand-loyal patients.

Obviously prices play an important role. In particular, note that:

$$\frac{\partial \tilde{x}_G}{\partial p_B} > 0$$  \hspace{1cm} (7)

and

$$\frac{\partial \tilde{x}_A}{\partial p_B} > 0$$  \hspace{1cm} (8)

Hence, an increase in $p_B$ reduces both the area CDEF and the area $\tilde{x}_A NA1$, mainly attenuating the impact of product hopping on market shares. In particular, since the only reason to buy a generic version of A is price, pre-emption of the market for the generic drugs should be associated to an aggressive pricing strategy. Of course, as long as $p_B > p_A$, product hopping might still be successful in increasing revenues, even if cannibalization is reduced to a minimum and limited to brand-loyal patients. This gain would not come, however, from facing generic competition, but rather from accommodating it and relying on the brand-loyal side of the market, representing another expression of the generic paradox often reported in the empirical and in the theoretical literature.

Although prices are important, in some highly regulated countries, there is not much firms can do in terms of pricing strategies. Moreover, it is clear that pricing is heavily influenced by how patients perceive the new product as similar to the old one. For example, assume for a moment that $c_A = c_B = c_G$. Then:

$$\frac{\partial \tilde{x}_G}{\partial t} > 0$$  \hspace{1cm} (9)
Hence, decreasing $t$ does not affect the demand for $A$ and reduces the demand for $G$. Indeed in this case when $t = 0$ all the M patients will buy product $B$. In other words, the more similar is product $B$ perceived to product $A$, the higher the benefits from product hopping. In the limit case of $t = 0$, the whole demand for $G$ would be covered by product $B$. On the other hand, if $c_B - c_G > V(H)(1 - \alpha)$, i.e. for price differences high enough, the sign of the first derivative of $\tilde{x}_G$ is reversed. In this case, if $t = 0$ all the demand of patients with $\alpha > \tau$ would stay on $G$.

Can the firm influence $t$? Since this parameter represents a psychological rather than a real cost, it probably can be affected by marketing and promotional efforts. Assuming that $t$ is at least partially endogenous to firms’ investment efforts, for product hopping to be successful a firm then needs to either homogenize prices and reduce $t$ or maintain high prices for $B$ while investing for increasing the perception of horizontal differentiation.

This simple description can then be useful to understand the case of Italy analyzed empirically in the following Sections. In the observation period and for the products used, in our study $c_B = 0$ (i.e. Esomeprazole was reimbursed with no co-payment), $c_G = 0$ (a Reference Price mechanism with

$\frac{\partial \tilde{x}_A}{\partial t} = 0$ (10)
no co-payment was at work) and $c_A = p_A - p_G \geq 0$ (patients would have to pay the difference between the price of product A and the price of the cheapest generic version of the same chemical) and $p_B \simeq p_A$. It follows that the best strategy for the incumbent would be to reduce the perceived distance between Omeprazole and Esomeprazole, i.e. decrease $t$ and shift as much demand as possible from the old to the new product.

3 Literature and Scientific Evidence

The question of whether a new product enlarges the overall market or just substitutes the existing goods is under-researched in the empirical Industrial Economics literature too. The most cited published paper in this area is Davis (2006), where the author evaluates business stealing, cannibalization and market expansion effects of entry in the US motion picture market. Using micro level data on the revenues and location of movie theaters, he performs a series of panel-data regressions in order to capture the effects of a new theater in a pre-specified distance-defined market. He finds that between 30% and 50% of a theater’s revenue is obtained by stealing revenue from rival products and this effect dissipates on average at a distance higher than 15 miles. He also shows that ownership counts, noting that there had been very little cannibalization due to limited strategic deterrence.

The study by Davis is very much related to ours, but its methodology can not be reproduced here because the structure of the data is different. In our case we have only one new product, and consequently only one firm that can cannibalize its revenues. The market is not based on thousands of small companies, but rather on a few big competitors. A different estimation strategy is therefore necessary, but the main questions and the basic approach (i.e. panel data reduced form analysis) are kept throughout the paper.

Another related study is Argentesi (2004) in which the author investigates the demand for Italian newspaper before and after the introduction of their weekly supplements. Using a macro-level logit approach on panel data, she evaluates the magnitude of market enlargement and business stealing effects, concluding that the latter is between 9% and 15% of pre-launch market shares. These data are closer to ours. However, innovation is a new characteristic in the existing products rather than a new product launched in the same market.

In the more specific literature on pharmaceutical empirical IO, the mea-
surement of market expansion has been traditionally related to the evaluation of the effect of Direct-To-Consumers advertisement. In particular Iizuka and colleagues (Iizuka, 2004, Iizuka and Ginger, 2007) come to the conclusion that Direct-To-Consumers advertisement is a public good for the drugs in the same class because it is related to a significant market expansion effect, with little business stealing.

3.1 Scientific Evidence

After Omeprazole, four other PPIs have been introduced in Italy: Lansoprazole (1995), Pantoprazole (1997), Rabeprazole (1999), and Esomeprazole (2002). Both Omeprazole and Esomeprazole are patented by the same company. Importantly, according to the British and Italian Health Authorities, none of the first four PPIs released has been shown to be more effective than another in healing erosive esophagitis.\(^6\)

Two points of the scientific literature are worth mentioning here. First of all, Omeprazole and Esomeprazole are chemically very similar, as already recognized also by the legal literature (Metzke, 2010):

A racemate, or racemic mixture, consists of exactly two stereoisomers called enantiomers. Coinciding enantiomers have the same molecular formula, connectivity and chemical and physical properties [.....] An issue then arises when a resolved enantiomer that offers little clinical improvement over its racemate is patented at the end of its parent racemate’s patent term [.....]

This is a much more attractive alternative to developing a wholly new Active Pharmaceutical Ingredient or an analog that may be synthetically challenging [.....] Esomeprazole is the single Omeprazole enantiomer.

Although enantiomers are very similar, they differ in some dimensions. Hence, potentially they may have different biological activity. It is thus important to see also what the pharmacoepidemiological literature has shown about the relation between Esomeprazole and the other PPIs.

The biggest (over 5000) double-blind study on the issue found a statistically significant difference in healing efficacy between Lansoprazole and

\(^6\)For Italy, we refer to the “nota 1” and “nota 48”, which serve as general guidelines for the prescriptions of antiulcers across the country. For Britain, the guidelines can be found here: http://www.nice.org.uk/page.aspx?o=292430
Esomeprazole. However, the difference was not clinically meaningful, as the healing rates differed by only 3.4\%(Howden et al, 2002) Moreover, many health professionals have expressed the view that the alleged improvement in efficacy is due to the dose of Esomeprazole recommended for the therapy rather than any superiority of Esomeprazole \textit{per se}. Indeed, in the cited study, and in all the other head-to-head analyses recently performed (see, for example, DrugDigest website for a review, http://www.drugdigest.org ), the comparison has always been between 40mg of Esomeprazole and lower dosages of other PPIs. In the above study described, for example, the counterfactual was 30mg of Lansoprazole. Importantly, Italian authorities consider Esomeprazole as equally effective as any other chemical within the PPI class.

As summarized by DrugDigest (accessed in October 2012), the accepted evidence on PPIs shows that:

- Most comparative clinical studies between PPIs have shown that all are about equally effective for relieving GERD, they all work in a similar manner, and they all have similar side effects. The effect of Rabeprazole may last slightly longer than the others.

- Along with Pantoprazole, Rabeprazole may have a slightly lower risk of side effects.

- Choosing which PPI to use depends on the doctor’s preference, the condition being treated, other drugs that are taken at the same time, past experience with a PPI, the prescription benefits formulary, and potential drug interactions.

In the present context, Rabeprazole and Pantoprazole are relatively irrelevant. Our data refer to a period when these drugs were not so well-known. Moreover, even if their efficacy was considered higher than other PPIs, this should be reflected in market shares both before and after the entry of Esomeprazole. To our purposes, the issues to point out from the scientific literature are that:

- From an economic point of view, PPIs products should be considered as substitutes of each other.

- The scientific evidence has not yet shown any convincing clinical superiority of Esomeprazole within the PPI class, as stated by various country specific health authorities.
• There is no evidence that Esomeprazole is a closer substitute of Omeprazole than of any other chemical in the PPI class.

This last point, although not directly stated in the literature, is particularly important for any test of substitution patterns.

4 Data

The data we use are from IMS Health Italy. The data include revenues and quantities of all the anti-ulcers sold in all regions in Italy through the Italian NHS. Quantities for every single pack are transformed in number of Defined Daily Doses. Summary statistics are provided in Table 1.

<table>
<thead>
<tr>
<th>Class</th>
<th>Chemical</th>
<th>$MS_R$</th>
<th>$MS_Q$</th>
<th>$N$ firms</th>
<th>$N$ observations</th>
<th>Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI</td>
<td>Esomeprazole</td>
<td>0.203</td>
<td>0.300</td>
<td>4</td>
<td>1711</td>
<td>2002</td>
</tr>
<tr>
<td>PPI</td>
<td>Lansoprazole</td>
<td>0.101</td>
<td>0.091</td>
<td>3</td>
<td>2268</td>
<td>1995</td>
</tr>
<tr>
<td>PPI</td>
<td>Omeprazole</td>
<td>0.508</td>
<td>0.435</td>
<td>4</td>
<td>3024</td>
<td>1989</td>
</tr>
<tr>
<td>PPI</td>
<td>Pantoprazole</td>
<td>0.161</td>
<td>0.156</td>
<td>6</td>
<td>4032</td>
<td>1997</td>
</tr>
<tr>
<td>PPI</td>
<td>Rabeprazole</td>
<td>0.027</td>
<td>0.018</td>
<td>1</td>
<td>756</td>
<td>1999</td>
</tr>
</tbody>
</table>

In the Table $MS_R$ and $MS_Q$ are the revenues and quantities market shares respectively. It is easy to note that the number of firms is greater than 1 even for in-patent chemicals. This is the consequence of the practice of marketing the same active compound as different brands under the originator license (i.e. “co-marketing”) (Ghislandi et al, 2005).

Omeprazole is the most popular chemical in the whole market for anti-ulcers. It was launched in 1989, but due to the Complementary Certificate Protection (CCP), its patent protection is extended for a further 18 years. As a result, in 2003 there was no off-patent PPI in 2003. Esomeprazole, despite its late entry (more or less at half of the sample length) has collected a significant sum of revenues and already represented the second most sold product in the PPI class.

In Italy, prices have been heavily regulated. In general, the approach of the Italian Authorities on this matter is to bargain with the pharmaceutical company on the basis of the prices existing in the same class and on the empirical evidence of efficacy improvements. So, it was possible to observe some
price differentials both among different types of similar drugs and among different packages inside the same chemical group. The situation changed after 2004, when prices per DDD were calculated and equated among all the drugs and packages inside the same "reference group". Esomeprazole was no exception. First launched in April 2002 in all the 21 Italian Regions, its price was initially a result of a bargaining process between Authorities and the company. However, since these bargaining processes were usually based on the prices of similar drugs already present in the market, prices, although not identical, did not change much across chemicals in the same group. After January 2004, Esomeprazole joined the other four "prazoles" in the same "reference group" and it is now sold with the same price per DDD as any other PPIs.

5 Market enlargement

An innovative product can change the market in many dimensions. If it tackles health needs that were not addressed before, what we should observe at aggregate level is an increase in the overall market for that category of products. The expansion of the market, however, could be associated also to a product that can improve over the existing ones on important dimensions, such as the side effect and the compliance. In this case, the new product reduces the costs for patients and this might well convince the marginal ones to enter a market that was not appealing before.

The first question to answer is then whether Esomeprazole increased the overall market for PPIs. If Esomeprazole is not a big scientific breakthrough as claimed by the scientific literature, its launch should not be associated with a significant market expansion effect. In other words, if the scientific literature is right, the launch of Esomeprazole should not have big consequences for the market.

Methodologically, what we are trying to test is whether the overall market size changed after the introduction of Esomeprazole. Given that we have 16 months before the launch and 18 months after, the sample is fairly balanced for a before/after type of analysis.

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7 A reference group is defined as a group of drugs that, for their medical and chemical characteristics, can be considered as substitute of each other.

8 This is a clear sign that the Italian authorities do not see Esomeprazole as different from the other PPIs.
In Figure 2 we report the trend of the quantities (DDDs) and revenues (in euros) for the overall market of PPIs.

The vertical line signals the launch of Esomeprazole in April 2002. Both revenues and quantities do not seem to grow at a faster rate. However, a positive trend is detectable in quantities. For this reason we focus our analysis of market enlargement only on DDDs. We proceed following the general to specific approach of Perron (Perron, 1997; 1989) for breaking trend functions. First, and most important, we need to understand whether the series for DDDs is Trend Stationary (TS) or Difference Stationary (DS). In the former case, the equation to run is:

\[ q_t = \mu + \varphi q_{t-1} + \sum_{k} \gamma_k \Delta q_{t-k} + \beta t + \alpha_1 DU_t + \alpha_2 DUT_t + \alpha_3 DT_t + \epsilon_t \]  \hspace{1cm} (11)

where \( DU_t = 1[x > T] \), \( DUT_t = 1[x = T+1] \) and \( DT_t = 1[x > T]*t \). The value of \( T \) is the value of the structural break as found by the methodology. In our case, we impose \( T \geq 16 \) (the month in which Esomeprazole was launched) and \( T \leq 24 \) (as with the new year new regulatory innovations might influence the trend independently from the effect of Esomeprazole). The variables...
$DU_t$ and $DT_t$ capture the change in the pattern of the series in the intercept and in the time trend respectively. The coefficients $\alpha_1$ and $\alpha_3$ are thus the important ones for our purposes.

If the series is DS, $\varphi = 1$ and the equation becomes:

$$\Delta q_t = \mu + \sum_k \gamma_k \Delta q_{t-k} + \alpha_1 DU_t + \alpha_2 DUT_t + \alpha_3 DT_t + \epsilon_t$$  \hspace{1cm} (12)$$

where the meaning of $\alpha_1$ and $\alpha_3$ is the same as for equation (11).

The test of whether the series is TS or DS is a test on $\varphi = 1$ in equation 11, i.e. is a unit root test. The Dickey-Fuller test might be applied, but if the trend has a break Perron has shown that the classical test tend to accept the unit root hypothesis too often. In order to correct for the bias, we need to manipulate the equations and the test in three ways.

First, we need to define the best value of T. Even if Esomeprazole entered in $t=16$, its effect might have taken a while before being detectable at macro level. As we can not know T in advance, the best way is to let the data speak and to choose the T closer to a break that we can find in the data. The regression for the unit root test is the performed separately for every possible date of the break and the coefficient $\alpha_3$ (or, alternatively, if we assume only a change in the intercept, $\alpha_1$) with the maximum absolute value of the t-statistic is the one that defines T.

Second, the lag length $k$ is chosen using Perron’s (Perron (1997)) $t$-sig criteria. We worked backward from $k=10$ and we chose the first value of $k$ for which the t-statistic on $\gamma_k$ is greater than 1.6 in absolute value and the t-statistic on $\gamma_l$ for $l > k$ is less than 1.6 in absolute value. Given we have only 16 months of observation before, and considering the encouraging fact that the t-statistics are very similar for all the $k$, we set $k=2$ as a maximum bound\(^9\).

Third, we choose the critical values for acceptance according to the ones given in Perron (1997).

The Perron test works fairly well on our data. The optimal lag is $k = 5$, the break is at $T = 16$, and the t-statistic for the unit root test is $t_\alpha = -2.7262344$. Thus the unit root null is not rejected and the series is difference stationary. As in Perron, we then run equation (12) as an OLS ($R^2 = 0.4,$):

\(^9\)Results do not change when considering higher values, but we think it is somehow odd to loose a high number of observation, asymmetrically, at the beginning of the period.
\[ \Delta q_t = 1743938 - 0.6220572^{**} \Delta q_{t-1} - 0.387428^{**} \Delta q_{t-2} + 
-8270177 \text{DU}_t + 3.63(10^7) \text{DUT}_t + 382948.2 \text{DT}_t \]

The results confirm our conclusion from graphical inspection. Both \( \alpha_1 \) and \( \alpha_3 \) are statistically not significant. The fact that \( \text{DU}_t \) is negative does not matter as the overall effect is given by all the three intervention variables.\(^{10}\)

Altogether, the provided evidence is robust in showing the lack of any significant market expansion effect related to the launch of Esomeprazole.\(^{11}\) More comments on the results are in the final Section.

6 Substitution among PPIs

Esomeprazole was not a breakthrough. However, it might still have introduced serious improvements. For example, a reduction in the side effects. For this reason in this Section we change target for the analysis and we evaluate how the equilibria among the incumbents have changed after the entry of Esomeprazole.

Looking at substitution patterns across the existing products can help in measuring two main issues. First, to what extent PPIs are really considered as perfect substitutes by actual decision makers? If perfect substitution holds, the entry of a new product should not significantly alter the pre-entry equilibrium market shares among incumbents. This implies that the proportion of revenues of one product is not expected to change before and after entry with respect to the total revenue of the PPI, Esomeprazole excluded.\(^{12}\) Second, how much of the demand of the new product come from existing products of the same firm?

---

\(^{10}\)If we consider the same regression but with \( \alpha_3 = 0 \), the coefficient on \( \text{DU}_t \) becomes positive but still not significant.

\(^{11}\)Here we note that the same results can be obtained if we consider the overall market for antiulcers rather than only the PPI. Actually, in that case the lack of a break for the DDD series is even more evident from simple graphical inspection. This implies that the increasing demand for Esomeprazole and PPIs in general came partly from the constant trend of substitution from H2 to PPIs.

\(^{12}\)In the language of the Industrial Organization, we could say that the ”displacement ratios” are identical among incumbents, where the displacement ratio is defined as the ratio of the post-entry change in revenues the entrant and an incumbent (Armstrong et al, 1996).
If different me-too drugs (i.e. drugs that are very similar to the original patented product) are present in the same competitive arena, product hopping requires a substitution pattern that does not reflect market shares. Reversely, if all the incumbents drugs are similar, a non-strategic launch of the new product should steal business from all the incumbents proportionally to the existing market-shares. A form of Independence of Irrelevant Alternatives (IIA) should then hold, provided that products are all similar to each other.\textsuperscript{13}

The dynamic in the revenues at chemical level is depicted in Figure 3.

![Figure 3: Revenues of PPIS by Chemical](image)

The most evident fact is that the entry of Esomepraole caused a change in the trend for Omeprazole. Before April 2002 sales where noisy but with something like an upward trend. After Esomeprazole entered, the trend clearly changed. The fact that the revenues at the beginning and at the end of the observation period are similar should be interpreted considering that the overall market has been constantly increasing since the mid 1990s.

\textsuperscript{13}Indeed, if the old and the new products are perfect substitutes, the only reason why the new product should gain market shares at the expenses of the competitors is that product hopping is accompanied by massive advertising investments or aggressive pricing. In this paper we do not control for advertising, since results are quite clear anyway. Pricing, on the other hand, is not a concern since we are considering heavily regulated markets.
Similar revenues at three years distance are thus a sign that the positive trend in PPIs has not been captured completely by Omeprazole. Pantoprazole shows a break in the series in January 2002. This is due to the (re)launch of Peptazol, a brand licensed to Altana, which turned out to be a commercial success.

What we need to test here is whether, considering common trends and different averages, Esomeprazole’s success could be explained by a more than proportional substitution from Omeprazole to the new drug. In other word, we are testing whether the proportion among drugs in the same PPI group has remained the same before and after Esomeprazole’s entry and, if not, how much it has changed. Note that this is conceptually equal to testing an independence of irrelevant alternatives (IIA) assumption among the four PPIs, with Esomeprazole representing the "irrelevant alternative".

For this part we run a series Difference in Difference (DD) models, where the effect of entry on one drug is compared with the average effects on the others. The estimation is based on a transformation of the original dependent variable, drug-level revenues. We use the subscript $j$ to indicate the firm, $l$ for the chemical, $h$ for the region and $t$ for the time.

The dependent variable is then defined as follows:

$$\tilde{y}_{jilt} \equiv \frac{(y_{jilt} - \bar{y}_{ht})}{\bar{y}_{ht}}$$

where $y_{jilt}$ is the revenue of one drug with chemical $l$ in region $h$ and time $t$; $\bar{y}_{ht} = \frac{\sum_j \sum_l y_{jilt}}{N_h}$, and $N_h$ is the number of firms in the four pre-entry chemicals' regional submarkets. In other words, $\bar{y}_{ht}$ represents the average of the revenues across firms and chemicals in the same region, excluding Esomeprazole.

Working on $\tilde{y}_{jilt}$, which represents the demeaned revenues at regional level, can then help in two important ways. First of all, by averaging across products, but not in time, we control for common trends. The problem here is that there might be a cross-section dependence among observations within a region. For example, imagine that the overall market size of the class in a region is stable in time or grows with a linear trend. Then, after controlling for the linear trend, an increase in the revenue of one drug is necessarily associated to a proportional decrease in the revenue of another product in the same region. This issue is commonly known as the problem of correlated panel and it has been shown to be an important source of bias if it is not taken
into account (Phillips and Moon, 2000). Demeaning is one of the solutions most commonly adopted.

Second, the behaviour of \( \tilde{y}_{jht} \) gives a natural test for the IIA hypothesis. Here we first give a definition of IIA as we intend it in our context. For simplicity imagine that there are only two periods, \( t = 0 \) and \( t = 1 \), corresponding to before and after the entry of the new chemical. Then, for each chemical \( l \) and region \( h \), the substitution patterns exhibit the IIA property if chemical-level revenues among incumbents within a region do not change before and after entry. Formally, indicating with \( l = 1 \) a “reference” chemical

\[
\text{IIA} \Rightarrow \left( \frac{y_l}{y_1} \mid t = 0 \right) = \left( \frac{y_l}{y_1} \mid t = 1 \right) = k_l
\]  

(13)

If the IIA property holds, \( \tilde{y}_{jht} \) must not change significantly after the introduction of the new chemical. This is shown formally in the Appendix, but can be understood intuitively: if the IIA holds, the revenues of the incumbents should change all in the same proportion. Consequently, the average distance from \( \bar{y}_{ht} \) (remember that \( \bar{y}_{ht} \) is the average only of the incumbents’ revenues) should be similar before and after the launch of Esomeprazole.

A test of the IIA is thus a test on the equality of \( \tilde{y}_{jht} \) before and after the introduction of Esomeprazole. For this purpose, we use a treatment effect approach. Specifically, we run a linear DD model for each (chemical \( L \)) of the four incumbent chemicals. In each regression, we consider the products that use chemical \( L \) as the treatment group and the products with chemicals \( l \neq L \) as the control group. In this setting, we are interested in understanding if, after the introduction of Esomeprazole, the change in \( \tilde{y} \) for the treated group is significantly different from the same change for the control group. Therefore, we run the following regression:

\[
\tilde{y}_{jht} = \mu_{jht} + \alpha_1 I_L + \alpha_2 DU_t + \alpha_3 I_L DU_t + \beta t + \gamma NHS_{ht} + \epsilon_{jht}
\]  

(14)

which is the most common specification for a linear DD model. Here \( I_L \) is a dummy indicating if firm \( j \)’s product uses chemical \( L \) (treated region). \( DU_t = 1[t > T_E] \) is the treatment period, where \( T_E \) is the time of entry of Esomeprazole. The interaction variable \( I_L DU_t \) represents the treatment effect we are interested in: products with chemical \( L \) in the post-entry period. The test of IIA then reduces to a test of the significance of \( \alpha_3 \).\(^{14}\) \( NHS_{ht} \) is

\(^{14}\) Note that taking a DD approach with time-trend correction we are actually testing whether IIA holds conditional on the trend.
Results are shown in Table 2. For each chemical, we perform only one random effect (GLS) estimation where the individual constant is treated as normally distributed with a first order autocorrelated variance-covariance matrix. The number of observations is common across all the regressions and equal to 10,060.

From the Table, substitution patterns for Omeprazole, Lansoprazole and Pantoprazole changed significantly. Importantly, Omeprazole lost revenues more than proportionally when compared with other PPIs. Approximately, the overall reduction in \( \tilde{y} \) is around 10%. On the other hand, Pantoprazole and Lansoprazole proportionally gained after the launch of Esomeprazole.

It could be pointed out that these results are sensitive to the way the sample is split into treated and control groups. In equation (14) the control group is represented by all the chemicals different from chemical \( L \). For example, in regression (2) of Table 2, \( \alpha_3 \) captures the difference between Pantoprazole and the average \( \tilde{y} \) of Omeprazole, Lansoprazole and Rabeprazole. As Omeprazole is by far the most important chemical in the market and its trend is negative, \( \alpha_3 \) is positive only with respect to this negative trend related to the control group.

In order to overcome this ”reference point” issue and to get a broader

### Table 2: IIA test

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<th>Rabeprazole</th>
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<td>.003 (.0008)**</td>
<td>.001 (.0008)</td>
<td>.001 (.0008)*</td>
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<tr>
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<td>-.021 (.008)**</td>
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<td>-.003 (.006)</td>
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<td>I</td>
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<td>.338 (.075)**</td>
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</tr>
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<td>.0002 (.0003)**</td>
<td>.0002 (.0003)**</td>
<td>.0003 (.0003)**</td>
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the overall NHS regional expenditure by year.
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<td>(.014)**</td>
<td>(.017)**</td>
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<td>.005</td>
<td>.105</td>
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<td>.115</td>
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<td>.0002</td>
<td>.0002</td>
</tr>
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</table>
picture of the substitution patterns, we run the following model:

\[
\tilde{y}_{jlt} = \mu_{jlt} + \sum_{j \neq L}^{4} \alpha_{1j} I_{j} + \alpha_{2} DU_{t} + \sum_{j \neq L}^{4} \alpha_{3j} I_{j} DU_{t} + \beta t + \gamma NHS_{lt} + \epsilon_{jlt} \tag{15}
\]

In this specification the situation is reversed with respect to equation (14): here the products belonging to chemical \(L\) are part of the control group, while all the chemicals \(l \neq L\) belong to the treatment group. Changing the chemical used as a control group, we obtain the results in Table 3, where the name of the column indicates compound \(L\). The value of \(\alpha_{3}\) for Omeprazole is basically identical to the one found in Table 2. On the other hand, Pantoprazole, Lansoprazole and Rabeprazole did not depart significantly from IIA, although, of course, they increase their presence in the market if Omeprazole is taken as a reference.

These findings\(^{15}\) are, we believe, perfectly consistent with what we could expect by looking at Figure 3. They imply that the four existing PPIs were not considered as perfect substitutes of Esomeprazole. More precisely, doctors substituted away mainly from Omeprazole, basically considering this chemical as the more direct substitute of the new entrant.

7 Entry and product replacement

7.1 Losses following entry

The magnitude of the loss of revenues following the entry of Esomeprazole can be analyzed using a Before and After (BA) approach. Note that this is basically the approach used in most of the economic literature. Davis (2006), for example, measures the impact on monthly revenues in any pre-defined market by regressing the total revenues on a set of dummies indicating the entry of new theaters. This reduces to a BA because the variation in revenues due to the new entry is measured as the change in the average revenues between the period preceding and the one following the change.

In Table 4 some simple BA test on the average revenues is performed. The means refer to the average revenues per firm per month in the specified Chemical sub-market. Period 0 is the period before entry, while period 1 is

\(^{15}\)Running the same models on regional aggregated chemical values gives exactly the same results: \(\tilde{y}_{t}\) for Omeprazole reduces by 10% after the introduction of Esomeprazole.
the period after. The test is a simple t-statistic. Results strongly confirm
the conclusions from the previous graphical inspection.

Table 4: t-tests on mean revenues

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<tr>
<th></th>
<th>$Y_0$</th>
<th>$Y_1$</th>
<th>$\sigma_{\pi_0 - \pi_1}$</th>
<th>$t$</th>
<th>$\mu_0 - \mu_1$</th>
<th>$N$</th>
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<td>5.50</td>
<td>&lt; 0***</td>
<td>84</td>
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<tr>
<td>Pantoprazole</td>
<td>52624</td>
<td>73799</td>
<td>30043.6</td>
<td>-7.91</td>
<td>&gt; 0***</td>
<td>126</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>129634</td>
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<td>34999.1</td>
<td>-5.89</td>
<td>&gt; 0***</td>
<td>63</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>224905</td>
<td>294206</td>
<td>54999.3</td>
<td>-5.77</td>
<td>&gt; 0***</td>
<td>21</td>
</tr>
</tbody>
</table>

***: significant at 1%,

$\bar{Y}$ revenues per firm per month before and after entry

The t-test indicates that the average revenues per firm have changed after Esomeprazole entered. However, we must take into consideration two aspects. First of all, there are 21 Regions in Italy and some are more important than others in terms of market size. Second, the overall market is subject to an upward trend that must be taken into account.

Using firm-level data, we refer to the same notation as in section 6. In order to take into account the time trend we run two models that differ in the ways the impact of entry is considered. All these models are run separately for each chemical, thus we do not include the subscript $l$. In this section $y$ refers to either quantities or revenues. The first model is:

$$
y_{jht} = \mu_{jh} + \beta t + \alpha_1 DU_t + \alpha_2 DT_t + \gamma X_{jht} + \epsilon_{jht}
$$

(16)

Here, $DT_t = (t \cdot 1[t > T_E])$ and it should capture the change in the trend of $y$ following entry. $X_{jht}$ is a vector of two control variables: $NHS_{ht}$ and $lead_j$, a dummy introduced to control for the likely different average revenues and quantities associated to being the patent holder. Our interest is in the $\alpha_2$ parameter, which should tell us if and how much the trend in the average firm-region revenues has changed after entry.

For the second model we use a version of model 3 of Perron (1997):

$$
y_{jht} = \mu_{jh} + \beta t + \alpha_1 DTP_t + \gamma X_{jht} + \epsilon_{jht}
$$

(17)

where $DTP_t = ((t - T_E) \cdot 1[t > T_E])$. Basically, $DTP_t$ tries to capture the difference between the coefficients of the linear trend before and the after entry. In this case, however, the after-entry trend line meets (and start from) the before-entry one exactly in $t=16$. 23
In all the specifications, we add a dummy named *break* for observations where $t > 13$ and the chemical is the Pantoprazole- This should take into account the launch of Peptazol in January 2002. Results of the first two models are reported in Tables 5.5 and 5.6.

For Omeprazole, the average loss in both revenues and quantities is confirmed by a significantly lower trend in both variables. With respect to the pre-entry positive trend, Omeprazole lost around 4,800 DDDs per unit of observation, which translates into a loss of around 16,000 euros per firm per region. Pantoprazole and Lansoprazole show a slight increase in DDDs, but the revenues tend not to grow as much. This is probably the effect of the intervention of regulators on prices. Depending on the pack and dosage sold, these cuts might affect more some markets than others.
<table>
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<td>DDDs</td>
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<td>(26)</td>
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7.2 Cannibalization

It is clear that Omeprazole is the chemical that mostly contributed to the increase in Esomeprazole’s revenues. Evidence comes from an analysis of both the substitution patterns and the revenues and quantities time trends. These results, however, do not yet give a precise answer to our original question: how much of the market for the new product comes from the cannibalization of the old one?

In order to understand the impact of entry, we need to define what we think would have happened without the entry of Esomeprazole. We believe that at this point the best solution is to provide two reasonable scenarios according to different hypothesis. In a sense, these scenario could just be seen as giving lower and upper bounds to the estimation of the real parameter of interest.

In all the scenarios we have to consider one main conclusion from the previous sections: Esomeprazole did not have an impact on the trend of the market for PPIs. Therefore, in the following we will always assume that the market is growing with a stable trend. What distinguishes one scenario from the other is the assumptions made on how incumbents’ market shares would have evolved without entry.

Scenario 1: Without Esomeprazole’s entry, the market for PPI would have been shared among incumbents according to their pre-entry market shares.

Results: This scenario implies that the constant growth in PPIs would have been shared between Lansoprazole, Omeprazole, Pantoprazole and Rabeprazole according the market shares in March 2002 (Omeprazole’s market share should thus be 65%). To this measure, however, we must add the fact that after Esomeprazole entered Omeprazole showed a negative trend. That is, it lost market share with respect to its pre-entry average. This loss can be calculated using Table 6. Setting the pre-entry average to the revenues in $t=15$, the loss due to the reduced trend are given by $rn \sum_{1}^{20} 8,000t = 141,100,000$, where $n$ is the number of firms, stable to 4, and $r$ is the constant number of regions, equals to 21. The value of 8,000 is absolute value of the difference between the pre-entry and the post-entry trend. This sum accounts for approximately half of the total revenues of Esomeprazole in the same period. Cannibalization is then the sum of this quantity and Omeprazole’s share in the growing trend of PPIs. Altogether, this accounts for 82.5% of Esomeprazole’s total market.
This scenario represents a lower bound. In our data, Omeprazole was growing faster than the other three chemicals. It makes sense, then, to take this trend into account.

**Scenario 2**: Without Esomeprazole’s entry, pre-entry trends in market shares would have continued.

**Results**: Remember that Omeprazole has shown the steepest trend in terms of market shares and revenues. This scenario implies a monthly growing trend of around 7,000 euros per firm per region for Omeprazole. Looking at Table 6, after April 2002 this trend was reduced by almost 15,000 euros, implying a new slope of around -8,000 per firm per region. The product replacement in the period April 2002-December 2003 can thus be calculated as: $15,000nr(\sum_{t=1}^{20} t) = 264,600,000$ euros. The sum of the revenues for Esomeprazole in the same period is around 286,000,000 euros. In this scenario, cannibalization accounts for 93% of the market of the new product.

This last result is mainly a consequence of the assumption of constant trend. As all the other PPIs in Model 2 (and in Figure 2) exhibit a flat trend, the *sic rebus stantibus* assumption implies that all the increase in the trend of PPIs should be captured by the only growing chemical, Omeprazole. As Esomeprazole did not significantly enlarge the market, the losses with respect to the expected trend from Omeprazole must approximate the total revenues of Esomeprazole.

Other scenarios would imply different rules for sharing the growing market for PPIs. However, we believe that, according to our analysis, placing the level of cannibalization somewhere between 82% and 93% of the market for Esomeprazole is a reasonable conclusion.

**8 Discussion**

Our empirical analysis points to three main findings. First, Esomeprazole did not expand the market for PPIs. We showed that despite the growing size of the market, the new entrant did not alter the pre-entry trends. PPIs are thus continuing to benefit from the reducing demand for H2 in the same way as they were doing before Esomeprazole was launched. Our second finding shows that the substitution patterns do not follow pre-entry market share. The IIA assumption does not hold in the PPI class because Omeprazole consistently lost revenues in relation to other PPIs. Thus, Omeprazole, more
than any other chemical, is actually "feeding" Esomeprazole. In the last part of the analysis we attempted to quantify the effects of the launch on the incumbent chemicals. The results here are consistent with the previous two sections. In particular, Omeprazole is the only product that shows a negative change in revenues’ trends. Comparing the loss from Omeprazole with the revenues of Esomeprazole, we were able to estimate two realistic levels of "cannibalization", which we have found to be particularly high but consistent with the whole situation.

One may wonder what is the relevance of these findings. The first encouraging result is that it was rather straightforward to extend the legal debate to the empirical analysis of market data. Of course, the context here is specific to a relatively small country and has no real connection with the real Antitrust case described in the Introduction. However, searching for consistency data checks through rigorous empirical analysis proved a fruitful approach in this case.

Concerns are however related with the policy consequences of our findings, in particular to the issue of the incentives to innovation. It is widely recognized that patents are required in order to boost innovation in an industry where massive R&D investments are generally followed by very low costs of production. Also, in the literature there is a strong feeling that on average patent-induced innovation is welfare improving. It is far from the objectives of this paper to enter the discussion about the role of intellectual property rights in the development of innovative drugs. However, the case of Esomeprazole might well represent what some critics have identified as one of the main costs related to the actual system. Our results showed a case in which a firm, being able to strategically influence the market, could keep its market shares by patenting and launching a new product similar to the existing ones. In the terminology of Boldrin and Levine (2004), this example can be described as a "rent seeking" behavior, where "abundant skills and resources are invested in keeping the competitive advantage by [...] making very hard for competitors to imitate and reproduce the good”. In this case, the competitors to be kept away are the generics.

Besides the patent related policy, these considerations should also have an impact on the way innovation is measured in most of the economic literature, i.e. by the number of the new products launched (e.g. Di Masi et al (2003), Giacotto et al (2005)). As the medical literature has pointed out in many circumstances, among the group of new drugs, there are probably
few particularly innovative products and many that make little or no thera-
peutic difference (e.g. Joppi et al (2005)). Any analysis that treats the new
chemicals as homogeneous fails to distinguish between these two sub-groups
and ultimately tends to overestimate the benefits from innovation.

Strategic patenting can also impose unwanted costs on the third payer (i.e.
private or public insurance). In this study, we have shown that one product
was able to bias the prescription patterns in its favor. From a welfare point
of view, there is nothing to be concerned about since this represents a clear
Pareto improvement over the previous situation. However, in systems where
regulators do not intervene on prices, the economic impact of a new drug
will depend on the behavior of the market forces. If price differentials do
not reflect relative health improvements, strategic launching can be more
problematic to deal with and cases like the one described in this paper can
impose an unnecessary burden on private/public insurance.

Finally, the results describe doctors’ behaviors in the Italian market.
Since all the PPIs in the period of observation were still under patent protec-
tion, our data represent doctors’ prescriptions more than consumers’ choices.
Certainly, patients’ preference have a role. However, it is sensible to assume
that what we are observing is mainly an aggregate of doctors’ decisions. If
this is the case, what do our results tell us about doctors’ preferences?

The clear finding is that doctors have served as demand shifters, prescrib-
ing away from the old to the new product of the same firm. Differently from
what the scientific evidence suggests, doctors have seen Omeprazole as the
principal substitute for Esomeprazole. From a theoretical point of view, this
represents another evidence that doctors’ choices are not independent from
market considerations. Of course, because there is no best drug, the failure
is not in the sense of the wrong prescription, but in the fact that doctors
somehow seemed to be heavily influenced by firms. What is surprising in our
results is the near 1 to 1 substitution between Omeprazole and Esomepra-
zole. This suggests that doctors that were prescribing Omeprazole before
started prescribing Esomeprazole after April 2002, while doctors that were
not prescribing Omeprazole, did not change their previous choices. Prob-
ably, doctors tend to keep some reference firm or seller, trusting them more
than others. Or maybe companies coordinate their advertising efforts and
one doctor listen mainly to one company. Or, again, the Company invested
more than any other competitor. In any case, it seems that doctors have
been somehow faithful to the firm.

The good news in our findings is the lack of evidence of market enlarge-
ment. From a public health point of view a market expansion, lacking any scientific evidence of the new product fulfilling needs not addressed by the existing chemicals, would have signaled a different type of moral hazard, with doctors overprescribing as a response to aggressive advertising campaigns. Overall, we can conclude that Italian doctors showed only a low degree of agency imperfection.

9 Conclusion

In this paper we have analyzed an important case of new entry in the pharmaceutical market.

Our analysis both in the assumptions and in the interpretation of the results relied on the existing scientific evidence in terms of the quality of the chemicals under consideration. Referring mainly to medical guidelines and previous literature, we showed that there is a consensus in treating all the existing PPIs as equally effective and in viewing Esomeprazole as a slightly more effective, but substantially similar to the other PPIs. Based on the idea that indications from the scientific literature should determine doctors’ prescription patterns and that the entry of a new drug can represent a good shock to the market, we performed mainly three types of analyses.

First, we checked whether Esomeprazole enlarged the market for PPI. We found that after the entry the revenues did not change much, while the quantities increased significantly. However, if we take the trend into account, there is no evidence of a break in the series of DDDs sold in the whole PPI class, neither at nor around the month of the launch of Esomeprazole. We interpreted this finding as Esomeprazole not affecting the size of the market for PPI.

Next, we analyzed the substitution patterns among the four incumbents chemicals. We expected to find a form of IIA, where the demand for the new product could be interpreted as coming from the existing ones proportionally to their market shares. We found that this is true only for the products not belonging to the same companies launching the new chemical.

Finally, we quantified the revenues and demand losses due to the entry of Esomeprazole. According to the previous findings, we expected more losses in the market for Omeprazole, and this is exactly what we found. Controlling for the trend and in a before and after analysis, we show, under reasonable scenarios, that between 82\% and 93\% of the demand for Esomeprazole came
from the substitution for Omeprazole.

Clearly, the incumbent is feeding its new product with the old one. In the discussion, we show how these findings are consistent with a story of strategic patenting in order to avoid future competition from generics. We also provide some brief insights about the consequences of our results on a broader set of topics.

References


10 Appendix

Here we show that if IIA holds, then the dependent variable used in section 4 ($\tilde{y}$) should not change after the entry of Esomeprazole. We show this for $n$ identical firms. Results can be extended to asymmetrical firms just using different weights.

Lemma 1 Consider a region (h) with $N$ chemical-level markets (l), each producing $y_{iht}$ in revenues, and each with $n_{lh}$ identical firms with firm-level revenues $y_{jlht} = \frac{y_{iht}}{n_{lh}}$. Indicating with $l=1$ the "reference" chemical and considering there are two periods, before ($t=0$) and after ($t=1$) entry, then IIA implies that:

$$\tilde{y}_{jht} = \frac{ak_{lh}}{k_{lh} + b} - 1$$

where $k_{lh} = \frac{y_{iht}}{y_{1ht}}$ and $a$ and $b$ are functions of $n_{lh}$ and $k_{i\neq lh}$.

Proof. Define $\tilde{n}_{lh} = \frac{n_{lh}}{n_{1h}}$. Then:

$$\bar{y}_{ht} = \frac{\sum_{l=2}^{N} \tilde{n}_{lh} y_{jht} + y_{j1ht}}{\sum_{l=2}^{N} \tilde{n}_{lh} + 1}$$

and

$$\tilde{y}_{jht} = \frac{y_{jht} - \frac{\sum_{l=2}^{N} \tilde{n}_{lh} y_{jht} + y_{j1ht}}{\sum_{l=2}^{N} \tilde{n}_{lh} + 1}}{\frac{\sum_{l=2}^{N} \tilde{n}_{lh} y_{jht} + y_{j1ht}}{\sum_{l=2}^{N} \tilde{n}_{lh} + 1}}$$

(18)

Now consider $k_{lh} = \frac{y_{iht}}{y_{1ht}} = \frac{n_{lh} y_{jht}}{n_{1h} y_{j1ht}} = \tilde{n}_{lh} \frac{y_{jht}}{y_{j1ht}}$. Under condition (13) (IIA), $k_{lh0} = k_{lh1} = k_{lh}$. Thus $y_{jht} = \frac{k_{lh} y_{j1ht}}{\tilde{n}_{lh}}$. Plugging this into (18) and
The Lemma states that under IIA the variable $\tilde{y}$ does not depend on any time related variable (i.e. neither $y_t$ nor $\overline{y}_t$). Consequently, a change in time must not imply a change in the relative size among the markets. The lemma applies easily to aggregated data. It is enough to impose $n=1$ for each market.