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# Innovation, loyalty and generic competition in pharmaceutical markets 

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#### Abstract

We analyze how a manufacturer with a brand-name drug close to patent expiration decides to launch a product-line extension (an upgrade through innovation) before it faces generic competition. There are two types of physicians: loyal physicians always prescribe first the product-line extension and then either the off-patent drug or a generic drug while the non-loyal ones prescribe taking into account the prices of the drugs. We consider a two-stage game. In the first stage, the incumbent firm decides the level of innovation. In the second-stage, all firms decide sequentially their prices, with the incumbent firm acting as a Stackelberg leader. We find two equilibria in the pricing-decision game. For relatively large levels of innovation, the incumbent firm competes for the price-sensitive physicians. However, for low levels of innovation, the incumbent firm prefers to exploit the loyal physicians and to charge the monopoly price. The equilibrium level of innovation exhibits an inverted U-shaped behaviour with respect to the degree of loyalty.


Keywords Brand-name drug • Line extension • Generic competition • Pharmaceutical markets . Innovation

## JEL Classification I10 • L13

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[^1]
## 1 Introduction

When brand-name drugs go off patent, they face generic competition. Historically, pharmaceutical firms have been able to maintain high prices after patent-expiration due to the existence of barriers to entry. During the eighties, new legislation to overcome entry barriers in pharmaceutical markets was enacted in the European Union and the US. In particular, the 1984 Drug Price Competition and Patent Term Restoration Act eased market entry for generic drugs as they only needed to prove bioequivalence to the brand-name drugs. Since then, the number of generic drugs entering the market has been continuously growing.

The economic literature has mainly focused on analyzing the effect of generic entry in the prices of brand-name drugs. However, less attention (specially from a theoretical perspective) has been paid to other strategies that pharmaceutical firms can use to cope with generic competition and protect their market shares and revenues. In particular, brand-name drug firms can limit generic entry by launching the so called 'pseudogenerics' (Kong 2009) or even by taking over generic firms (European Commision 2009). Alternatively, pharmaceutical firms can launch product-line extensions (Hong et al. 2005). A line extension is a variation of an existing product or a modification of an existing molecular entity. This strategy allows brand-name drug firms extend the original drug with a new modification, and shifts demand from the original brand to the new extension. These line extensions of off-patent drugs allow the firm to introduce a differentiated product to compete with the generic drugs, and they often substitute for the original drug. ${ }^{1}$

Product line extensions require, compared to blockbuster drugs, lower R\&D expenditures. ${ }^{2}$ According to global figures, most of the new drugs are not based on really new chemical ingredients. Grabowski and Wang (2006) reported that worldwide and for the period 1982-2003, 919 new chemical ingredients were introduced, being only 115 of them first in class, i.e. strictly new. ${ }^{3}$ Hong et al. (2005) report that only $15 \%$ of the 1,035 new drugs approved by the US Food and Drug Administration from 1989 through 2000 were innovative drugs. In Spain, according to the Ministry of Health and Consumption (2005), 782 new specialities were registered in 2004, from which 747 were based in already known chemical ingredients (about 300 were generic drugs) and 35 in new ones. These figures indicate that new drugs (new registered products with their corresponding patents) come basically from developments of known chemical

[^2]ingredients and only a low proportion (less than 5\% in Spain) are derived from really new ones.

The pharmaceutical industry seems to have opted for the strategy of introducing new drugs based on minor innovations (upgrades and product-line extensions). The new drug is usually protected by additional periods of patent exclusivity. ${ }^{4}$ The original drug, the new product (line-extension) and the generics may coexist in the market.

In this paper, we consider a manufacturer of a brand-name drug close to patent expiration that must decide whether to introduce a product-line extension (upgrade) of the existing brand-name drug to cope with generic competition. Specifically, we focus on the situation of a leading firm that produces a successful drug (a star product) with high loyalty from prescribers and close to patent expiration. The firm can, of course, try to get another first-in-class drug after a long and expensive R\&D process. However, the firm can also take advantage of brand-loyalty and, with low R\&D expenses, obtain a new differentiated product (through a minor innovation, upgrading or just designing a line extension) before generic drugs similar to the off-patent drug enter the market and price competition takes place. This situation is frequently observed when the off-patent drug has been very successful in the market. ${ }^{5}$

To simplify the analysis, we assume that the outcome of $R \& D$ expenditures is deterministic, and that there is free pricing for new drugs. ${ }^{6}$ We consider a standard model of vertical product differentiation where the incumbent firm faces the competition of $n$ generic drug firms. The demand for drugs is determined by physicians. We consider that there are two types of doctors. On the one hand, a proportion of physicians prefers the innovative drug and prescribes it first as long as the patient's net utility is non-negative. In case the line extension prescription causes negative net utility to a patient, these doctors may prescribe her either the off-patent drug or any of the available generic drugs. Throughout the paper, we call these doctors "loyal" physicians. These physicians prefers the new drug produced by the incumbent firm to any other drug available. Here, loyalty means that these physicians always prescribe the line extension regardless of the prices as long as the patient's net utility is non-negative. They remain loyal to the firm that initially developed the off-patent drug, and now, they prefer first to prescribe the upgraded drug (the line extension) produced by the same firm. On the other hand, the remaining physicians base their prescribing decisions on efficiency considerations and take into account both the effectiveness and the prices of the drugs.

[^3]We model the interaction between firms as a two-stage game. In the first stage, the producer of the brand-name drug decides the degree of product differentiation through innovation. In the second stage, firms sequentially set their prices. We assume that the producer of the brand-name drug acts as a Stackelberg leader in the pricing game. Brand-name drug firms often introduce the line extension previously to the generic entry to shift demand through brand-loyalty. So, the choice of Stackelberg leadership seems to be a good approximation to real world.

Our goal is to characterize the equilibrium prices and the equilibrium level of innovation. We also analyze how both the equilibrium level of innovation and the sales of generic drugs behave when the proportion of loyal physicians changes. We find that, for a sufficiently high proportion of loyal physicians, the equilibrium price of the line extension is such that the line extension is only prescribed by the loyal physicians. When the proportion of loyal physicians is low, however, both type of physicians prescribe in equilibrium the line extension. We also find that the higher the proportion of price-sensitive physicians, the larger the sales of generic drugs are. Regarding the level of innovation, we find that the equilibrium level of innovation exhibits an inverted U-shaped behavior with respect to the proportion of loyal physicians: it increases when this proportion is low and decreases when it is high. From a social welfare perspective, the level of innovation chosen by the firm is too low. When the proportion of loyal physicians is relatively high, it seems to be desirable to reduce it. The level of innovation would be higher as well as the social welfare. Health authorities could act on detailing as, after all, pharmaceutical firms rely on this marketing activity to generate loyalty to their products.

Our paper contributes to the theoretical literature of pharmaceutical markets and generic competition. Theoretical analysis of competition in pharmaceutical markets began with the seminal paper by Frank and Salkever (1992). They focused on analyzing the effect of generic competition on the prices of off-patent drugs to explain the puzzling increase in the prices of brand-name drugs after generic entry ('Generic Competition Paradox'). They concluded that one possible explanation was that generic entry could make the demand of brand-name drugs steeper. (See also Lexchin 2004; Regan 2008; Mestre 1999; Kong 2009; Ferrara and Kong 2008 for alternative explanations of the 'Generic Competition Paradox'.) Innovation in pharmaceutical markets has been recently analyzed by Bardey et al. (2010). They focus on how reference pricing affects the type of innovations brought to the market, but they do not analyze the relationship between innovation and generic entry. Another strand of research has focused on advertising as the mechanism by which pharmaceutical firms try to influence the prescribing behavior of physicians. (See Königbauer 2006, 2007) These papers endogenize the proportion of price-sensitive physicians by determining the optimal level of advertising expenditures, leaving as exogenous the level of product differentiation (the quality of the brand-name and the generic drug). On the contrary, our paper takes as exogenous the proportion of price-sensitive physicians and endogenizes the degree of product differentiation through innovation. Finally, other papers (Brekke et al. 2007; Cabrales 2003; Kyle 2007; Ekelund and Peersson 2003; Dalen et al. 2006; Danzon and Chao 2000) have analyzed the effects of market regulation in drug prices. To the best of our knowledge, our paper is the first attempt to analyze, from
a theoretical perspective, the role that product-line extensions play in pharmaceutical markets following generic entry.

The paper is structured as follows. Section 2 describes the model, and in Sect. 3, the equilibrium prices are determined. Section 4 characterizes the equilibrium level of innovation, and analyses its behavior with the proportion of brand-loyal physicians, variable through which public policy can influence prescription in our model. In Sect. 5, welfare analysis is carried out and public policy considerations are described. Finally, conclusions are presented in Sect. 6.

## 2 The model

We consider a standard model of vertical product differentiation applied to pharmaceuticals markets. ${ }^{7}$ There are $n+1$ firms where firm 1 is the incumbent firm producing a brand-name drug and a line extension while the remaining $n$ firms produce generic drugs. Firm 1 faces patent expiration for its brand-name prescription drug and must decide the degree of product differentiation through innovation for its new drug (a line extension) before $n$ firms enter the market with generic drugs.

There is a continuum of consumers (patients) with the same illness that can be treated with either of the three drugs. ${ }^{8}$ Consumers are indexed by $\theta$, which is uniformly distributed in the interval $[0,1]$ with density one. The parameter $\theta$ measures the severity of the illness. Each consumer is assumed to buy (to be prescribed) at most, one unit of the product (drug). In the case of drugs, patients do not choose directly the drug but this is, instead, prescribed by physicians. So, the demand for drugs is determined by physicians. We assume that there is a population of physicians of size one. Physicians, when they treat a patient, observe the parameter $\theta$ and decide which drug to prescribe. Let $s_{i}$ be the quality of the good (drug) from firm $i$ perceived by all physicians, $i \in\{1,2, \ldots, n+1\}$. Perceived quality is a combination of baseline and innovative attributes, such that we can write $s_{i}=f_{i}+k_{i}$, where $f_{i}$ and $k_{i}$ denote respectively the baseline and innovative attributes of the drug produced by firm $i$. From the physicians perspective, patients' utility depends on the severity of their illness and on the prescribed drug so that we can write $\theta s_{i}$ as the gross utility that a patient with a severity of illness $\theta$ obtains when she is prescribed the good (drug) from firm $i .{ }^{9}$

All drugs have the same baseline attribute, $f_{i}=f \forall i$, but only firm 1 produces a drug (the line extension) with the innovative attribute: $k_{1}=k$ and $k_{i}=0$ for $i \neq 1$ For the sake of simplicity and without loss of generality, we will assume that $f=1$. Firm 1 can produce the innovative attribute $k \geq 0$ at a $\operatorname{cost} C(k)$, with $C(0)=0$, $C^{\prime}(k)>0, C^{\prime \prime}(k)>0$ and $C^{\prime}(0)=0$. To simplify the analysis, we assume that marginal production costs for all firms and drugs are zero. The line extension is assumed to be protected by the patent system.

[^4]Among the population of physicians, a proportion $\alpha \in(0,1)$ consists of physicians who take only into account the innovative attribute, and therefore, they prescribe first the drug with the highest perceived innovative quality (the line extension) regardless of its price as long as the patients' net utility is non-negative. ${ }^{10}$ Type $\alpha$ physicians also consider that the off-patent drug is therapeutically equivalent to the generic drugs. For patients whose net utility was negative if they were prescribed the line extension, these physicians may prescribe either the off-patent or a generic drug. The off-patent drug and the generic drugs have the same chemical entity. In some countries, doctors prescribe taking into account the chemical entity, and for them, both types of drugs are therapeutically equivalent. Alternatively, we could think that drugs are dispensed by pharmacists that take into account the chemical entity of the drugs. Both situations fit well within the framework of the model. Type $\alpha$ physicians are loyal to the innovation, although they may also prescribe the off-patent drug or a generic drug. The remaining doctors take into account both the total perceived quality and the prices, and prescribe the drug for which patients' net utility is higher. We assume that they prescribe generic drugs instead of the off-patent drug for equal prices. They prescribe the line-extension if it provides a higher net utility. Net utility when the line extension is prescribed is given by $\theta s_{1}-p_{1}=\theta(1+k)-p_{1}$, where $p_{1}$ is the price of the line extension. For generic drugs, the net utility is $\theta s_{i}-p_{g i}=\theta-p_{g i}$, where $p_{g i}$ is the price for the generic drug of firm $i$. When the off-patent drug is prescribed, the net utility is $\theta-p_{b}$, where $p_{b}$ is the price of the off-patent drug. All physicians prescribe as long as the net utility is non-negative. ${ }^{11}$

We consider a two-stage game. In the first stage, firm 1 decides the level of innovation $k$. In the second stage, firms set their prices. We assume that firm 1 acts as a Stackelberg leader and chooses its prices ( $p_{1}, p_{b}$ ) first. ${ }^{12}$ The remaining firms, taking as given the level of innovation $k$ and firm 1's prices decide simultaneously their prices $p_{g i}$. We solve the game by backward induction, and find the subgame perfect equilibrium.

Our goal is to characterize the equilibrium prices and the equilibrium level of innovation. Note that, in equilibrium, the price of the line extension $p_{1}$ must be higher than both the price of the off-patent drug and the price of the generic drugs. If $p_{1} \leq p_{g i}$ for any $i$, firm $i$ has incentives to lower its price as otherwise, it would end up with zero demand. If $p_{1} \leq p_{b}$, firm 1 can increase its profit by increasing $p_{1}$.

[^5]
## 3 The determination of the equilibrium prices

### 3.1 The second stage subgame

Given $k$ and ( $p_{1}, p_{b}$ ), the firms producing generic drugs simultaneously decide their prices. As all the generics drugs are equivalent, price competition drives their prices to zero, the marginal cost, for all $k$ and $\left(p_{1}, p_{b}\right)$. Firm 1, taking the level of innovation as given, set its prices $\left(p_{1}, p_{b}\right)$ to maximize its profits taking into account that the price of the generic drugs is equal to zero. Firm 1 will set $p_{b}$ equal to zero. ${ }^{13}$ As the off-patent drug is considered to be equal to the generic drug by both types of physicians, firm 1's profits from the sales of the off-patent drug are equal for any $p_{b}$. If $p_{b}>0$, the off-patent drug is not sold, and the profits are zero. Likewise, if $p_{b}=0$, the off-patent drug is sold but the profits are zero. So, the relevant problem for firm 1 is to determine the price of the line extension $p_{1}$ that maximizes its profits.

Let us first derive the firm 1's demand function for the line extension. As the price of the generic drugs is zero, the consumer indifferent between the line extension and the generic drug has a severity of illness $\hat{\theta}$ that satisfies:

$$
\hat{\theta}(1+k)-p_{1}=\hat{\theta}
$$

Therefore, $\hat{\theta}=\frac{p_{1}}{k}$. If the consumer with a severity of illness $\hat{\theta}$ obtains a non negative net utility $\left(\hat{\theta}(1+k)-p_{1} \geq 0\right)$, he buys (is prescribed) the line extension, and so do all consumers with a higher severity of illness. All physicians prescribe the line extension to these patients. Let $\tilde{\theta}=\frac{p_{1}}{1+k}$ be the severity of illness of the consumer indifferent between the line extension and not buying. Note that $\hat{\theta}>\tilde{\theta}$.

When $p_{1}<k$, it follows that $\hat{\theta}$ is lower than 1 and firm 1 , on the one hand, sells to all consumers whose severity of illness is greater or equal to $\hat{\theta}$. Thus, its demand is $1-\hat{\theta}$, as both types of physicians prescribe the line extension. These consumers obtain a strictly positive net utility. On the other hand, there are consumers (those with severity of illness between $\tilde{\theta}$ and $\hat{\theta}$ ) that would obtain a higher net utility consuming the generic drug, although their net utility is also positive if they are prescribed the line extension. Therefore, a proportion $\alpha$ of physicians (physicians that do not compare prices) prescribe the line extension to these consumers, and firm 1's demand is $\alpha(\hat{\theta}-\tilde{\theta})$. Then, firm 1's total demand is $1-\hat{\theta}+\alpha(\hat{\theta}-\tilde{\theta})$. When $p_{1} \geq k$, it follows that $\hat{\theta} \geq 1$. In this case, firm 1's total demand is given by $\alpha(1-\tilde{\theta})$ : the line extension is only prescribed by the loyal physicians as long as patients' net utility is non-negative. The demand for the line-extension is depicted in Fig. 1. The demands for the off-patent drug and the generics are respectively $\alpha \tilde{\theta}$ and $(1-\alpha) \tilde{\theta}$.

[^6]

Fig. 1 The demand for the line extension

Thus, firm 1's demand for the line extension is given by:

$$
D_{1}\left(p_{1}, \alpha, k\right)= \begin{cases}\alpha(1-\tilde{\theta}) & \text { if } p_{1} \geq k \\ 1-\hat{\theta}+\alpha(\hat{\theta}-\tilde{\theta}) & \text { if } p_{1}<k\end{cases}
$$

Firm 1 can follow any of two available strategies. On the one hand, it may choose a high price such that the line extension is prescribed only by the loyal physicians. Alternatively, it may choose a lower price such that both types of physicians prescribe the line extension.

If the line extension is prescribed only by the loyal physicians, the price that maximizes firm 1's profits is the solution to:

$$
\begin{aligned}
& \max \alpha p_{1}(1-\tilde{\theta})=\alpha p_{1}\left[1-\frac{p_{1}}{1+k}\right] \\
& \text { s.t. } \quad p_{1} \in[k, 1+k]
\end{aligned}
$$

It is easy to see that the solution to this problem is $p_{1}=\frac{1+k}{2}$ if $1>k$. Otherwise, the solution is $p_{1}=k$. Let $\Pi_{1}^{l}(\alpha, k)$ denote firm 1 's profits when the line extension is prescribed only by the loyal physicians. By taking into account the solution to the above problem, we have:

$$
\Pi_{1}^{l}(\alpha, k)= \begin{cases}\frac{\alpha(1+k)}{4^{4}} & \text { if } 1>k  \tag{1}\\ \frac{\alpha k^{2}}{1+k} & \text { if } 1 \leq k\end{cases}
$$

Alternatively, firm 1 can maximize its profits by choosing a price such that $\hat{\theta}<1$. In this case, it solves the problem:

$$
\begin{array}{ll}
\max & p_{1}[1-\hat{\theta}+\alpha(\hat{\theta}-\tilde{\theta})]=p_{1}\left[1-\frac{p_{1}}{k}+\alpha\left(\frac{p_{1}}{k}-\frac{p_{1}}{1+k}\right)\right] \\
\text { s.t. } & p_{1}<k
\end{array}
$$

The solution to this problem is $p_{1}=\frac{k(1+k)}{2(1+k-\alpha)}$ if $2 \alpha<1+k$. Firm 1's profits in this interior solution are:

$$
\begin{equation*}
\Pi_{1}(\alpha, k)=\frac{k(1+k)}{4(1+k-\alpha)} \tag{2}
\end{equation*}
$$

Which is the best strategy for firm 1 ? When $2 \alpha \geq 1+k$, the best strategy is to set a price such that only the loyal physicians prescribe the line extension. When $2 \alpha<1+k$, firm 1 chooses the strategy for which profits are higher. Both strategies are feasible for parameter values within this range and the firm compares its profits under both strategies. If $1>k$, we have from (1) and (2):

$$
\frac{\alpha(1+k)}{4} \gtreqless \frac{k(1+k)}{4(1+k-\alpha)} \quad \text { if and only if } \alpha \gtreqless k
$$

When $k \geq 1$, we have from (1) and (2):

$$
\begin{aligned}
\Pi_{1}(\alpha, k)-\Pi_{1}^{l}(\alpha, k) & =\frac{k(1+k)}{4(1+k-\alpha)}-\frac{\alpha k}{1+k} \\
& =\frac{k\left[(1+k)^{2}-4 \alpha(1+k-\alpha)\right]}{4(1+k)(1+k-\alpha)}>0
\end{aligned}
$$

The next Proposition summarizes the equilibrium prices for the line extension based on the above analysis.

Proposition 1 For a given ( $k, \alpha$ ), firm 1 chooses a price such that only the loyal physicians prescribe the line extension if $\alpha>k$. If $\alpha \leq k$, the price for the line extension is such that both types of physicians prescribe it. The equilibrium prices are
$p_{1}^{*}(\alpha, k)=\frac{k(1+k)}{2(1+k-\alpha)}$ if $\alpha \leq k$ and $p_{1}^{*}(\alpha, k)=0.5(1+k)$ if $\alpha>k$.
For a given $k$, if the proportion of loyal physicians is relatively low (below the level of innovation), firm 1 will prefer to compete for the price-sensitive physicians and it chooses a price such that they prescribe the line extension to some patients. The larger $k$, the higher $\alpha$ must be to find profitable to sell only to the loyal physicians. Alternatively, for a given $\alpha$, the level of innovation must be sufficiently high to have both types of doctors prescribing the line extension. As $\alpha$ grows, the minimum level of innovation that firm 1 needs to find it profitable to compete for these physicians is higher. For lower levels of innovation, product differentiation is not large enough and firm 1 then prefers to exploit the loyal physicians.

### 3.1.1 Case $\alpha \leq k$

The equilibrium price increases with the level of innovation $k$ and with $\alpha$. Plugging the equilibrium prices into the definitions of $\hat{\theta}$ and $\tilde{\theta}$ yields:

$$
\begin{aligned}
& \hat{\theta}^{*}(\alpha, k)=\frac{1+k}{2(1+k-\alpha)} \\
& \tilde{\theta}^{*}(\alpha, k)=\frac{k}{2(1+k-\alpha)}
\end{aligned}
$$

Note that $\hat{\theta}^{*}(\alpha, k) \in(0,1)$ and $\hat{\theta}^{*}(\alpha, k)>\tilde{\theta}^{*}(\alpha, k)$. Firm 1 's customers are mostly consumers with a high severity of illness. Although the line extension is more expensive than the generic drugs, even the price-sensitive physicians prefer to prescribe the line extension as the increase in utility derived from the innovative attribute outweighs paying a higher price. It can be easily shown that $\tilde{\theta}^{*}(\alpha, k)$ grows with $k$ :

$$
\frac{d \tilde{\theta}^{*}(\alpha, k)}{d k}=\frac{(1-\alpha)}{2(1+k-\alpha)^{2}}>0
$$

When the level of innovation grows, the valuation of the line extension increases ( $1+k$ is larger) and firm 1 chooses a higher price. The consumer indifferent to being treated with the line extension or not is now a consumer with a higher degree of illness. On the contrary, $\hat{\theta}^{*}(\alpha, k)$ lowers with $k$ :

$$
\frac{d \hat{\theta}^{*}(\alpha, k)}{d k}=\frac{-\alpha}{2(1+k-\alpha)^{2}}<0
$$

The higher the level of innovation, the higher the difference between drug prices. Nevertheless, the severity of illness of the consumer indifferent between the line extension and the generic drugs is now lower. It can be easily checked that, for a given $k, \hat{\theta}^{*}(\alpha, k)$ and $\tilde{\theta}^{*}(\alpha, k)$ grow with $\alpha$.

We analyze now the effect of $k$ in the sales of the generic drugs. The total sales of generic drugs $G$ (assuming that loyal physicians prescribe the off-patent drug instead of a generic drug for equal prices) are given by:

$$
G^{*}(\alpha, k)=(1-\alpha) \hat{\theta}^{*}(\alpha, k)=\frac{(1-\alpha)(1+k)}{2(1+k-\alpha)}
$$

For a given $\alpha$, the larger the level of innovation, the lower the sales of generic drugs are. For a given $k$, the sales of generic drugs grow as $\alpha$ gets lower:

$$
\begin{aligned}
\frac{d G^{*}(\alpha, k)}{d k} & =-\frac{\alpha(1-\alpha)}{2(1+k-\alpha)^{2}}<0 \\
\frac{d G^{*}(\alpha, k)}{d \alpha} & =-\frac{k(1+k)}{2(1+k-\alpha)^{2}}<0
\end{aligned}
$$

The sales of the line extension are:

$$
D_{1}^{*}(\alpha, k)=1-\hat{\theta}^{*}(\alpha, k)+\alpha\left(\hat{\theta}^{*}(\alpha, k)-\tilde{\theta}^{*}(\alpha, k)\right)=0.5
$$

The sales of firm 1 do not change with $k$ and $\alpha$. When the level of innovation increases, $\hat{\theta}^{*}(\alpha, k)$ decreases, being now larger the number patients for which both types of physicians strictly prefer to prescribe the line extension. However, $\hat{\theta}^{*}(\alpha, k)-$ $\tilde{\theta}^{*}(\alpha, k)$ decreases, being lower now the number of patients for which the loyal physicians prescribe the line extension. Both effects cancel each other out leaving the sales of firm 1 unaltered. When $\alpha$ grows, firm 1 , on the one hand, loses some line extension sales as $1-\hat{\theta}^{*}(\alpha, k)$ decreases but, on the other hand, gains sales as $\alpha$ and $\hat{\theta}^{*}(\alpha, k)-\tilde{\theta}^{*}(\alpha, k)$ increases. On aggregate, sales of the line extension do not change. Note that, for a given $k$, the sales of firm 1 are equal to those it made before generic competition. Generic competition initially reduces firm 1's market share. However, innovation increases the valuation of the line extension, compensating for the competition effect.

### 3.1.2 Case $\alpha>k$

The price of the line extension increases with $k$. Plugging the equilibrium prices into the definitions of $\hat{\theta}$ and $\tilde{\theta}$ yields:

$$
\begin{aligned}
& \hat{\theta}^{*}(\alpha, k)=\frac{1+k}{2 k}>1 \\
& \tilde{\theta}^{*}(\alpha, k)=0.5
\end{aligned}
$$

Total sales of generics are $1-\alpha$ : all price-sensitive physicians prescribe generic drugs to all patients. It follows that the generic sales decrease with $\alpha$. The sales of the line extension do not depend on the level of innovation, but they increase with $\alpha$ :

$$
D_{1}^{*}(\alpha, k)=\alpha\left(1-\tilde{\theta}^{*}(\alpha, k)\right)=0.5 \alpha
$$

## 4 The determination of the level of innovation

In the first stage of the game, firm 1, taking into account the second stage equilibrium prices, chooses the level of innovation $k \geq 0$ to maximize its profits, where profits equal revenues minus innovation costs:

$$
\Pi_{1}(k, \alpha)=p_{1}^{*}(\alpha, k) D_{1}^{*}(\alpha, k)-C(k)= \begin{cases}\frac{k(1+k)}{4(1+k-\alpha)}-C(k) & \text { if } k \geq \alpha \\ \frac{\alpha(1+k)}{4}-C(k) & \text { if } k<\alpha\end{cases}
$$

It is difficult to analyze the determination of the equilibrium level of innovation with a general cost function. From now on, we will assume that the innovation costs are
given by $C(k)=\frac{c k^{2}}{2}$ with $c \in(0,0.25] \cdot{ }^{14}$ The equilibrium level of innovation will depend on the parameter $c$ and on the proportion $\alpha$ of loyal physicians.

First, note that the equilibrium level of innovation cannot be below $\alpha$ as the profit function is continuous for all $k$ and increasing for $k<\alpha$ :

$$
\left.\frac{d \Pi_{1}}{d k}\right|_{k<\alpha}=\frac{\alpha}{4}-c k>\frac{\alpha}{4}-0.25 \alpha=0
$$

Therefore, the equilibrium level of innovation $k^{*}(\alpha)$ solves the following problem:

$$
\begin{align*}
& \max \Pi_{1}(k, \alpha)=\frac{k(1+k)}{4(1+k-\alpha)}-\frac{c k^{2}}{2} \\
& \text { s.t. } \quad k \geq \alpha \tag{P1}
\end{align*}
$$

As the objective function is strictly concave (see Appendix), the solution to this problem is determined by the first order conditions.

Proposition 2 The equilibrium level of innovation $k^{*}(\alpha, c)>\alpha \forall \alpha \leq 1$ and $c<0.25$.

Proof (See Appendix.)
Corollary 1 For $c=0.25$, the equilibrium level of innovation $k^{*}(\alpha)$ is 1 if $\alpha=1$ and $k^{*}(\alpha)>\alpha$ if $\alpha<1$.

It is interesting to analyze how the equilibrium level of innovation in the interior solution behaves when the proportion $\alpha$ of loyal physicians changes. We have the following result:

Proposition 3 Let $c \leq 0.25$. Then, $\exists \alpha^{*}(c) \in(0,1)$ such that the equilibrium level of innovation $k^{*}(\alpha, c)$ grows with $\alpha$ for $\alpha<\alpha^{*}(c)$ and decreases with $\alpha$ for $\alpha>\alpha^{*}(c)$. Furthermore, $\alpha^{*}(c)$ grows with $c$.

## Proof (See Appendix.)

Figure 2 depicts the equilibrium level of innovation. ${ }^{15}$ As it can be seen, the equilibrium level of innovation $k^{*}(\alpha)$ exhibits an inverted U-shaped behavior with respect to $\alpha$. There is a trade-off between the equilibrium level of innovation and the proportion of loyal physicians.

The equilibrium level of innovation can be larger if the proportion $\alpha$ of loyal physicians decreases. For this to happen, the requirement is a sufficiently large $\alpha$ (above

[^7]Fig. 2 The equilibrium level of innovation

$\left.\alpha^{*}(c)\right)$. Intuitively, when $\alpha$ decreases within that range, firm 1 increases the level of innovation and the price. Note that its sales do not change. Firm 1 increases the degree of product differentiation to reduce competition. When all physicians are loyal ( $\alpha=1$ ), firm 1 does not need a high level of innovation as it would be the case if some physicians were price-sensitive. Product differentiation is less important and firm 1 chooses a relatively low level of innovation as innovation is costly. As $\alpha$ decreases, firm 1 increases the level of innovation. Now, there are some price-sensitive physicians, and product differentiation becomes important. Firm 1 invests in innovation to soften competition, increases the price of the line extension and some patients are prescribed the line extension by the price-sensitive physicians. This pattern of behaviour holds as long as the proportion of loyal physicians remains above $\alpha^{*}(c)$.

However, for low values of $\alpha$ (below $\alpha^{*}(c)$ ), as $\alpha$ decreases, the equilibrium level of innovation is lower. In this case, the captive market is not large enough to make higher levels of product differentiation profitable. Intuitively, when all physicians are price-sensitive $(\alpha=0)$, firm 1 launches the line-extension with a positive level of innovation to differentiate the product. Otherwise, its profits would be zero. As all physicians prescribe (at least, to some patients) the line extension and innovation is costly, the equilibrium level of innovation is relatively low. As $\alpha$ grows, firm 1 increases the level of innovation and the price of the line extension to compensate for the fewer price-sensitive physicians and to exploit the loyal ones. Although loyal physicians are captive and would prescribe the line extension at a higher price even for the same level of innovation, they also prescribe it if both the price and the innovation
are larger. Let us suppose that there were some physicians loyal to the innovation ( $\alpha$ strictly positive) and that the firm kept the same level of innovation as before. Now, the price of the line extension would be higher as $\alpha$ is larger. Although sales from price-sensitive physicians would be lower, aggregate revenues would be higher and, consequently, profits would be larger as innovation costs remain constant. However, this is not a profit-maximizing strategy as it does not take into account the effect on profits due to a change in the level of innovation. Profits will be larger if the level of innovation is modified accordingly. When $\alpha$ is relatively low, both the price and the level of innovation increase, although the demand for the line-extension from the price-sensitive physicians does not change too much. Proportionally, the increase in price is larger than the increase in $k$. As most of the physicians are price-sensitive, the firm cannot afford to lose a large amount of sales, and the patient indifferent between the line-extension and the generic drugs has now a severity of the disease slightly larger than before. On the one hand, revenues from the prescriptions by the loyal physicians increase while revenues from the prescriptions from the price-sensitive physicians decrease. On aggregate, total revenues are higher. On the other hand, innovation costs are larger. Overall, increasing the level of innovation is optimal from a profitmaximization perspective. The firm needs to balance $k$ and the price of the line extension to modify the demands from both type of physicians in such a way that profits are maximized. This pattern of behavior holds as long the proportion of loyal physicians remains below $\alpha^{*}(c)$.

## 5 Welfare analysis and public policy

In this section, we characterize the level of innovation that maximizes social welfare and discuss the welfare effects of public policies that reduce the proportion of loyal physicians. Social welfare is defined as the sum of consumers' surplus and firms' profits minus the cost of the innovation. In the model, pharmaceutical expenses are equal to firms' profits and, from a social perspective, they cancel each other out. Thus, social welfare $W(k, \alpha)$ takes into account the surplus enjoyed by the treated patients (notice that all the patients are treated) and the costs of the innovation:

$$
W(k, \alpha)=\left\{\begin{array}{l}
\int_{0}^{\hat{\theta}^{*}} \theta d \theta-\alpha \int_{\tilde{\theta}^{*}}^{\hat{\theta}^{*}} \theta d \theta+(1+k)\left[\int_{\hat{\theta}^{*}}^{1} \theta d \theta+\alpha \int_{\tilde{\theta}^{*}}^{\hat{\theta}^{*}} \theta d \theta\right]-C(k) \text { if } k \geq \alpha \\
(1-\alpha) \int_{0}^{1} \theta d \theta+\alpha \int_{0}^{0.5} \theta d \theta+\alpha(1+k) \int_{0.5}^{1} \theta d \theta-C(k) \quad \text { if } k<\alpha
\end{array}\right.
$$

where $\hat{\theta}^{*}$ and $\tilde{\theta}^{*}$ have been defined in Sects. 3.1.1 and 3.1.2 for $k \geq \alpha$ and $k<\alpha$ respectively. In the appendix (see Lemma 1) we show that the level of innovation that maximizes social welfare is above $\alpha$. Recall that the equilibrium level of innovation chosen by firm 1 is also above $\alpha$. A question remains as to whether the level of innovation that maximizes social welfare is above the level chosen by the firm. In the context
of our model, as it happens in real world, innovation increases product differentiation, reduces competition and increases revenues for firm 1 . So, firm 1 has incentives to choose a relatively high level of innovation. From a social perspective, a high level of innovation makes competition be less intense. As a result, the price of the line extension is higher but the size of the covered market remains unchanged. However, some of the treated patients benefit from the innovation and enjoy higher levels of utility. In aggregate, consumers' surplus increases. From a social perspective, as well as in the case of the firm, there are incentives to choose a high level of innovation. However, innovation is costly. Thus, there are two forces pulling in different directions. The relationship between both levels of innovation will depend on how both firm 1's revenues and consumers' surplus change with innovation.

Proposition 4 The level of innovation that maximizes social welfare $k^{s}(\alpha, c)$ is higher than the level of innovation $k^{*}(\alpha, c)$ chosen by firm $1 \forall(\alpha, c)$.

Proof (See Appendix.)
From a social perspective, the firm invests in innovation less than the level that it would be desirable. From this result, some policy implications arise. Health authorities can act on $\alpha$ given the relationship between $k^{*}$ and $\alpha$ found in the previous section.

Health authorities have traditionally tried to promote generic prescription, not only to reduce the pharmaceutical expenses, but also because it is perceived that new brandname drugs incorporate minor innovations that do not bring about health outcomes substantially better than those from generic drugs, and brand-name drugs are much more expensive. Within the framework of our model, the promotion of generic prescription is formally equivalent to a reduction in $\alpha$, and, a priori, it is not clear if this policy is socially desirable.
Proposition 5 For $\alpha \in\left[\alpha^{*}(c), 1\right]$, social welfare decreases with $\alpha$ if $1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right) \geq 0$. For $\alpha \in\left[0, \alpha^{*}(c)\right]$, social welfare increases with $\alpha$ if $1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right) \leq 0$.

## Proof (See Appendix.)

When the level of loyal physicians is sufficiently high, policies that reduce loyalty are desirable as they increase social welfare. However, these policies can also be counterproductive when the proportion of loyal physicians is relatively low. In this case, they induce less innovation and may lower welfare. While $\frac{\partial W}{\partial \alpha}<0, \frac{\partial W}{\partial k} \frac{d k^{*}(\alpha)}{d \alpha}$ is positive and the sign of $\frac{d W}{d \alpha}$ is ambiguous. If the direct effect of $\alpha$ dominates the indirect effect in welfare through $k^{*}$, then reductions in $\alpha$ would lead to higher levels of welfare. Otherwise, welfare would be smaller, and the correct policy would be to encourage loyalty.

## 6 Conclusions

In this paper, we have considered a model of product differentiation applied to a pharmaceutical market with $n+1$ firms. In particular, we have analyzed how a
manufacturer of a brand-name drug whose patent is close to expiration decides the degree of product differentiation of a line extension through innovation before it faces generic competition. Decisions on innovation and prices are taken within an environment characterized by loyalty to innovative drugs, where some physicians prescribe first the line extension while others base their prescribing decisions on efficiency considerations. We have considered a game with two stages. In the first stage, the brand-name drug manufacturer decides the level of innovation. In the second stage, all firms play a sequential pricing game, where the brand-name drug firm acts as a Stackelberg leader. Depending on the level of innovation and the degree of loyalty, we have found two equilibria in the pricing game. For high enough levels of innovation, it is optimal for the incumbent firm to compete for the price-sensitive physicians. However, for levels of innovation lower than the degree of loyalty, such firm prefers to exploit the loyal physicians and charges the higher monopoly price.

Regarding the level of innovation, we have characterized the equilibrium level of innovation and analyzed how it changes with the proportion of loyal physicians. We find that the equilibrium level of innovation exhibits an inverted $U$-shaped behavior with respect to the proportion of loyal physicians. For high levels of loyalty, the equilibrium level of innovation grows when loyalty is reduced. Alternatively, for low levels of loyalty, the equilibrium level of innovation decreases when loyalty is reduced.

From a social perspective, the firm chooses a level of innovation that is too low. When the proportion of brand-loyal physicians is sufficiently high, we find that public policies that reduce loyalty are socially desirable. However, these policies can have a negative effect on social welfare if the proportion of loyal physicians is relatively low. In this case, the right policy would be to promote loyalty.

The basic model can be used to analyze several extensions. We have implicitly assumed that the patients pay the full price of drugs. An extension of the model would be to introduce a co-payment system and analyze its relationship with the level of innovation. Co-payment would affect the patient's net utility, but qualitatively, the analysis would not be very different. We have also considered that pricing decisions are taken sequentially. Another possible extension could consist of carrying out the analysis when pricing decisions are taken simultaneously. We have also assumed a deterministic innovation process to simplify the analysis. In reality, the outcome of the innovation effort is random. While considering stochastic innovation outcomes adds realism to the model, it also complicates its analytical tractability. The model can be used to analyze also the marketing decisions that endogenize the proportion of loyal physicians as pharmaceutical firms devote an important proportion of their sales revenues to marketing activities to generate loyalty to their products.

We have carried out our analysis within a framework of free pricing. In many European countries, pharmaceutical markets are highly regulated and a reference pricing system operates. The introduction of such a system in our model would not bring about qualitatively different results. If the reference pricing system is based on bioequivalence principles (as in Spain), the off-patent drug and the generics would be subject to such a system, but the line extension would remain out of it. Price competition would drive the prices of the off-patent drug and the generics to zero and the line extension would be priced freely, as in our model. If the reference pricing system is based on therapeutical equivalence principles (as in Germany), besides the off-patent
drug and the generics, line extensions that incorporate low levels of innovation would likely be also subject to such a system, and the results of our model could change. We hope to explore these issues in further research.

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## Appendix

Concavity of the profit function of firm 1
The profit function of firm 1 is strictly concave for $k \geq \alpha$.

$$
\begin{aligned}
\left.\frac{d \Pi_{1}}{d k}\right|_{k \geq \alpha} & =\frac{(1+k)^{2}-\alpha(1+2 k)}{4(1+k-\alpha)^{2}}-c k \\
\left.\frac{d^{2} \Pi_{1}}{d k^{2}}\right|_{k \geq \alpha} & =-\frac{\alpha(1-\alpha)}{2(1+k-\alpha)^{3}}-c<0
\end{aligned}
$$

Proof of Proposition 2 The Lagrangian function for problem $P 1$ is:

$$
\mathcal{L}=\frac{k(1+k)}{4(1+k-\alpha)}-\frac{c k^{2}}{2}+\lambda_{1}(k-\alpha)
$$

where $\lambda_{1}$ is the Lagrange multiplier. The first order conditions are:

$$
\begin{equation*}
\frac{d \mathcal{L}}{d k}=\frac{(1+k)^{2}-\alpha(1+2 k)}{4(1+k-\alpha)^{2}}-c k+\lambda_{1}=0 \tag{A.1}
\end{equation*}
$$

plus the restrictions and the complementary slackness conditions. In the solution, the restriction $k \geq \alpha$ cannot be binding. If it were binding, $\lambda_{1} \geq 0$, and from (A1), it should be that $\left.\frac{d \Pi_{1}}{d k}\right|_{k=\alpha} \leq 0$. However:

$$
\left.\frac{d \Pi_{1}}{d k}\right|_{k=\alpha}=\frac{1+\alpha(1-\alpha)-4 c \alpha}{4}>0 \quad \forall \alpha \in[0,1] \quad \text { if } c<0.25
$$

Therefore, $\forall \alpha \in[0,1]$ and $c<0.25$, the solution to the optimization problem is interior: $k^{*}(\alpha, c)>\alpha$

Proof of Proposition 3 As $k^{*}(\alpha, c)$ is interior, it satisfies $\left.\frac{d \Pi_{1}}{d k}\right|_{k \geq \alpha}=0$ :

$$
\begin{equation*}
\left[1+k^{*}(\alpha, c)\right]^{2}-\alpha\left(1+2 k^{*}(\alpha, c)\right)=4 c k^{*}(\alpha, c)\left[1+k^{*}(\alpha, c)-\alpha\right]^{2} \tag{A.2}
\end{equation*}
$$

Differentiating this expression with respect to $\alpha$ yields:

$$
\begin{equation*}
\frac{d k^{*}(\alpha, c)}{d \alpha}=\frac{1+2 k^{*}(\alpha, c)-8 c k^{*}(\alpha, c)\left[1+k^{*}(\alpha, c)-\alpha\right]}{2\left[1+k^{*}(\alpha, c)-\alpha\right]\left[1-2 c\left(1+k^{*}(\alpha, c)-\alpha\right)-4 c k^{*}(\alpha, c)\right]} \tag{A.3}
\end{equation*}
$$

From (A.3):

$$
\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=1}=\frac{1+2 k^{*}(1, c)-8 c k^{*}(1, c)^{2}}{2 k^{*}(1, c)\left[1-6 c k^{*}(1, c)\right]}
$$

where $k^{*}(1, c)$ is the equilibrium level of innovation for $\alpha=1$. From (A.2), it follows that $k^{*}(1, c)=\frac{1}{4 c}$. Therefore:

$$
\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=1}=-4 c<0
$$

It remains to shows that $\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=0}>0$. From (A.3), it follows:

$$
\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=0}=\frac{1+2 k^{*}(0, c)-8 c k^{*}(0, c)\left[1+k^{*}(0, c)\right]}{2\left[1+k^{*}(0, c)\right]\left[1-2 c\left(1+k^{*}(0, c)\right)-4 c k^{*}(0, c)\right]}
$$

where $k^{*}(0, c)$ is the equilibrium level of innovation for $\alpha=0$. From (A.2), it follows that $k^{*}(0, c)=\frac{1}{4 c}$. Therefore:

$$
\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=0}=\frac{4 c}{(1+4 c)^{2}}>0
$$

Thus, $\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=0}>0$ and $\left.\frac{d k^{*}(\alpha, c)}{d \alpha}\right|_{\alpha=1}<0$. Therefore, there exists a value $\alpha^{*}(c) \in(0,1)$ such that $\frac{d k^{*}(\alpha, c)}{d \alpha}=0$. From (A.3), it follows:

$$
1+2 k^{*}\left(\alpha^{*}(c), c\right)-8 c k^{*}\left(\alpha^{*}(c), c\right)\left[1+k^{*}\left(\alpha^{*}(c), c\right)-\alpha^{*}(c)\right]=0
$$

Differentiating with respect to $c$ yields:

$$
\frac{d \alpha^{*}(c)}{d c}=\frac{1+k^{*}\left(\alpha^{*}(c), c\right)-\alpha^{*}(c)}{c}>0
$$

Lemma 1 From a social perspective, the equilibrium level of innovation must be above $\alpha$.

Proof It suffices to show that the social welfare function is strictly increasing for $k<\alpha$ and that $\left.\frac{\partial W}{\partial k}\right|_{k=\alpha}>0$. When $k<\alpha$, social welfare can be written as:

$$
\left.W(k, \alpha)\right|_{k<\alpha}=\frac{3 \alpha k}{8}+\alpha-\frac{1}{2}-\frac{c k^{2}}{2}
$$

and its derivative is:

$$
\frac{\left.\partial W(k, \alpha)\right|_{k<\alpha}}{\partial k}=\frac{3 \alpha}{8}-c k
$$

This expression is strictly positive for all $k<\alpha$ and $c \leq 0.25$. When $k \geq 0.5 \alpha$, social welfare is:

$$
\begin{align*}
\left.W(k, \alpha)\right|_{k \geq \alpha}= & 0.5(1-\alpha)\left(\hat{\theta}^{*^{2}}-\tilde{\theta}^{*^{2}}\right)+0.5 \tilde{\theta}^{*^{2}} \\
& +0.5(1+k)\left(1-\hat{\theta}^{*^{2}}+\alpha \hat{\theta}^{*^{2}}-\alpha \tilde{\theta}^{*^{2}}\right)-0.5 c k^{2} \\
= & 0.5\left(1+\frac{3 k}{4}-\frac{k \alpha(1-\alpha)}{4(1+k-\alpha)^{2}}-c k^{2}\right) \tag{A.4}
\end{align*}
$$

and its derivative is:

$$
\begin{align*}
\frac{\left.\partial W(k, \alpha)\right|_{k \geq \alpha}}{\partial k} & =\frac{3}{8}-c k-\frac{\alpha(1-\alpha)}{8(1+k-\alpha)^{4}}\left[(1+k-\alpha)^{2}-2 k(1+k-\alpha)\right] \\
& =\frac{3}{8}-c k-\frac{\alpha(1-\alpha)(1-2 k)}{8(1+k-\alpha)^{3}} \tag{A.5}
\end{align*}
$$

It follows that:

$$
\left.\frac{\left.\partial W(k, \alpha)\right|_{k \geq \alpha}}{\partial k}\right|_{k=\alpha}=\frac{3}{8}-c \alpha-\frac{\alpha(1-\alpha)(1-2 \alpha)}{8}=\frac{3-8 c \alpha-\alpha(1-\alpha)(1-2 \alpha)}{8}
$$

This expression evaluated at $c=0.25$ is strictly positive:

$$
\left.\frac{\left.\partial W(k, \alpha)\right|_{k \geq \alpha}}{\partial k}\right|_{k=\alpha, c=0.25}=\frac{3-\alpha[2+(1-\alpha)(1-2 \alpha)]}{8}>0
$$

Proof of Proposition 4 Recall that both $k^{s}(\alpha, c)$ and $k^{*}(\alpha, c)$ are above $\alpha$. In particular, $k^{*}(\alpha, c)$ satisfies:

$$
\begin{equation*}
\frac{\partial \Pi_{1}}{\partial k}=0 \Leftrightarrow \frac{\left(1+k^{*}(\alpha, c)\right)^{2}-\alpha\left(1+2 k^{*}(\alpha, c)\right)}{4\left(1+k^{*}(\alpha, c)-\alpha\right)^{2}}=c k^{*}(\alpha, c) \tag{A.6}
\end{equation*}
$$

and $k^{s}(\alpha, c)$ satisfies:

$$
\begin{equation*}
\frac{\partial W}{\partial k}=0 \Leftrightarrow \frac{3}{8}-\frac{\alpha(1-\alpha)\left(1-2 k^{s}(\alpha, c)\right)}{8\left(1+k^{s}(\alpha, c)-\alpha\right)^{3}}=c k^{s}(\alpha, c) \tag{A.7}
\end{equation*}
$$

It suffices to show that $\left.\frac{\partial W}{\partial k}\right|_{k=k^{*}(\alpha, c)}>0$. From (A.5) and (A.6), the derivative of the social welfare function evaluated at $k=k^{*}(\alpha, c)$ is:

$$
\begin{aligned}
& \left.\frac{\left.\partial W(k, \alpha)\right|_{k \geq \alpha}}{\partial k}\right|_{k=k^{*}(\alpha, c)} \\
& \quad=\frac{3}{8}-\frac{\left(1+k^{*}(\alpha, c)\right)^{2}-\alpha\left(1+2 k^{*}(\alpha, c)\right)}{4\left(1+k^{*}(\alpha, c)-\alpha\right)^{2}}-\frac{\alpha(1-\alpha)\left(1-2 k^{*}(\alpha, c)\right)}{8\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}} \\
& \quad=\frac{3}{8}-\frac{1}{4}-\frac{\alpha(1-\alpha)}{4\left(1+k^{*}(\alpha, c)-\alpha\right)^{2}}-\frac{\alpha(1-\alpha)\left(1-2 k^{*}(\alpha, c)\right)}{8\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}} \\
& \quad=\frac{1}{8}-\frac{\alpha(1-\alpha)(3-2 \alpha)}{8\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}}
\end{aligned}
$$

As $1+k^{*}(\alpha, c)-\alpha>1$, it follows that $\frac{\alpha(1-\alpha)(3-2 \alpha)}{\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}}<1$ and therefore $\left.\frac{\partial W}{\partial k}\right|_{k=k^{*}(\alpha, c)}>0$.

Proof of Proposition 5 The effect of $\alpha$ in social welfare is given by:

$$
\begin{equation*}
\frac{d W}{d \alpha}=\frac{\partial W}{\partial k} \frac{d k^{*}(\alpha, c)}{d \alpha}+\frac{\partial W}{\partial \alpha} \tag{A.8}
\end{equation*}
$$

From Proposition 4, as $k^{*}(\alpha, c)<k^{s}(\alpha, c)$, it follows that $\frac{\partial W}{\partial k}$ is positive. Let $\alpha \in\left[\alpha^{*}(c), 1\right]$. From Proposition $3, \frac{d k^{*}(\alpha)}{d \alpha}<0$ and social welfare will decrease with $\alpha\left(\frac{d W}{d \alpha}<0\right)$ if $\frac{\partial W}{\partial \alpha}<0$. From (A.4), the effect of $\alpha$ in social welfare, keeping the level of innovation constant, is given by:

$$
\begin{align*}
\frac{\partial W}{\partial \alpha} & =-\frac{k^{*}(\alpha, c)}{8\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}}\left[\left(1+k^{*}(\alpha, c)-\alpha\right)(1-2 \alpha)+2 \alpha(1-\alpha)\right] \\
& =-\frac{k^{*}(\alpha, c)}{8\left(1+k^{*}(\alpha, c)-\alpha\right)^{3}}\left[1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right)\right] \tag{A.9}
\end{align*}
$$

When $1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right) \geq 0$, it follows from (A.8) that $\frac{d W}{d \alpha}<0$. If $1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right)<0$, the effect of $\alpha$ in social welfare is ambiguous. Let $\alpha \in\left[0, \alpha^{*}(c)\right]$. From Proposition $3, \frac{d k^{*}(\alpha)}{d \alpha}>0$ and social welfare will increase with $\alpha\left(\frac{d W}{d \alpha}>0\right)$ if $\frac{\partial W}{\partial \alpha}>0$. From (A.9), it is required that $1+k^{*}(\alpha, c)-\alpha(1+$ $\left.2 k^{*}(\alpha, c)\right) \leq 0$. If $1+k^{*}(\alpha, c)-\alpha\left(1+2 k^{*}(\alpha, c)\right)>0$, the effect of $\alpha$ in social welfare is ambiguous.

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[^2]:    ${ }^{1}$ According to a recent classification for drug innovations suggested by Caprino and Russo (2006), productline extensions could be considered as type D (new chemical ingredients structurally related to a chemical class already described for a similar therapeutic indication); type E (known pharmaceutical products generated through biotechnology or other very innovative techniques); type F (known pharmaceutical products with either new characteristics or more relevance due to its pharmaceutical form or administration path) and type G (known pharmaceutical products that have new characteristics or that have less relevance due to its pharmaceutical form, administration path, safety or handling improvements).
    ${ }^{2}$ DiMasi et al. (2003) found a cost of over 800 million US dollars to produce a new pharmaceutical product, including the whole $\mathrm{R} \& \mathrm{D}$ process to discover the new chemical ingredient.
    ${ }^{3}$ Among the 804 minor innovations, there are also follow-on drugs produced by competing firms and prod-uct-line extensions (upgrades) produced by leading firms. New registered drugs based on minor innovations overwhelmingly exceed new first-in-class drugs.

[^3]:    ${ }^{4}$ When the line-extension is based on a new chemical entity, it is always granted patent protection. However, it may be the case that slight modifications of existing drugs are not protected by a patent or are protected by weak patents. Manufacturers of line-extensions seek the highest protection for their new product through a patent to replace sales lost when the original drug goes off patent.
    ${ }^{5}$ For instance, the firm Lundbeck that produced "citalopram", a band-name drug for moderate-severe depression with patent protection, developed, before patent expiration, a minor innovation "escitalopram" to reduce the immediate generic competition.
    ${ }^{6}$ In European countries, pharmaceutical markets are highly regulated, and reference pricing systems are used. Our model considers free pricing, and therefore it is better applied to a situation like the US market. See the conclusion section for some comments on how our results might change if a reference pricing system is in place.

[^4]:    ${ }^{7}$ See Gabszewicz and Thisse (1979), Mussa and Rosen (1978) and Shaked and Sutton (1982) for standard product differentiation models.
    8 Throughout the paper, we use the terms consumers and patients interchangeably.
    9 The parameter $\theta$ can be also interpreted as the patients' marginal valuation for quality.

[^5]:    10 These physicians have been prescribing the off-patent drug during patent protection, and inertia makes them keep on prescribing the same drug improved with the innovation (the line-extension). See Coscelli (2000).

    11 Based on the 1989 National Ambulatory Medical Care Survey for the US, Hellerstein (1998) points out that almost all physicians prescribe both brand-name drugs and generic drugs, although some physicians tend to prescribe more often brand-name drugs while others prescribe generic drugs instead.
    12 From a theoretical point of view, the decision on prices could have been modelled as a simultaneous move game. However, in real world, pharmaceutical firms often introduce the line extension previously to the generic entry to shift demand through loyalty. So, the choice of Stackelberg leadership seems to be a good approximation to real world. Kong (2009), Ferrara and Kong (2008) and Frank and Salkever (1992) also model competition between brand-name drugs and generics as a sequential price-setting game.

[^6]:    13 Given the assumptions of the model, the price of the off-patent drug must be equal to the price of generic drugs. Although we have considered a free pricing framework, a possible justification for this price equalization can be found in the reference pricing system in place in most European countries. For example, in Spain, the reference pricing implies that off-patent drugs are priced similarly to generic drugs.

[^7]:    ${ }^{14}$ For this parameter range, firm 1 competes for the price-sensitive physicians in the second stage, and in equilibrium, these physicians prescribe the line-extension to some patients. This situation is the one empirically relevant as Hellerstein (1998) points out. For higher values of $c$, the profit function $\Pi_{1}(k, \alpha)$ has two local maxima but we have not been able to find analytically the global maximum. For low values of $c$, however, it is possible to characterize the global maximum. So, we have focused on this range of $c$ to illustrate the determination of the equilibrium level of innovation.
    ${ }^{15}$ It can be shown that $\alpha^{*}(c)>0.5$. A proof is available from the authors upon request.

