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Private versus social incentives for pharmaceutical innovation

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ABSTRACT

We provide a theoretical framework to contribute to the current debate regarding the tendency of pharmaceutical companies to direct their R&D toward marketing products that are "follow-on" drugs of already existing drugs, rather than toward the development of breakthrough drugs. We construct a model with a population of patients who can be treated with drugs that are horizontally and vertically differentiated. In addition to a pioneering drug, a new drug can be marketed as the result of an innovative process. We analyze physician prescription choices and the optimal pricing decision of an innovative firm. We also characterize the incentives of the innovative firm to conduct R&D activities, disentangling the quest for breakthrough drugs from the firm effort to develop follow-on drugs. Our results offer theoretical support for the conventional wisdom that pharmaceutical firms devote too many resources to conducting R&D activities that lead to incremental innovations.

1. Introduction

It is widely recognized that of all the industrial sectors, the pharmaceutical industry is the sector that traditionally invests most heavily in research and development (R&D). In 2012, for instance, US biopharmaceutical research companies invested an estimated $48.5 billion in R&D (PhRMA, 2013). Regarding R&D intensity, and according to a recent report by the European Commission, spending on R&D in 2012 by the pharmaceutical industry amounted to 15.3% of its GDP in the US, 16.3% in Japan, and to 14.7% in the European Union (European Commission, 2013).

However, there is a great deal of debate surrounding pharmaceutical R&D activities. Pharmaceutical companies are often accused of devoting too many resources to the marketing of apparent new products that are "follow-on" drugs of already existing drugs, rather than toward the development of breakthrough (first-in-class) drugs.[1] In fact, a successful new first-in-class drug will often face competition from a series of follow-on drugs that are therapeutically similar to the pioneering drug. The angiotensin converting enzyme (ACE) inhibitors, a class of drugs used to manage high blood pressure, is illustrative of this. The first ACE inhibitor, captopril, was introduced in the US in 1981. Since then over 10 ACE inhibitors have been launched (Hernandez and Harrington, 2008).[2] The development of follow-on drugs is cheaper and less risky than drugs with a novel mechanism of action, but they supposedly do not bring significant therapeutic progress to patients (see, for instance, the discussions by Angell, 2004; Avorn, 2004; Goozner, 2004). Defenders of incremental innovations argue, however, that medicines based on incremental improvements often represent advances in safety and efficacy, along with providing new formulations and dosing options that increase patient compliance (see diMasi and Paquette, 2004; Wertheimer and Santella, 2009; Miller, 2014).

This paper aims at contributing to this social debate. We build a theoretical model of innovation to investigate whether there exist arguments that allow us to support the conviction that pharmaceutical firms devote too many resources to marketing me-too drugs and too few to launching breakthrough drugs. Our model

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[1] Follow-on drugs are sometimes called "me-too" drugs as they are close copies of existing drugs.

[2] Another example is omeprazole, the first proton pump inhibitor launched in 1989 to reduce gastric acid production. Proton pump inhibitors have since become the mainstay of treatment for acid-related gastrointestinal disease in adults, and omeprazole was followed by other proton pump inhibitors, with the most recent launched in 2009.

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emphasizes the distinction between radical and incremental innovation processes.[3] Radical innovation processes may lead to breakthrough drugs, while incremental innovation processes pursue me-too drugs.

In our model there is a continuum of patients in need of medical treatment. Patients can be treated with drugs that are horizontally and vertically differentiated. Vertical differentiation refers to the quality of the drug and includes the health gains experienced by patients. Horizontal differentiation reflects the adequacy of the drug for patients, as different patients in the population will experience different effects of a given medication in terms of tolerability, side effects or interaction with other medicines. In the market, there is a pioneering drug. We assume that the price of this drug is fixed, for example, because the patent protection that covered it has already expired and the drug is sold at its marginal cost. Moreover, a new drug can be marketed as the result of an innovative process by a pharmaceutical firm that seeks to achieve an improvement over the existing medicine. Finally, there is a physician who makes drug prescription decisions. The physician acts as a perfect agent for the health system (which includes both patients and the health authority) and, hence, he makes prescription choices based on the price-effectiveness of the drugs.

In this simple set-up we first describe physician prescription choices, given the prices and the characteristics of the two drugs (when the innovation process is successful). Second, we characterize the optimal pricing decision of the innovative firm, which anticipates the physician prescription behavior. The optimal price for the new drug depends on the differences in cost-effectiveness and the horizontal distance between the new drug and the pioneer. When the new drug is much more cost-effective than the pioneer, the innovative firm sets a price that leads the physician to prescribe the new drug to all patients. When the improvements in the cost-effectiveness of the new drug are not substantial, or the two drugs are very horizontally differentiated, then the price set by the innovative firm leads to a drug replacement treatment only for some patients. In all other situations the new drug is not marketed.

Finally, we characterize the incentives of the innovative firm to conduct R&D activities and compare these private incentives with those that would be optimal from a social point of view. The paper distinguishes between radical innovation processes, seeking breakthrough drugs, and incremental innovation processes that aim at launching a me-too drug. In order to differentiate these two kinds of innovations, we follow the approach of measuring the degree of innovativeness of a drug as the size of the differences (either small or large) between the new drug and the pioneer. These differences can emerge either in the horizontal or the vertical characteristics of the drugs. Innovations in the vertical dimension imply a better quality of treatment (or a lower production cost) for all the patients suffering from the disease.[4] Horizontal innovations would be advances that benefit some but not all patients because drugs may have lower side effects for a certain group of patients.[5] Moreover, in order to account for the fact that the level of risk (or uncertainty of the final outcome) is typically larger in the case of radical innovations, we consider that the outcome of a radical innovation process by the innovative firm takes values on a large support and has a greater variance.

The paper provides some interesting findings. We show that for incremental innovation processes pursuing me-too drugs, the social value of the innovation coincides with the private benefits of the firm (as the innovative firm appropriates all the health system benefits derived from the launching of the me-too drug). If we consider, instead, R&D activities searching for breakthrough drugs, then private and social incentives for conducting research are not aligned. In particular, the incentives for conducting research by the firm are inferior to those socially optimal as there are patients that – despite the larger price of the new drug – benefit from it. These results allow us to show that if a pharmaceutical company can only adopt one of the two types of innovation processes due, for instance, to budget constraints, it may happen that the firm has an incentive to seek a me-too drug although R&D activities oriented to search for a radical innovation are socially superior. At the same time, it never happens that the innovative firm prefers to develop a radical innovation when devoting the resources to incremental innovations is preferable from a social point of view. Our results thus offer theoretical support for the conventional wisdom that pharmaceutical firms devote too many resources to conducting R&D activities that lead to me-too drugs.

The theoretical literature on incentives for pharmaceutical innovations is not abundant, although there is an increasing number of papers that study the interaction between the pricing policy constrained by various forms of regulation and the effort of innovation by pharmaceutical firms. Ganuza et al. (2009) find a bias in the pharmaceutical industry toward small innovations. Their result relies on the low sensitivity of a part of the demand (due to the loyalty of some physicians) to changes in prices. This lack of price-sensitivity provides an excessive reward for small innovations and consequently downwardly distorts the incentives of pharmaceutical firms. In our model, the physician acts as a perfect agent for the health system, so that the difference between the social value and the private benefits that the firm obtains from innovation arises from a different source: the ability of the pharmaceutical firm to appropriate or not the health system surplus through the price. The existence of physicians that are loyal to innovative drugs also plays an important role in Antoñanzas et al. (2011). They study the incentives of an incumbent pharmaceutical firm to launch an upgraded drug through innovation before it faces generic competition. The paper shows that the equilibrium level of innovation exhibits an inverted U shape, as innovation increases when the proportion of loyal physicians is low and decreases when it is high. Finally, Bardey et al. (2010) focus on the long-run impact of reference pricing on pharmaceutical innovation by firms. Their model shares some similarities with ours as it makes a clear distinction between incremental and radical innovations in a setting where drugs are horizontally and vertically differentiated. However, the distinction they make between the two types of innovations differs notably

[3] The labels "radical" and "incremental" belong mostly to the managerial literature and does not offer a unique description of the difference between the two concepts. In fact, the literature reveals that the definitions of radical and incremental innovations are still puzzling, both at the theoretical and at the empirical level (see García and Calantone, 2002, for a critical review of the innovativeness terminology). In particular, the degree of innovativeness of a product is measured using various dimensions including the level of risk implied in the innovation strategy, the type of knowledge to be processed or the level of investment needed to move onto a new trajectory.

[4] Examples of innovations that would be classified as vertical in our model would include the aforementioned captopril (ACE-inhibitor) and omeprazole (protone pump inhibitor), and also cimetidine (H2-receptor antagonist), propranolol (β-adrenoceptor antagonist), lovastatin (HMG-CoA-reductase inhibitor), and sumatriptane (5-HT1B/1D-receptor agonist) among others. All these are drugs that, when marketed, met a given need much more effectively than available treatments and were beneficial for all patients in the treatment of their disease. Also, innovations in antibiotics that allow administration once a day, giving patients the possibility of being treated at home, or at least the possibility to reduce hospitalization time, are vertical innovations according to our classification. Finally, second-generation antihistamines have some (vertical) improvements over first-generation antihistamines like, for instance, less frequent dosing.

[5] For example, in the market for statins, Lovastatin, pravastatin, and fluvastatin represent the class members with the lowest potency to reduce cholesterol levels but which are attractive candidates for use in treating patients who have proven intolerant of more potent statins such as atorvastatin, simvastatin or rosuvastatin (Kapur and Musunuru, 2008).

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