External Reference Pricing and Sequential Launching of Drugs

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Abstract

This paper analyzes the countries decision to adopt external reference pricing (ERP) for drugs together with the firms decision to sequentially launch drugs in various countries. We show that sequential launching of drugs is a firm’s best response to ERP only when prices can be revised periodically and countries are different enough from each other, both in terms of market size and WTP. Otherwise, the firm is always better off simultaneously launching the drug in all countries. Countries are better off announcing ERP beforehand and revising prices accordingly after potential launch delays in other countries.

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1. Introduction

The French Cour des comptes has identified the following interesting case.\(^3\) Plavix ® is an antiplatelet drug marketed in the US in 1997 and in the EU in 1998. It is the second most sold drug worldwide, and it is the first one in France. The cost of a DDD (defined daily dose) of Plavix is about 1.23 € in France. In June 2009, the European Medicines Agency (EMEA) gave authorization to six generic versions of the drug. Their cost of a DDD is about 0.65 € in France. In 2010, a new antiplatelet drug, Efient, has been marketed in France and elsewhere. According to the French Transparency Commission, Efient has no therapeutic added value compared to Plavix. Despite the advice of the Transparency Commission, the CEPS has negotiated a price of 1.43 € for a DDD of Efient on the French market. Still, the price of Efient in France is lower than in other EU countries.

This is only a piece of anecdotic evidence about a possible phenomenon that is not yet empirically proven: the influence of external reference pricing of drug prices among EU countries. External reference pricing (ERP) is a policy that has been widely used recently in EU countries with the aim of controlling pharmaceutical prices. Its principle is to refer to prices of identical drugs in foreign countries to influence the negotiated price on the domestic market. In the EU 24 out of 27 countries use ERP to regulate pricing for new pharmaceuticals coming onto the market in their country. Only Germany, Sweden and the UK have resisted using this price-control mechanism so far.

What has been reported so far is an observed convergence in EU prices resulting from ERP.\(^4\) Nothing has been empirically proven about the possible detrimental effect of ERP. The paper by Garcia-Marinoso, Jelovac and Olivella (2011) provides some theoretical arguments to stress the importance of the ERP design to avoid detrimental effects.

According to the WHO/HAI Project on Medicine Prices and Availability, the

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\(^3\) The French Cour des comptes is an independent agency that evaluates the activities of the French government and of some public agencies such as the CEPS (Comité économique des produits de santé – Economic committee for health products). CEPS is the public agency in charge of negotiating the pharmaceutical prices with the pharmaceutical companies.

\(^4\) Add references.
pharmaceutical companies might strategically respond to ERP policies. In particular, “companies may try to initially market a new product in countries where prices are not regulated or where high prices are common. Launches in lower-price countries may be delayed so as not to influence other countries. This company strategy will not work if the high-price country revises its prices downwards after launch. Companies can reduce price transparency in many different ways. They can list high prices in reference countries while granting confidential rebates or discounts to them. As a result of these strategies, the objectives of countries using ERP may be hindered and the country might end up paying higher prices than intended. Smaller, lower-income countries might end up paying higher transaction prices than the higher income countries taken as reference.”

In this paper, we argue that this effect can be true even in the absence of confidential rebates or discounts to reference countries. In particular, the firms' strategic timing of drug launches is sometimes sufficient to make the ERP policy counterproductive if it is applied blindly. We provide a formal analysis of the conditions under which this can happen. We analyze the countries decision to adopt ERP for the pricing of drugs together with the firms decision to sequentially launch drugs in various countries. We model a situation where two countries have the choice between applying either the cost-benefit criteria or the ERP to price their drugs. The pharmaceutical firm has the choice between launching its drugs in one or another country first, or in both countries simultaneously. The sequence of launches a fortiori determines the possibility of a country to apply ERP. The possibility for countries to revise their drugs price is also considered.

We show that when we force the launching of drugs to be sequential and price revisions are not allowed, the pharmaceutical firm launches the drug in the country with the highest WTP first and thereby discourages any ERP attempt by the following country, unless the other country (the one with a lower WTP) has a very large market. In the latter case, the firm launches the drug in the very large market first, even though ERP becomes advantageous for the following country. We also show that when price revisions are not possible, the firm is better off launching the drug simultaneously in both countries so that ERP is never an active policy, no matter whether it is announced beforehand or not. It is only when price revisions are possible that both ERP and
sequential launching of a drug become rational. Last, when we allow for periodical price revisions, the firm prefers to simultaneous launch the drug in both countries when the countries are similar enough in terms of market size and WTP. When one country largely outperforms the other in terms of both market size and WTP, the firm is better off foregoing selling in the less interesting market in the first period to delay the revision to a binding ERP price to a further period of time in the large market.

The paper is organized as follows. We describe the theoretical setting in Section 2. Section 3 presents the analysis excluding the possibility to periodically revise prices. Section 4 extends to the latter possibility. Section 5 concludes.

2. The Model

We consider one firm launching a patented drug in two countries, A and B. Countries differ in their maximum willingness to pay (WTP) for the drug, \( v_i, i = A, B \). Even though we do not explicitly model the determinants of the maximum WTP for a drug; we can reasonably consider that it depends positively on a country's wealth and on its willingness to offer a comprehensive range of health goods and services.

We assume that patients are completely insured against expenses associated with drug consumption. Therefore, demands in both countries are assumed constant for each period of time and denoted \( q_i, i = A, B \). This is a simplifying assumption that approximates the situation in many health care systems where patients are relatively well insured against health care expenditure and where the demand for health care consumption is relatively inelastic for most of the population.

In our model, the firm decides the country in which it starts marketing the drug. It also decides the price \( p_i \) of the drug in each country. We reasonably assume that the variable cost of production is zero while the fixed cost can be positive and sunk already. Once the drug is launched in a country, it can be consumed in any period (infinite time horizon). The above defined demand \( q_i, i = A, B \), relates to the demand in each period. We denote the temporal discount factor by \( \delta \).
We assume that both countries apply a cost-benefit analysis. This means in the present model that a country $i$ authorizes the marketing of a drug if and only if its price does not exceed the maximum WTP in country $i$: $p_i \leq v_i$. On top of that, a country can adopt an ERP policy. If it does, it authorizes the marketing of the drug only if its price does not exceed the price of the same drug abroad: $p_i \leq p_j, j \neq i$, when the drug is already marketed abroad.

The timing of the game is the following. In the first stage, countries A and B decide whether to adopt an ERP policy. In the second stage, the firm decides the sequence of launches and the prices of the drug. We start the analysis forcing the drug launches to be sequential. We then extend the game to possibly launching the drug simultaneously in both countries. Last, we allow periodic revisions of the prices in each country.

3. No revision of drug prices

We first force the launching of drugs to be sequential and do not allow for price revisions. In the long run, the firm is always better off selling a drug in a country than not because we assume that the variable costs of production are zero. Therefore, except for the one period delay in launching the drug in one of the countries, the firm always proposes a price that is acceptable in regard of the countries regulations. This is why we directly include the regulatory price caps as constraints in the firm’s profit maximization programs.

If the firm launches the drug in country A first, the prices $p_i, i = A, B$, are the solution to the following program:

$$\begin{align*}
\max_{\{p_A, p_B\}} & \quad \Pi_{AB} = \frac{1}{1-\delta} p_A q_A + \frac{\delta}{1-\delta} p_B q_B \\
\text{s.t.} & \quad p_A \leq v_A; \quad p_B \leq v_B; \quad p_B \leq p_A
\end{align*}$$
The solution prices are thus

\[ p_A = v_A; \quad p_B = \min\{v_A, v_B\}. \]

If the firm launches the drug in country A first, country B effectively applies ERP if its maximum WTP for the drug is higher than the one of country A: \( v_A \leq v_B \). The interest of ERP is therefore to take advantage of the lower WTP for the drug abroad. If country B had purely replaced its cost-effectiveness policy by an ERP policy, it would have ended up with a higher price if the WTP were higher abroad: \( v_B \leq v_A \). The firm is obviously better off when the ERP is not binding.

The firm’s solution profit when launching the drug in country A first depends on the relative WTP in both countries:

\[
\Pi_{AB} = \begin{cases} 
\frac{v_A}{1-\delta}(q_A + \delta q_B) & \text{if } v_B \geq v_A \\
\frac{v_A}{1-\delta}(q_A + \delta v_B q_B) & \text{if } v_A \geq v_B 
\end{cases}
\]

Similarly, if the firm launches the drug in country B first, the prices \( p_i, i = A, B, \) are the solution to the following program:

\[
\max_{\{p_A, \phi_A\}} \Pi_{BA} = \frac{1}{1-\delta} p_B q_B + \frac{\delta}{1-\delta} p_A q_A \\
\text{s.t.} \quad p_A \leq v_A; \quad p_B \leq v_B; \quad p_A \leq p_B
\]
The solution prices are thus

\[ p_A = \min\{v_A, v_B\}; \quad p_B = v_B. \]

As in the previous case, ERP is binding if and only if it allows the country to take advantage of a lower WTP abroad. Otherwise, it would be detrimental to the country adopting ERP. ERP is always detrimental to the firm.

Again, the firm’s solution profit when launching the drug in country B first depends on the relative WTP in both countries:

\[
\Pi_{BA} = \begin{cases} 
\frac{v_B}{1-\delta} \left( q_B + \delta q_A \right) & \text{if } v_A > v_B \\
\frac{v_B}{1-\delta} \left( q_B + \delta \frac{v_A}{v_B} q_A \right) & \text{if } v_B > v_A
\end{cases}
\]

To decide whether to launch the drug in country A or B first, the firm compares its profits under each scenario, i.e. \( \Pi_{(AB)} \) and \( \Pi_{(BA)} \). The following lemma summarizes the findings of this section and Figure 1 illustrates it graphically.
Lemma 1.

The firm launches the drug in country A first and at a price $p_A = v_A$ if and only if both the WTP in A relative to the one in B ($v_A/v_B$) and its specific demand relative to the one in B ($q_A/q_B$) are high enough:

$$\Pi_{AB} > \Pi_{BA} \iff \text{either } \frac{v_A}{v_B} > \text{Max}\left\{1, \delta + (1 - \delta) \frac{q_B}{q_A}\right\} \text{ or } 1 < \frac{v_B}{v_A} < \delta + (1 - \delta) \frac{q_A}{q_B}.$$  

Conversely, the firm launches the drug in country B first at a price $p_B = v_B$ when $v_B$ and $q_B$ are high relative to $v_A$ and $q_A$, respectively:

$$\Pi_{BA} > \Pi_{AB} \iff \text{either } \frac{v_B}{v_A} > \text{Max}\left\{1, \delta + (1 - \delta) \frac{q_A}{q_B}\right\} \text{ or } 1 < \frac{v_A}{v_B} < \delta + (1 - \delta) \frac{q_B}{q_A}.$$  

As already discussed, the country suffering from a launch delay is not necessarily better off referencing the price abroad.\(^5\) The following lemma states the conditions under which it is optimal to reference the other country’s price.

Lemma 2.

When launches are sequential and prices are never revised,

Country B references country A’s price if and only if $1 < \frac{v_B}{v_A} < \delta + (1 - \delta) \frac{q_A}{q_B}$.

Country A references country B’s price if and only if $1 < \frac{v_A}{v_B} < \delta + (1 - \delta) \frac{q_B}{q_A}$.

\(^5\) By referencing the price abroad we mean, having a binding ERP policy.
Figure 1 helps interpreting the results obtained so far.

When both the WTP ($v_A$) and the size of the market ($q_A$) are larger in country A than in country B, the pharmaceutical firm faces no trade-off. It is better off first launching the drug in country A because the latter is more interesting than country B in all respects. In the short run, i.e. during the first period, the firm foregoes the less interesting market only, the one in B. In the long run, it extracts the maximum rent from both countries since both countries pay exactly their maximum WTP. Indeed, country B is better off not binding its ERP policy because the WTP in A is higher. The opposite argument holds in the symmetric case, that is, when $v_B$ and $q_B$ are larger than $v_A$ and $q_A$, respectively.

When the WTP is lower in the largest market, the firm starts to face a trade-off between preventing ERP by first launching the drug in the high-WTP country and not foregoing an important market in the first period by first launching the drug in the large-market country. Preventing ERP in the high-WTP country is more important than not foregoing the large-size market when the difference in WTP is high relative to the difference in market sizes. Conversely, when the difference in market sizes is large relative to the difference in WTO, it is more important to launch the drug in the large market first, allowing for ERP in the small market.
To summarize, when we force the launching of drugs to be sequential, the pharmaceutical firm will first launch the drug in the country with the highest WTP and thereby discourage any binding ERP in the following country, unless the other country (the one with a lower WTP) has a very large market. In the latter case, the firm launches the drug in the very large market first, even though binding the ERP becomes advantageous for the following country.

When we allow the firm to simultaneous launch the drug in both countries, then its profits are higher than in any of the previous configurations with sequential launches:

$$\Pi_{\text{sim}} = \frac{1}{1 - \delta} \left( v_A q_A + v_B q_B \right).$$

With simultaneous launches, the firm a fortiori prevents the activation of an ERP policy and extracts the maximum WTP out of both countries. Furthermore, the firm does not forego profits in any period. Both countries apply the cost-effectiveness criterion only, just as they would do if no ERP were announced beforehand. We observe that the countries are better off in some cases announcing ERP beforehand, while the opposite never happens.

**Lemma 3.**

*When prices are never revised, the firm is better off launching its drug simultaneously in both countries rather than sequentially and no country ever apply ERP. The situation is equivalent to one without any ERP announcement. The countries are worse off with a simultaneous launch of drugs or, equivalently, with no previous announcement of a non-binding ERP policy.*
In real life, we do observe sequential launches of drugs. Price revisions may help explaining them.

4. Possible revisions of drug prices

We now allow for periodical revisions of prices as well as either simultaneous or sequential launches of drugs. Periodical revisions of prices allow for applying the ERP policy in every period and, in particular, once the drug is marketed in all countries.

We start considering that the WTP is higher in A than in B, whatever the market size. If the firm launches the drug in A first, the price in A is \( p_A = v_A \) in the first period. In the second period, the drug is marketed in country B at a price \( p_B = v_B \), while country A still has \( p_A = v_A \). Because of the difference in WTP, country B is better off sticking to the cost-effectiveness criterion and its ERP restriction is not binding. It is only in period 3 that country A is able and willing to revise its price to \( p_A = v_B \). In this case, the total expected profit of the firm is the following:

\[
\Pi_{AB} = (1 + \delta) v_A q_A + \delta v_B q_B + \frac{\delta^2}{1 - \delta} v_B (q_A + q_B).
\]

If the firm launches the drug in country B first, the firm sells in B at a price \( p_B = v_B \) from period 1 on, and in country A at a (binding ERP) price \( p_A = v_B \) from period 2 on. No further revision will ever take place since prices in both countries are set at the minimum level. In this case, the total expected profit of the firm is the following:

\[
\Pi_{BA} = \frac{v_B}{1 - \delta} (q_B + \delta q_A).
\]
If the firm launches the drug in both countries simultaneously, it does so in period 1 at prices $p_A = v_A$ and $p_B = v_B$ since ERP cannot be binding now. It is thus in period 2 that country A is able and willing to revise its price and bind the ERP to $p_A = v_B$. In this case, the total expected profit of the firm is the following:

$$\Pi_{\text{sim}} = v_A q_A + v_B q_B + \frac{\delta}{1 - \delta} v_B (q_A + q_B).$$

Comparing the firm’s profits, we deduce that the firm should never launch the drug in country B first when $v_A > v_B$. It should launch the drug in country A first when the difference in WTP is high enough so that it is more interesting to postpone the price revision to period 3 at the cost of foregoing the market in country B in the first period. Conversely, when the difference in WTP is not that high, a simultaneous launch in both countries with an early revision (in period) is more interesting for the firm.

Similarly, when $v_A < v_B$, the firm never launches the drug in country A first. It launches the drug in country B first when the difference in WTP is large enough. Otherwise, the firm prefers to simultaneously launch the drug in both countries. The following lemma formalizes this comparison and Figure 2 depicts it.

**Lemma 4.**

The firm launches the drug in country A first at a price $p_A = v_A$ that is revised in period 3 if and only if both $v_B$ and $q_B$ are high relative to $v_A$ and $q_A$, respectively:

$$\Pi_{AB} > \Pi_{\text{sim}} > \Pi_{BA} \iff \frac{v_A}{v_B} > 1 + \frac{1}{\delta} \frac{q_B}{q_A}.$$

Conversely, the firm launches the drug in country B first at a price $p_B = v_B$ that is revised in period 3 if and only if $v_B$ and $q_B$ are low relative to $v_A$ and $q_A$, respectively:
\[ \Pi_{RA} > \Pi_{sim} > \Pi_{AB} \iff \frac{v_B}{v_A} > 1 + \frac{1}{\delta q_B} . \]

Otherwise, the firm simultaneously launches the drug in both countries and prices are revised in the second period.

To summarize, the firm prefers to simultaneously launch the drug in both countries when the countries are similar enough in terms of market size and WTP. When one country largely outperforms the other in terms of both market size and WTP, the firm is better off foregoing selling in the less interesting market in the first period to delay the revision to a binding ERP price to a further period of time in the large market. It is straightforward to show that countries are better off announcing ERP beforehand and revising prices accordingly after potential launch delays in other countries.

Figure 2.

**Lemma 5.**

Countries are better off announcing ERP beforehand and revising prices accordingly after potential launch delays in other countries.
5. Conclusion

In this paper, we have shown that sequential launching of drugs is a firm’s best response to ERP only when prices can be revised periodically and countries are different enough from each other, both in terms of market size and WTP. Otherwise, the firm is always better off simultaneously launching the drug in all countries. Countries are better off announcing ERP beforehand and revising prices accordingly after potential launch delays in other countries.
References

