SHIFTING THE RISK IN PRICING AND REIMBURSEMENT SCHEMES. A NEW MODEL OF RISK-SHARING AGREEMENTS FOR INNOVATIVE DRUGS

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1. Introduction

The rapid increase in pharmaceutical expenditure and the need to control the health care budget has sparked renewed interest in pricing policies (Claxton, 2007).

Rising costs are a challenge to healthcare policy makers because high prices put budgetary pressure on governments who try to maintain access to drugs for the population at an affordable cost.[3] For this reason, most EU member states control the prices of reimbursable medicines.

The aim of these regulatory mechanisms is to find an optimal trade-off between the need to incentivate R&D, to protect consumers and to secure value for money in the use of public funds. The market for pharmaceuticals is not, for various reasons, a competitive market.[4] The demand side is characterized by uncertainty on the effectiveness of the drug and patients' inability to translate their need for improved health into the demand for a specific treatment. The agency relationship between the patient and the physician[5] means that that choice of the drug is largely entrusted to the latter, with a possible distortion of the market. The regulations and restrictions laid down by Government agencies in this sector are themselves a source of distortion. Pharmaceutical price regulation methods in non-US markets are heterogeneous and include, for example, direct price regulation through a negotiation process (e.g. France and Italy) and indirect price regulation through limits on reimbursement under social insurance programmes (e.g. Germany and Japan) (Danzon and Chao, 2000b; Capri and Levaggi, 2002; 2007).

One of the most innovative methods applied in pricing schemes is represented by the risk-sharing agreements. Risk sharing occurs when the risks involved (in this case the cost of a particular drug therapy) are shifted from one stakeholder to another, from the government to the industry and vice versa, in order to alleviate some of the concerns about uncertainty. There are two types of risk sharing: performance-based and financial-based contracts. Performance-based contracts focus on the efficacy of the product, whereas risk-sharing financial-based agreements involve cost per patient.

Such risk-sharing arrangements for pharmaceuticals can be used to report high quality when product quality is not fully observable. While there may be difficulties in devising such schemes for every product, risk-sharing agreements may become an essential feature of the market in the future (Cook et al, 2008).

The aim of this paper is to study the effects of risk-sharing in markets for highly targeted new drugs. In this environment we can assume that ex ante the treatment is always appropriate and that the effectiveness of the drug does not depend on the number of patients to be treated.

2. Risk-sharing concepts

In the listing process the industry has an interest in showing that the drug is very effective in order to increase its probability of being listed and, possibly, to obtain a high price. The number of patients have a countervailing effect on expected profits since they reduce the probability of being listed, but they increase profits if the outcome of the listing process is positive.

Once the drug has been introduced, almost all regulatory systems require greater effort in the post-marketing monitoring of drugs, not only from a purely medical perspective (DePouvourville, 2006). Public authorities, in fact, schedule procedures to control the drug for possible side effects. However, only a few of them verify the real ex post value for money of the drug. In particular, only a few regulators impose a form of penalty if the effectiveness falls short of the declared efficacy and/or the volume is greater than what was agreed.

This failure to verify efficacy and volume ex post creates perverse effects on the regulatory system. The industry, in fact, has an interest in overestimating the efficacy and underestimating the number of people that will benefit from the drug in the listing process, given that both parameters will not be controlled by the regulator ex post.

In general, it is very difficult and costly to verify the discrepancy between efficacy and effectiveness. For very costly and targeted drugs such as cancer drugs it is possible to verify their effectiveness ex post. This is because the number of patients is limited and already controlled. In Italy, for instance, a specific registry for expensive cancer drugs has been created and for some of these drugs the risk-sharing scheme is applied.[6] The patient is registered in the website and treatment is initially paid by the Italian NHS. If treatment fails (progressive disease or unacceptable toxicity at or before the agreed time), the pharmaceutical company reimburses (money or corresponding amount of drug) the whole delivered treatment or 50% of it. An example for the UK is Janssen-Cilag's Velcade (bortezomib, see NICE, 2007) in which patients who demonstrate a 50% response rate at first relapse are eligible to continue treatment on the NHS, otherwise the manufacturer refunds the NHS.

On the theoretical side, a new strand of literature is developing to study risk-sharing. Zaric and O'Brien (2005) study the effects of rebates in the pricing mechanism when the quantity sold exceeds the negotiated quantity. As for the effectiveness of the drug, Barros (2010) studies the welfare properties of specific risk-sharing mechanisms while Zaric and Xie (2009) examine two different risk-sharing agreements in an intertemporal setting. In their model the company applies for listing, proposes a price and sets a marketing

strategy to sell the drug. The efficacy of the latter is a random variable and a penalty is imposed on the firm if the ex post efficacy (the effectiveness) falls below a specific threshold. The penalty may consist in delisting in the second period or in a rebate. The authors show that depending on the environment, one or the other instruments perform better both from the industry and the purchaser point of view.

In this paper we propose a very general modelling framework that allows study of the risk-sharing properties of several pricing schemes, their effects on the number of patients treated and on the expected profit of the company selling the drug. Our framework allows for differentiation between risk-sharing and risk-shifting schemes and has important policy implications: the number of patients that are treated is not necessarily affected by risk-sharing/risk-shifting unless the listing procedure itself is changed; the price for which the drug is listed may be higher than without risk-sharing, but the expected profit of the industry is: a) always lower for risk-shifting schemes; b) for true risk-sharing it depends on the bargaining power of the company.

The article will be organised as follows: in the following section we present the model, in section ; in section and we present our pricing scheme with and without risk-sharing respectively; in section we show how our pricing mechanism can be used to represent most of the systems used by regulators; in section we show the difference between a risk-sharing and a risk-shifting scheme and argue why a company may still prefer to be listed with risk-shifting. Finally in section the main conclusions of our paper are drawn.

3. The model

In the market we analyse, patients are treated using a drug that is currently listed and has the following characteristics:

- the drug is relatively new; data on the theoretical efficacy are available, the results concerning ex post effectiveness are not known;

- the effectiveness E° of the drug lies within a range of values $(0, L)$ with a known uniform probability so that the expected effectiveness ED° is equal to $\frac{L}{2}$;

- the listed price of this drug is p° while the quantity that maximises expected profit is equal to x°. As a consequence, the expected budget is $B^\circ = p^\circ x^\circ$;

- the regulatory process by which the drug has been approved and listed is the same as the one that will be used for the new product.

A new drug is about to be marketed to treat the same condition. Its effectiveness E lies within a range of values $(0, A)$ with a known probability distribution $g(E)$ with $G(0) = 0; G(A) = 1.$ To simplify the exposition, we assume that the distribution of this function is uniform, i.e. $g(E) = 1/A$ so that the expected effectiveness ED is equal to $\frac{A}{2}$. The marginal cost c to produce the drug is approximated to zero, but the firm has to incur a fixed cost F for research into the drug and marketing.

The outcome of the listing process (i.e. the approved price, the level of reimbursement, the limitations) is uncertain and depends on the efficacy (D), the price (p) and the number of patients to be treated (x).

The expected effectiveness (ED) is derived from the randomised clinical trials the firm has to carry out before the drug is approved. To simplify matters, we assume that one unit of the drug is sufficient to treat one patient so that the number of doses and the number of patients are equivalent.

The price p and the number of patients to be treated, x, are usually the result of a bargaining between the company and the regulator where the price and the quantity may be decided by the firm, by the regulator or by the market depending on the regulatory framework (Capri and Levaggi, 2007; Jelovac, 2003; Claxton, 2007).

In this bargaining process the regulator takes account of the budget that is necessary to treat patients and the value for money of the drug. At the listing stage the latter can observe the expected effectiveness (ED) which can be verified by both parties through the results of the randomised clinical trials. However, the true effectiveness $(E$: the ex-post efficacy) is not known when the price is set. Such uncertainty depends on several elements such as the role of compliance, the interactions with other drugs when patients have several pathologies and the appropriateness of physicians' prescription behaviour. The firm may have more precise information on the likely effectiveness of the drug because it has access to more information than the minimum required by the regulatory process. In our paper we show that the risk of effectiveness falling short of expected efficacy can be partly shifted onto the company that applies for listing.

We formalise the listing process by assuming that the price of the drug depends on three parameters:

- α which reflects cost effectiveness considerations. It may be interpreted as society's willingness to pay in a class of specific treatments and it is set by the regulator. We assume that it is set outside the model.

- D which is the efficacy of the drug that is declared by the company for reimbursement purposes; it must lie in the range ($0, A$) but it may not necessarily be equal to expected effectiveness, $A/2$. This is because the firm may be more or less optimistic about the success of the drug in treating patients outside the randomised clinical trial;

- z, a rebate on the price if the ex post effectiveness (E) is lower than D . z represents the risk-sharing element of our formula.

The pricing rule can be written as:

$$p = \alpha D - z\alpha \int_0^D (D - E)\frac{1}{A} dE$$

(1)

x is the number of patients that will be treated. We assume that this number is contractible and can be verified.

If the effectiveness falls short of what is declared, the firm will have to pay a rebate proportional to the difference between the declared efficacy and true effectiveness $(D - E)$, but other schemes are compatible with our risk-sharing formula as we will show later.

The company applies for the drug to be reimbursed by the regulator. The latter may or may not decide to grant reimbursement; this decision depends on D and on the budget $B = px$ that is necessary to take care of the possible benefiter (x) of the new drug. Both variables are measured in relation to the market in which the new drug is introduced.

In particular, we assume that the probability of being reimbursed can be defined by $\pi(\frac{D}{D°}, \frac{B}{B°})$ where $D°$ and $B°$ is the efficacy of the drug and the budget spent for the active principle that is currently used to treat patients with the same condition. As in Zaric and O'Brien (2005), the function is assumed to be separable and additive in $\frac{D}{D°}$ and $\frac{B}{B°}$. The probability of being listed is increasing in ED and decreasing in px .[7]

This function is common knowledge to the actors in the decision process, i.e. the company knows the parameters of this function before setting D . Given that during the negotiation process neither party knows the true effectiveness, the budget that the regulator uses in the decision to list the drug is $p^* = \alpha D.$

The expected profit from listing can be written as:

$$E\Pi = \pi(ED; px)(p - c)x - F$$

(2)

The company aims to maximise its expected profit and to do so it has to choose the level of efficacy ($D)$ and the number of patients (x) that maximises the following function:

$$Max_{D,x}E\Pi = \left(\pi_1\left(\frac{D}{D°}\right) - \pi_2\left(\frac{\alpha Dx}{p°x°}\right)\right)\left(\alpha D - z\alpha\int_0^D (D - E)\frac{1}{A}dE\right)x - F$$

(3)

In order to show the differences in terms of price and expected profits between our model and a more conventional listing process, we now show how the pricing mechanism would be in our model if there were no risk-sharing.

4. The pricing mechanism without risk-sharing

In this section we compare the results of our model with a system where there is no risk-sharing. In the absence of any other information, the pricing rule set by the regulator will depend on expected efficacy $(ED = \frac{A}{2})$:

$$p^{NR} = \alpha \frac{A}{2}$$

(4)

If listed, the industry receives a price equal to $\alpha \frac{A}{2}$, independently of E, the effectiveness verified ex post. The idea behind this pricing mechanism is that in the short run the industry has a limited bargaining power in setting the price of the drug that it is about to market. The price is in fact determined by α and by the expected efficacy resulting from the randomised clinical trials which the industry has to perform.

The only discretionary variable for the company is x, the number of patients, which will be determined through the maximisation of its expected profit:

$$Max_x E\Pi = \left(\pi_1 \left(\frac{A/2}{L/2} \right) - \pi_2 \left(\frac{\alpha \frac{A}{2} x}{p^\circ x^\circ} \right) \right) \alpha \frac{A}{2} x - F$$

(5)

As in Zaric and O'Brien (2005) we assume that the marginal probability of being listed is linear; the F.O.C. can be written as:

$$-\frac{1}{2} \alpha A^2 \frac{\pi_2 \alpha x L - \pi_1 p^\circ x^\circ}{L p^\circ x^\circ}$$

(6)

The optimal solution for x can be written as:

$$x^* = \frac{x^\circ}{2} \frac{\pi_1}{\pi_2}$$

(7)

The price of the new drug is outside the control of the industry in the listing process, unless the industry can influence the value of $A/2$ through the randomised clinical trial. The number of patients that the industry will target for the new drug may be greater or smaller than for the drug already listed. It will depend on the parameters of the probability of listing set by the regulator. $\frac{\pi_1}{\pi_2}$ is in fact the ratio of the marginal effect on the probability of being listed deriving from an increase in the effectiveness and in the budget.

This ratio may be controlled by the regulator. For example, if the latter wants the same number of patients treated with the old and the new drug ($x^* = x^\circ$), it will have to put greater weight on the efficacy compared to the budget[8]. To some extent, this may not be a perverse effect of regulation given that the new drugs are more effective, but also more targeted on a restricted number of patients (Pirmohamed and Lewis 2004; Danzon and Towse, 2002).

Substituting equation (4) into (5) we can write the expected profit as:

$$E\Pi^{NR} = \frac{1}{8} \frac{A^2}{L} \alpha \frac{\pi_1^2}{\pi_2} - F$$

(8)

The profit is increasing in α and in the efficacy of the new drug, as may be expected.

5. The pricing mechanism with risk-sharing

In this section we introduce our proposed risk-sharing formula. The price will be set according to equation ( ) and the probability of listing depends on declared efficacy and the maximum budget.

The company chooses the level of efficacy and the number of patients that maximises the following function:

$$Max_{D,x} E\Pi = \left(\pi_1 \left(\frac{D}{D^\circ} \right) - \pi_2 \left(\frac{\alpha D x}{p^\circ x^\circ} \right) \right) \left(\alpha D - z\alpha \int_0^D (D - E) \frac{1}{A} dE \right) x - F$$

$$s.t$$

$$D \le A$$

(9)

If the marginal probability of being listed is linear as in the previous example, the optimal level for D and x can be written as:[9]

$$D^* = \frac{4}{3} \frac{A}{z} \text{ if } z \ge \frac{4}{3}$$

$$D^* = A \quad \text{ if } z < \frac{4}{3}$$

$$x^* = \frac{x^\circ}{2} \frac{\pi_1}{\pi_2}$$

(10)

In this model where the efficacy of the drugs belonging to the same therapeutical class is rewarded in the same way, D^* does not depend on the threshold set by the regulator (α) but on the rebate it will have to pay if the effectiveness falls short of the declared efficacy. α is an important element in determining the profit of the firm, but it does not distort the choices of the company as regards D^*. It interesting to note that unless $z \ge \frac{4}{3}$, the company will always apply using the maximum possible level of efficacy (A). This result is driven by the fact that by increasing D^* the expected profit increases (listing is more certain) even if the risk of paying a fine is higher.

By comparing equation (7) with equation (10) we can see that the number of patients which the company is applying to treat is the same, i.e. our risk-sharing formula does not alter the decisions of the company as regards the number of patients for whom it is agreed the new treatment will be made available if listed.

Through substitution of the optimal quantities in the profit function we can determine the expected profit:

$$
\begin{aligned}
&\frac{4}{27}\alpha\frac{\pi_1^2}{\pi_2}p^\circ\frac{A^2}{z^2D^\circ}-F \quad if \ z \geq \frac{4}{3} \\
&\frac{1}{4}\alpha\frac{\pi_1^2}{\pi_2}p^\circ\frac{A^2}{L}\left(1-\frac{1}{2}z\right)-F \ if \ z < \frac{4}{3}
\end{aligned}
$$

(11)

As in the previous case, the profit is increasing in α. In this case it is also decreasing in z, as might be expected.

6. Other risk-sharing mechanisms

The agreement presented in the previous section envisages a rebate proportional to the difference between declared efficacy and effectiveness. In everyday application of risk-sharing, other mechanisms are often used. Some cancer drugs are reimbursed to the company only if they are effective by different combination of schemes: e.g. in Italy nilotinib and sorafenib are not reimbursed after the second cycle of therapy if the patient does not respond to the first cycle; avanstin is fully reimbursed only for respondent patients after 15 cycles; sprycell is reimbursed at 50% of the price if there is a progression of the disease after the first cycle. In this case a threshold for reimbursement is defined in relation to the level of declared efficacy. In other words, the agreement between the pharmaceutical company and the regulator takes this form:

$$
\begin{aligned}
p &= \alpha D \quad if \ E \geq sD \\
p &= 0 \quad\ if \quad E < sD
\end{aligned}
$$

where $0 \leq s \leq 1$ is a parameter set by the regulatory authority. For $s = 1$ the company is reimbursed only if the ex post effectiveness is at least equal to the declared efficacy; for values smaller than one, the company has more room for manoeuvre.

This risk-sharing mechanism is similar to the one proposed by Barros (2010). In this case the profit for the company can be written as:

$$
Max_{D,x}E\Pi = \left(\pi_1\left(\frac{D}{D^\circ}\right)-\pi_2\left(\frac{\alpha Dx}{p^\circ x^\circ}\right)\right)\left(\alpha D\int_{sD}^A\frac{1}{A}dE\right)x-F
$$

$$
s.t
$$

$$
D \leq A
$$

(12)

As in the previous examples, if the marginal probability of being listed is linear, the optimal level for D and x can be written as:[10]

$$D^* = \frac{2}{3}\frac{A}{s}\; \text{if}\; s > \frac{2}{3}$$

$$D^* = A \quad \text{if}\; s < \frac{2}{3}$$

$$x^* = \frac{x^\circ}{2}\frac{\pi_1}{\pi_2}$$

(13)

The quantity for which the company requests listing is the same as in the no risk-sharing case. In this case our model does not predict an increase in the number of cases treated, a possible problem that Barros (2010) points out for risk- sharing agreements. The difference in the results of the two models is explained by the presence in our approach of a listing process also in the case in which the drug is reimbursed only if it is effective. Such result has important policy implications: risk-sharing does not necessarily mean that more patients will be treated, unless the listing process is changed. In our example the rules for being listed do not change: the probability of being listed still depends on the effectiveness of the drug and the budget and in this case the number of patients that will be treated is independent of the pricing mechanism.

Instead of paying for the effective therapies, the regulator may envisage a rebate if effectiveness falls below a specific level. In this case the company is paid a price $p = \alpha D$, but it will have to pay a fixed rebate $k\alpha D$ if the effectiveness falls short of a specific threshold sD.

In other words, the agreement between the pharmaceutical company and the regulator takes this form:

$$p = \alpha D \quad \text{if}\; E \geq sD$$
$$p = (1-k)\alpha D \quad \text{if}\quad E < sD$$

(14)

where $0 \leq k \leq 1$ is a parameter set by the regulator authority. *For $k = 1$ the payback is equal to the price paid to the company the price is equivalent to the one we have described in the previous section.* This risk-sharing mechanism is similar to the one proposed by Zaric et al. (2009). In this case the profit for the company can be written as:

$$Max_{D,x}E\Pi = \left(\pi_1\!\left(\frac{D}{D^\circ}\right) - \pi_2\!\left(\frac{\alpha D x}{p^\circ x^\circ}\right)\right)\!\left(\alpha D - k\alpha D \int_0^{sD}\frac{1}{A}\,dE\right)x - F$$

$$s.t$$

$$D \leq A$$

(15)

As in the previous examples, if the marginal probability of being listed is linear, the optimal level for D and x can be written as:

$$D^* = \frac{2}{3}\frac{A}{ks} \text{ if } ks > \frac{2}{3}$$

$$D^* = A \quad \text{ if } ks < \frac{2}{3}$$

$$x^* = \frac{x^{\circ}}{2}\frac{\pi_1}{\pi_2} \tag{16}$$

The parameters k and s play a similar role in this model. From a policy point of view this means that the regulator may choose the payback level and the threshold independently, but it is the combination of these two parameters that determine the choice of the industry.

Through substitution of the optimal quantities in the profit function we can determine the expected profit:

$$\frac{1}{27}\frac{A^2}{k^2 s^2 D^{\circ}}\alpha\frac{\pi_1^2}{\pi_2}p^{\circ} - F \quad \text{if } ks \geq \frac{2}{3}$$

$$\frac{1}{4}\alpha\frac{\pi_1^2}{\pi_2}p^{\circ}\frac{A^2}{L}(1 - ks) - F \quad \text{if } ks < \frac{2}{3} \tag{17}$$

This formula represents the profit both for the case in which only the effective therapies are paid for (in which case $k = 1)$ and the more general case of a rebate. As in the previous case, the profit is increasing in α. In this case it is also decreasing in ks, as might be expected. From a policy point of view it is interesting to note that if $ks = \frac{z}{2}$ the two systems are equivalent, i.e. the industry fixes the same price and has the same profit.

For this reason, below we study the effects of risk-sharing only with reference to the first model proposed.

7. Policy implications

In this session we try to answer the following question: who are the gainers and the losers of a risk-sharing mechanism?

From a purely economic point of view, one of the most important arguments for not introducing risk-sharing mechanisms is that they may increase the price of the drugs, hence public expenditure. The company on the other hand may feel that the system is depressing expected profit. In our model, given the assumption of no marginal production costs as regards the drug, we can simply compare the expected profit of the company under the two arrangements. In fact, given the assumption of zero marginal costs to produce the

drug, public expenditure and expected profit differ because of F, hence the comparison can be made simply for the profits.

In the model presented here there is no effect on the target number of patients which is the same under the two systems, provided that the listing process is the same for drugs with and without risk-sharing agreements. As for the profit, it is necessary to compare equation (11) with equation (8).

In appendix 2 we show that independently of the level chosen for z (i.e. $z \leq 4/3$ and $z > 4/3$)), the profit for the company is always lower under a risk-sharing agreement.

This allows us to conclude that a risk-sharing mechanism like the one we have proposed is always preferred by the regulator. In fact, the number of patients that are going to be treated is the same, but the ex post price (net of the rebate) is lower than in a system where the expected effectiveness is reimbursed.

This means that from an economic point of view such a scheme should not be defined risk-sharing but risk-shifting (Towse and Garrison, 2010). The company in fact agrees to receive an expected profit that is lower than without this scheme. For a true risk-sharing mechanism, the cost per QALY threshold (α) should be set higher in the risk-sharing mechanism. Let's call this value α_1. In particular, it can be shown that for $\alpha_1 = \frac{9}{8}\alpha z$ the company is indifferent between the two agreements. This equation shows two interesting facts: the first is that $\alpha_1 > \alpha$ as expected; the second is that α_1 is increasing in z, i.e. the higher the penalty, the higher the price under a risk-sharing scheme.

This result has important policy implications; for very expensive drugs when α is the maximum value that society is willing to pay for QALY [11], the agreements currently proposed are in fact risk-shifting practices. The company, confronted with an all or nothing offer, prefers to reduce its expected profit against the alternative of not being listed and it is for this reason that it accepts the agreements. Some experts argue that risk-sharing is second option for the pharmaceutical industry: if the normal process fails because the drug is too costly, the company enters a risk-sharing agreement. Our model adds one important element to this discussion: entering such a risk-shifting agreement is equivalent to accepting a reduction in the price of the new drug. The company may prefer this solution for several reasons:

the price will be based on a declared efficacy which may be higher than the expected value. In the short run this declaration may be used as a message to physicians and competitors on the confidence the company has in the healing properties of the new drug;

the company may have acquired new evidence on the effectiveness of the new drug or how to better target the patients and it may prefer to risk paying a penalty than receive a lower price.

When the threshold α is not the maximum willingness to pay, a true risk-sharing mechanism may arise. In this case the company will ask to be reimbursed at a higher rate than α and effects on the expected profit depend on the bargaining ability of the company. In this case, part of the risk is in fact shifted from the regulator to the industry as regards the effectiveness of the new drug a cost that is represented by the increase in the expected profit.

8. Conclusions

In this paper we propose a pricing mechanism to be used both for risk sharing and risk shifting purposes based on the effectiveness of the new drug.

Our model shows the basic difference between risk-sharing and risk-shifting. The first mechanism may be used by a regulator that wishes to reduce uncertainty concerning the ex post cost effectiveness of the drug. The second mechanism is instead used to reduce the expected price of the drug and is compatible with situations where the drug is very costly and its effectiveness highly uncertain. In this framework the company may have an interest in accepting a reduction in its profit through a risk-sharing mechanism instead of through a straight price reduction. In this way it may have advantages in terms of market signalling about the confidence the company has in the effectiveness of the new drug. Furthermore, the company may be able to use new evidence on the true effectiveness of the treatment to target the patients, hence improving the expected effectiveness.

The price at which the new drug is listed is always higher than in a system without risk sharing, but the expected profit is lower unless the efficacy is reimbursed at an higher rate. This consideration has important policy implications: in the presence of risk sharing the listing price is not a good proxy for value for money. It is only ex post, when the true effectiveness will be known that value for money can be evaluated. In a risk-sharing agreement in fact it is necessary to take account of the rebates that the firm may incur if the effectiveness falls short of what promised.

At the time of listing, the expected profit of the firm is a better proxy for value for money because it takes account of these rebates.

Our formula creates incentives for the company to target the number of people that will be treated instead of increasing it like the risk-sharing mechanism proposed by NICE in 2007 for bortezomib (Barros 2010).

The reason for this different result can be explained as follows: in our approach we use the probability of listing of the new drug and risk sharing on the price while NICE substitutes the listing process with the risk sharing agreement on the price. Our model shows that risk sharing is not a substitute for total expenditure considerations; on the contrary the two instruments should be used together.

The framework we use highlights the effects of the listing process on the number of patients that the company propose to treat in the long run. Our model shows in fact that the number of patients the company proposes to treat depends on the relative weight that is given in the decision process to the efficacy and to budget considerations. This means that all the parameters of the pricing formula have to be carefully assessed to avoid perverse effects (Claxton et al. 2008). For this reason, this note represents just a first step in studying new ways of defining prices for drugs in a regulated market.

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Appendix 1: The optimal D* and x*

The maximisation problem can be written as:

$$Max_{D,x}E\Pi = \left(\pi_1\left(\frac{D}{D^\circ}\right) - \pi_2\left(\frac{\alpha Dx}{p^\circ x^\circ}\right)\right)\left(\alpha D - z\alpha\int_0^D (D-E)\frac{1}{A}dE\right)x - F$$

$$s.t$$
$$D \le A$$

We can take account of the constraint using Khun Tucker conditions:

If the marginal probability of being listed is linear, the F.O.C. can be written as:

$$\frac{1}{2}\alpha Dx(\pi_1 p^\circ - \pi^2 x)\frac{4A-3zD}{D^\circ p^\circ A} = 0$$

$$\frac{1}{2}\alpha D^2(2A-zD)\frac{\pi_1 p^\circ - 2\pi^2 x}{D^\circ p^\circ A} = 0$$

Let's assume that the constraint is not binding. The above equations can be solved as a system of linear equations. The non-negative solutions are the following couples:

$$\left(x = x^\circ\frac{\pi_1}{\pi^2}; D = 2\frac{A}{z}\right)\!;\!\left(x = \frac{x^\circ}{2}\frac{\pi_1}{\pi^2}; D = \frac{4}{3}\frac{A}{z}\right)$$

The first solution is not feasible, only the second can be considered. However this solution is valid only if $z > \frac{4}{3}$

For $z < \frac{4}{3}$ the constraint is binding and the problem can be written as:

$$Max_x E\Pi = \left(\pi_1\left(\frac{A}{L}\right) - \pi^2\left(\frac{\alpha Ax}{\alpha Lx^\circ}\right)\right)\left(\alpha A - z\alpha\int_0^A (D-E)\frac{1}{A}dE\right)x - F$$

The FOC can be written as:

$$\frac{1}{2}A^2(z-2)\frac{\pi\pi_1 p^\circ - 2\pi^2 x}{Lp^\circ} = 0$$

which implies $x = \frac{x^\circ}{2}\frac{\pi_1}{\pi^2}$

Appendix 2: Profit under the two pricing mechanisms

Given that there are two solutions for risk-sharing, we have to compare two different cases

$a) z > 4/3$

In this case the difference in the profit can be written as:

$$\tfrac{1}{8}\pi_1^2 \tfrac{A^2}{D^\circ}\alpha \tfrac{p^\circ}{\pi^2} - F - \tfrac{4}{27}\pi_1^2 \tfrac{A^2}{z^2 D^\circ}\alpha \tfrac{p^\circ}{\pi^2} + F$$

Given that $D^\circ = \tfrac{4}{3}\tfrac{L}{z}$

the equation above can be written as:

$$\alpha\left(\tfrac{1}{8} - \tfrac{1}{9z}\right)\tfrac{\pi_1^2 A^2 p^\circ}{\pi_2 L}$$

which is equal to 0 for $z = 8/9$. For values above this threshold, the equation is negative, for values below it is positive. Since the equation for the profit with risk-sharing is valid only if $z > 4/3$ the difference is always negative.

b) $z < 4/3$

In this case the difference in the profit can be written as:

$$\tfrac{1}{8}\pi_1^2 \tfrac{A^2}{L}\alpha \tfrac{p^\circ}{\pi_2} - F \quad - \tfrac{1}{4}\pi_1^2 \tfrac{A^2}{L}\alpha\left(1 - \tfrac{1}{2}z\right)\tfrac{p^\circ}{\pi_2} + F$$

which can be written as

$$\left(\tfrac{1}{8} - \tfrac{1}{4} + \tfrac{1}{8}z\right)\pi_1^2 \tfrac{A^2}{L}\alpha \tfrac{p^\circ}{\pi_2}$$

This expression is equal to zero if $z = 1$ which, however, implies no risk-sharing. For $z < 1$ *it* is negative, but has no economic meaning.

Notes

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[3] In Europe, about 75% of pharmaceutical expenditure is reimbursed from public funds (OECD, 2009)

[4] See Zweifel, Breyer and Kifmann (2009) chap.12 and Capri and Levaggi (2007).

[5] See Barigozzi and Levaggi (2008) and references therein

[6] See http://antineoplastici.agenziafarmaco.it/

[7] i.e. $\frac{\partial \pi(ED;px)}{\partial ED} > 0$ and $\frac{\partial^2 \pi(ED;px)}{\partial ED^2} \leq 0$ and $\frac{\partial \pi(ED;px)}{\partial px} < 0$ and $\frac{\partial^2 \pi(ED;px)}{\partial px} \geq 0$

[8] i.e. if π^1 (the marginal probability *of being* listed directly correlated with the efficacy) is twice π^2 (the probability *of being* listed inversely correlated with the budget).

[9] See appendix one

[10] See appendix one.

[11] For instance, in the UK, NICE (National Institute for Health and Clinical Excellence) has fixed the maximum cost for a QALY (quality-adjusted life year) gained *at* £ 30,000.