Reference Pricing of Pharmaceuticals*

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Abstract

We consider a therapeutic market with potentially three pharmaceutical firms. Two of the firms offer horizontally differentiated brand-name drugs. One of the brand-name drugs is a new treatment under patent protection that will be introduced, if the profits are sufficient to cover the entry costs. The other brand-name drug has already lost its patent and faces competition from a third firm offering a generic version perceived to be of lower quality. This model allows us to compare generic reference pricing (GRP), therapeutic reference pricing (TRP), and no reference pricing (NRP). We show that competition is strongest under TRP, resulting in the lowest drug prices (and medical expenditures). However, TRP also provides the lowest profits to the patent-holding firm, making entry of the new drug treatment least likely. Surprisingly, we find that GRP distorts drug choices most, exposing patients to higher health risks.

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1 Introduction

Pharmaceutical markets are characterised by price inelastic demand mainly due to extensive medical insurance. Since individuals – once they are ill – only pay a small fraction of the medical cost, prices are likely to have a limited effect, not only on the choice of whether or not to consume a drug, but also on the choice between alternative drug treatments. On the supply-side, there are large, sunk R&D costs associated with the discovery of new drug treatments. To stimulate innovation, pharmaceutical firms are granted market power (for a given period) by patent protection.

The combination of supply-side market power and price inelastic demand has induced purchasers to employ various means to control medical expenditures.[1] We can distinguish between two price control mechanisms: (i) regulation of drug prices (price caps); and (ii) regulation of the reimbursement level, frequently referred to as *reference pricing* (RP). While price caps limit the pharmaceutical firms' ability to exploit market power by charging high prices, RP aims at stimulating competition by making demand more price elastic. In this paper, we analyse in detail the effects of RP on the price-setting strategies of the pharmaceutical firms. On the basis of this analysis, we discuss implications for market entry of new drug treatments, patient health risks, and optimal drug reimbursement policies. While these issues have received some empirical attention, theoretical contributions are very limited.[2]

RP of prescription drugs is quite novel, but has rapidly become a widely used price control mechanism in the pharmaceutical market. Germany's Statutory Health Insurance System, generally viewed as the pioneer in this regard, introduced RP for prescription drugs in 1989, which was followed in Europe by the Netherlands in 1991, Denmark and Sweden in 1993, Spain in 2000, and Belgium and Italy in 2001. Norway adopted RP in 1993, but abandoned it in 2001, because the expected cost savings did not materialise. Outside Europe, RP has been adopted by Australia, the Canadian province of British Columbia, and New Zealand.[3]

The reference price is constructed as follows: drugs are classified into clusters based on

[1] Danzon (1997) provides an excellent overview and discussion of various regulatory mechanisms in the pharmaceutical industry.

[2] According to the extensive literature survey by Lopez-Casasnovas and Puig-Junoy (2001), the bulk of the RP literature is mainly descriptive, and there is a pronounced lack of theoretical studies analysing the effects of RP systems. See also Danzon (2001).

[3] In the US, RP has been proposed as a possible approach to drug reimbursement for a comprehensive Medicare drug benefit (Huskamp et al., 2000). Kanavos and Reinhardt (2003) argue that RP for drugs is compatible with US health care. Notably, generic reference pricing is well-established in the US through "maximum allowable charge" programs used by, e.g., Medicaid.

similar therapeutic effects. The regulator sets a reference price based on a relatively low-priced drug (e.g., the minimum or median price) in the cluster. The reference price is the maximum reimbursement for all products in the group. Pharmaceutical firms can set prices above the RP, but in this case the patient must pay the surcharge.[4]

The construction of therapeutic clusters for RP is by far the most controversial task in the development of such systems. These clusters may be narrowly or broadly defined: (i) products with the same active chemical ingredients, (ii) products with chemically related active ingredients that are pharmacologically equivalent, and (iii) products that may be neither chemically identical nor pharmacologically equivalent, but have comparable therapeutic effects. By its nature, the first type of cluster includes only off-patent brand-name drugs and their generic substitutes. The second and third may include on-patent drugs. They differ in breadth, but are qualitatively similar. As is commonly done, we refer to the first type as *generic reference pricing* (GRP), and the second and third as *therapeutic reference pricing* (TRP).

We construct a theoretical model that allows us to analyse the effects of the two RP systems, as well as the benchmark case of no reference pricing (NRP), where patients pay a fixed share (co-payment rate) of the drug price.[5] The basic set-up is a therapeutic market with potentially three pharmaceutical firms, where two of the firms offer original brand-name drugs with different chemical ingredients. One of the brand-name drugs is an old treatment (e.g., the breakthrough drug) that has lost its patent protection and faces competition from a third firm offering a generic version, perceived to be of lower quality than the off-patent brand-name drug.[6] The other brand-name drug is a new, horizontally differentiated treatment under patent protection that will be introduced in the market, if the profits are sufficient to cover the entry costs.[7] This modelling approach enables us to discuss the arguments for

[4] On the other hand, if a firm's price is below the RP, the savings may be shared between the payer and the dispensing pharmacist.

[5] The NRP regime is often referred to as 'free pricing', but we find this somewhat imprecise, since RP in itself does not restrict price-setting of drugs by pharmaceutical firms. Only the reimbursement level is regulated, not drug prices.

[6] Empirical evidence strongly suggests that generic drugs are not perceived to be perfect substitutes to the original brand-name drug, despite being chemically identical. After generic entry, the original brand-name firm typically charges a higher price than its generic version and still has positive market shares (e.g., Grabowski and Vernon, 1992, Frank and Salkever, 1997, Scott Morton, 2000). These findings fit well with predictions of vertical differentiation models. Two recent papers applied to branded-generic competition are Cabrales (2003) and Königbauer (2005).

[7] One can think of the entry costs as a marketing cost associated with entering a new country-specific market. Alternatively, the entry costs can be thought of as (expected) R&D costs, which must be recouped for the discovery of a new drug treatment to take place.

and against RP systems in general, and between TRP and GRP in particular.

The main argument in favour of RP is, that it stimulates price competition by making demand more elastic and thus results in lower medical expenditures. Intuitively, the effect on price competition should be stronger, the wider the cluster is defined. Our model confirms this line of argument. We show that the price of every drug in the therapeutic market is highest under NRP and lowest under TRP. It is worth noting that GRP not only reduces the prices of the drugs in the reference cluster, but also puts a downward pressure on the price of the non-included, but therapeutically equivalent drug. This is due to prices being strategic complements.[8]

The inclusion of on-patent drugs is perhaps the main source of controversy over RP-systems. It is argued that TRP per se effectively eliminates patent protection and will stifle innovation in drug therapy, while GRP, on the other hand, is considered to have a minimal effect on incentives for R&D since it applies only to off-patent drugs (see e.g., Danzon, 2001, and Lopez-Casasnovas and Puig-Junoy, 2000). Our model confirms the first line of the argument, but not the second. We show that TRP provides the lowest profits to the patent-holding firm, making market entry (and innovation) of the new drug treatment least likely.[9] However, we also find that a patent-holding firm can be negatively affected by RP, even if on-patent drugs are exempted from this particular reimbursement system. Stronger price competition induced by GRP forces the patent-holding firm to lower the price of its drug in order to reduce the loss of market shares.

Another important concern about TRP is that this system forces a large number of patients to opt for a less suitable drug simply to avoid the extra co-payment. The broader the therapeutic cluster, the more severe is the trade-off between surcharges and increased health risks to patients.[10] GRP, on the other hand, is said to conserve third party funds

[8] Pavcnik (2002) provides strong evidence from Germany that the introduction of RP has induced pharmaceutical prices to drop, the effect being stronger for branded drugs facing generic competition. Aronsson et al. (2001) provide similar evidence from Sweden.

[9] This result has empirical support from Danzon and Ketcham (2004) who analyse the effect of RP on the availability of drugs in Germany, the Netherlands and New Zealand.

[10] Lopez-Casasnovas and Puig-Junoy (2000, p. 111) formulate this problem as follows:

> "First, if there is no interchangeability at the level of the individual patient [...] then the co-payment may become not avoidable and the RP system may discriminate against some patients. Second, selection of a drug under a RP category may result in a lower level of effectiveness and potentially harmful side effects for the patient because the drug is chosen simply with a view to avoiding the copayment".

The same argument is presented by Danzon (2001).

without exposing patients to significant risks, because it applies to substitution only among generically equivalent drugs that have demonstrated bioequivalence to the original brand-name drug. For *given prices*, this is, of course, trivially true. However, the intention of the RP systems is to induce price responses from the pharmaceutical firms. Taking this into account, we show that, in fact, GRP distorts drug choices most, exposing patients to higher health risks. Since the on-patent drug is exempted from reference pricing under GRP, the patent-holding firm faces a less price-elastic demand than its competitors and can thus charge a considerably higher price. This induces a larger fraction of patients to choose the drugs that are included in the reference cluster, which are less suitable, but have a lower co-payment.

In terms of policy implications, our results suggest no clear-cut conclusions about the optimal choice of reimbursement system. We can, however, make distinctions among the following general cases. If market entry costs are low, with a corresponding low risk of no market entry for new drugs, then TRP is clearly socially favourable. However, if this is not the case, then either NRP or GRP might be necessary to stimulate market entry. The choice between NRP and GRP implies a trade-off, since the former yields higher drug expenditures but lower health risks to patients. A social planner's evaluation of this particular trade-off is determined by the importance of drug expenditures in the planner's objective function. GRP might thus be the favoured reimbursement system in countries where the pharmaceutical industry is insignificant or non-existent, while NRP might be preferred otherwise.

The theoretical literature on RP is, as mentioned above, very limited with only a couple of notable exceptions. Zweifel and Crivelli (1996) analyse the pricing responses to the introduction of a RP system using a Bertrand duopoly model. They frame their analysis in the context of the introduction of the TRP system in Germany in 1989. Danzon and Liu (1997) use a monopolistic competition model with kinked demand and imperfect physician agency to predict price responses to RP. The modelling approaches are distinctly different from ours. The combination of horizontal and vertical differentiation allows us to analyse and compare GRP and TRP closely. Moreover, our model also enables the analysis of market entry and health risks to patients, which are lacking in the above mentioned studies.[11]

Our paper contributes also to the more general literature on horizontal and vertical prod-

[11] These important aspects of RP-systems are also absent in Merino-Castelló (2003), who studies the price effects of generic reference pricing in a vertical differentiation model.

uct differentiation. Most papers within this field allow firms to invest in quality, but assume consumers to differ only along the horizontal dimension (taste).[12] The present paper explicitly combines the horizontal differentiation framework of Hotelling (1929) with the vertical differentiation framework introduced by Gabszewicz and Thisse (1979, 1980) and Shaked and Sutton (1982, 1983). While these two approaches typically are applied separately, the pharmaceutical market – with both inter-brand (branded vs. branded) and intra-brand (branded vs. generic) competition – serves as a natural example for combining these frameworks.

The paper is structured as follows: in section 2, the model is presented. In section 3, the equilibrium prices are derived and characterised for all three regimes. Section 4 analyses the market entry decision of the firm with the new drug treatment. Section 5 analyses the welfare properties of the three different regimes and presents some policy implications. Finally, in section 6, the paper is concluded.

2 The Model

Consider a particular therapeutic market for prescription drugs with the following characteristics. There are two patient types, indexed by $j = H, L$, differing with respect to their gross valuation of drug treatment, due to, e.g., different degrees of illness. A fraction λ of the patients are H-types, with a gross valuation v. The remaining patients – the L-types – have a gross valuation γv, where $\gamma \in (0, 1)$. Both patient types are uniformly distributed on the line segment $S = [0, 1]$, with a total mass of 1, where the location of an arbitrary patient, $x \in S$, is associated with the patient's susceptibility towards specific drug characteristics. A 'mismatch cost' parameter t measures the utility loss per unit of distance between a patent's ideal treatment – given by his location on S – and the drug actually consumed. We can think of such mismatch costs as reflecting various side-effects or contraindications that reduce the gross valuation of drug treatment.

There are potentially three pharmaceutical single-product firms, indexed by $i = 0, 1, G$, operating in the market. Firms 0 and 1 offer original brand-name drugs at prices p_0 and p_1,

[12] Several papers have added quality competition to a standard Hotelling-framework, see e.g., Ma and Burgess (1993) for the case of fixed locations under both price competition and price regulation, Economides (1989) for the case of endogenous locations and price competition, and Brekke et al. (2006) for the case of endogenous locations and price regulation. However, none of these papers allow consumers to differ with respect to their willingness-to-pay for quality, which means that the vertical differentiation framework is not explicitly dealt with.

respectively. These drugs, which differ with respect to chemical compounds, are located at either end of the unit interval S, reflecting their horizontally differentiated treatment effects. We assume that drug 1 is a new treatment version – still under patent protection – that will be introduced in this particular market, if variable profits are sufficient to cover entry costs. Drug 0, on the other hand, has already lost its patent protection and faces generic competition from a third pharmaceutical firm G, offering a generic drug version at a price p_G. In terms of horizontal differentiation, the generic drug is (naturally) also positioned at 0. However, in the eyes of the patients, 0 and G are *vertically differentiated*. This is captured by assuming that patients' gross valuation of the generic drug is deflated by a factor $\theta \in (0,1)$. Thus, the perceived quality difference between the two versions of drug treatment 0 is given by $(1-\theta)$. This vertical differentiation might be due to differences in advertising intensity that creates perceived quality differences, or simply due to the brand-name drug being perceived to be safer, because of its longer life in the market.

Each patient needs one unit of either drug version. A patient of type j who is located at x and consumes a unit of drug i obtains utility

$$U_j(x,i) = \begin{cases} u_j - t|x-i| - c_i & if \quad i = 0,1 \\ \theta u_j - tx - c_i & if \quad i = G \end{cases}, \tag{1}$$

where

$$u_j = \begin{cases} v & if \quad j = H \\ \gamma v & if \quad j = L \end{cases}, \tag{2}$$

and c_i is the patient co-payment for drug i.

Patients are (partially) insured and face a co-payment rate $\alpha \in (0,1)$. In the absence of a reference price system, the co-payment is simply given by $c_i = \alpha p_i$. On the other hand, in the presence of a reference price system, the co-payment is based on a reference price $\overline{p}$, and the patients must additionally pay the full price difference if choosing a drug in the reference group which is priced in excess of the reference price. Thus, if drug i is included in a reference price system, the co-payment is given by

$$c_i = \begin{cases} \alpha p_i & if \quad p_i \leq \overline{p} \\ \alpha \overline{p} + (p_i - \overline{p}) & if \quad p_i > \overline{p} \end{cases}. \tag{3}$$

We analyse a three-stage game with the following sequence of events:

1. A benevolent regulator decides on the socially optimal drug reimbursement policy to implement. She chooses among the following policies: (i) no reference pricing (NRP), (ii) therapeutic reference pricing (TRP), or (iii) generic reference pricing (GRP).

2. Firm 1 decides whether to enter the market and thus to offer a new treatment, given that treatment 0 already exists and is offered in the form of both an original version (drug 0) and a generic substitute (drug G).

3. All pharmaceutical firms in the market play a simultaneous pricing game.

As usual, the game is solved by backward induction.

3 Drug pricing

In this section we derive the optimal pricing strategies of the pharmaceutical firms for each of the three possible reimbursement regimes. We look for an equilibrium where all firms are active and compete in terms of prices. This requires some restrictions on the parameters. More specifically, we assume that the mismatch cost parameter t is bounded from both below and above, i.e., $t \in \left(\underline{t}, \overline{t}\right)$, where the lower and upper bounds are functions of the other parameters. In the Appendix we show that, when $t \in \left(\underline{t}, \overline{t}\right)$, there exists a vertically separating equilibrium, where the brand-name drug 0 is priced 'high' and consumed by the H-types only, while the generic substitute G is priced 'low' and consumed by the L-types only.[13] This is the only possible type of equilibrium, where the generic drug can survive in the market, since all patients prefer drug 0 over drug G if $c_0 \leq c_G$. On the other hand, the horizontally differentiated brand-name drug 1 is consumed by both types in equilibrium.

It is worth noting that, in this context, it makes considerable intuitive sense to focus on *intermediate* values of the mismatch cost parameter t. On the one hand, a very low t is not compatible with patent protection, since a new drug must be sufficiently differentiated to obtain a patent. On the other hand, a very high t is not compatible with the notion of a

[13] To be more precise, we show that an equilibrium exists when $t \in \left(\underline{t}, \overline{t}^k\right)$, $k = NRP, TRP, GRP$. In other words, there is a common lower bound on t in all three regimes, whereas the upper bound generally differs between the regimes.

'therapeutic market'. In particular, the idea of therapeutic reference pricing requires that the drugs included in a reference group are not too differentiated.

Demand and profits

Let us first derive drug demand for each firm under the assumption of vertical market segmentation. This requires the identification of two indifferent patients; one for each of the two patient types.

The H-types choose between the two brand-name drugs, and the location of the indifferent H-type patient, denoted $\widetilde{x}_H$, is given by the solution to

$$U_H\left(\widetilde{x}_H, 0\right) = U_H\left(\widetilde{x}_H, 1\right),$$

yielding

$$\widetilde{x}_H = \frac{1}{2} + \frac{c_1 - c_0}{2t}. \tag{4}$$

The L-types, on the other hand, choose between the generic drug G and the horizontally differentiated brand-name drug 1. The location of the indifferent L-type patient, denoted $\widetilde{x}_L$, is given by the solution to

$$U_L\left(\widetilde{x}_L, G\right) = U_L\left(\widetilde{x}_L, 1\right),$$

yielding

$$\widetilde{x}_L = \frac{1}{2} + \frac{c_1 - c_G - \gamma v\left(1 - \theta\right)}{2t}. \tag{5}$$

Under the additional assumption of full market coverage, so that all patients obtain non-negative utility from the consumption of their most preferred drug, the demand facing firm i is given by

$$D_i = \begin{cases} \lambda \widetilde{x}_H & if \quad i = 0 \\ \lambda\left(1 - \widetilde{x}_H\right) + \left(1 - \lambda\right)\left(1 - \widetilde{x}_L\right) & if \quad i = 1 \\ \left(1 - \lambda\right)\widetilde{x}_L & if \quad i = G \end{cases}. \tag{6}$$

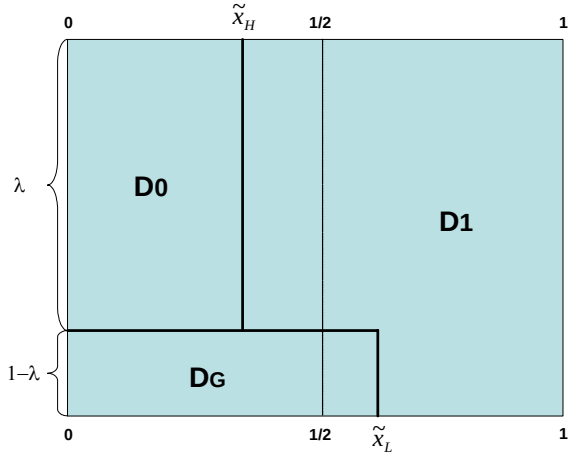

Figure 1: Illustration of the demand system

Finally, assuming zero production costs, (variable) profits for firm i are simply given by[14]

$$\pi_i = p_i D_i. \tag{7}$$

Figure 1 illustrates the demand system. Firm 0 providing the old breakthrough drug serves only the high valuation (high severity) patients, represented by a fraction λ, whereas the generic firm serves the low valuation (low severity) patients, given by the fraction $1-\lambda$. The new, on-patent drug, producer serves both segments.

3.1 No reference pricing (NRP)

In the absence of any reference price system, the patient co-payment for drug consumption is simply given by

$$c_i^{NRP} = \alpha p_i^{NRP}. \tag{8}$$

Explicit expressions for the profit functions under the NRP-system are easily found by using (8) in (4)-(7). In equilibrium, the two brand-name producers choose prices p_0^{NRP} and p_1^{NRP} that maximise π_0 and π_1, respectively, as defined by (7). The optimal strategy for the generic producer, on the other hand, is to choose a price p_G^{NRP} that is just low enough to make it unprofitable for firm 0 to deviate from p_0^{NRP} by setting a 'low' price that also captures the

[14] At this stage, market entry costs (R&D costs and/or marketing costs) are sunk and thus play no role for the analysis.

L-types. The equilibrium drug prices are given by[15]

$$p_0^{NRP} = \frac{3t}{\alpha}\Delta_0, \tag{9}$$

$$p_1^{NRP} = \frac{t}{\alpha}\Delta_1, \tag{10}$$

$$p_G^{NRP} = \frac{1}{\alpha}\left[3t\Delta_G - \gamma v\left(1-\theta\right)\right], \tag{11}$$

where

$$\Delta_0 := \frac{3-(1-\lambda)\sqrt{1-\lambda}}{8+\lambda\left(\lambda^2+3(1-\lambda)\right)} > 0, \tag{12}$$

$$\Delta_1 := \frac{10-\lambda\left(\lambda^2+3(1-\lambda)\right)-6\left(1-\lambda\right)\sqrt{1-\lambda}}{8+\lambda\left(\lambda^2+3(1-\lambda)\right)} > 0, \tag{13}$$

$$\Delta_G := \frac{4-\lambda(2-\lambda)-(4-\lambda)\sqrt{1-\lambda}}{8+\lambda\left(\lambda^2+3(1-\lambda)\right)} > 0. \tag{14}$$

We see that all prices are increasing in t and decreasing in α. Higher mismatch costs reduce the substitutability, and thus the degree of competition, between the brand-name drugs, leading to higher prices. A higher co-payment rate, on the other hand, increases the price elasticity of drug demand, leading to lower prices in equilibrium. It is also straightforward to show that $\partial\Delta_i/\partial\lambda > 0$, implying $\partial p_i/\partial\lambda > 0$, for all $i = 0, 1, G$. A higher fraction of H-types implies an increase in the overall willingness to pay, with a corresponding price increase for the original drugs. This price increase also enables the generic producer to charge a higher price in equilibrium.[16] Note also that a reduction of the perceived quality difference between the two versions of treatment 0 (i.e., an increase in θ) leads to a higher price for the generic drug version, as expected.

On the other hand, a higher gross valuation of drug treatment for the L-types – i.e., an increase in γ – leads to a *lower* generic price in equilibrium. The reason is that a higher gross valuation for the L-types, implying a higher willingness-to-pay for drugs, makes it more profitable for firm 0 to lower its price in order to capture the L-segment of the market. Consequently, the generic firm must reduce its price in order to prevent this price-undercutting strategy from the brand-name firm. If the difference in gross valuations between the two patient types becomes sufficiently small – i.e., if γ becomes sufficiently close to 1 – it

[15] A full derivation of the equilibrium is given in the Appendix.

[16] From (11) and (14) we see that λ must be sufficiently high to secure a non-negative generic drug price and thus equilibrium existence. See the Appendix for exact conditions.

is not possible for the generic firm, with a (perceived) lower-quality product, to prevent the brand-name firm from serving both patient types in equilibrium. In this case, the generic drug is driven out of the market.

From (9)-(11) we can easily establish the following ranking of equilibrium drug prices:

$$p_0^{NRP} > p_1^{NRP} > p_G^{NRP}. \tag{15}$$

These price differences are reflected in the allocation of equilibrium market shares:

$$\widetilde{x}_H^{NRP} = \frac{3\left[3-(1-\lambda)\sqrt{1-\lambda}\right]}{2\left[8+\lambda\left(\lambda^2+3(1-\lambda)\right)\right]} \in \left(\frac{3}{8}, \frac{1}{2}\right), \tag{16}$$

$$\widetilde{x}_L^{NRP} = \frac{3\left[2+(2-\lambda)\lambda+(2+\lambda)\sqrt{1-\lambda}\right]}{2\left[8+\lambda\left(\lambda^2+3(1-\lambda)\right)\right]} \in \left(\frac{1}{2}, 0.77\right). \tag{17}$$

The allocation of market shares allows us to assess if and how drug consumption is distorted in equilibrium for the two patient types.[17]

Proposition 1 *Under NRP, the brand-name drug with a generic substitute always charges the highest price in equilibrium. Both patient groups are distorted: H-type patients consume more of the new, patent-protected brand-name drug, while L-type patients consume more of the generic drug.*

It might seem counterintuitive that the price level is higher for the brand-name drug with a generic substitute, since, normally, we would expect prices to be lower for products that face stronger competition. The reason for this result is that, due to generic competition, the optimal strategy of firm 0 is to concentrate exclusively on serving the H-type patients and leave the L-types to the generic competitor. Since firm 0 competes only for H-patients with less price-elastic demand, while firm 1 competes for both patient types, firm 0 sets a higher price than firm 1 in equilibrium. This theoretical result tallies well with several empirical findings of price increases for brand-name drugs after the entry of generic substitutes in the market.[18]

[17] 'Distortion' refers to allocations of consumption (or market shares) that differ from the one that minimises patients' mismatch costs, i.e., $\widetilde{x}_j = \frac{1}{2}$.

[18] The empirical study by Grabowski and Vernon (1992) shows that generic entry was followed by price increases by the branded producer, a result later confirmed by Frank and Salkever (1997). This finding was called the 'generic competition paradox' by Scherer (1993).

Inserting the equilibrium prices into (7), we derive the equilibrium profits:

$$\pi_0^{NRP} = \frac{3t\lambda\Delta_0}{2\alpha}\left(1+\Delta_1-3\Delta_0\right), \tag{18}$$

$$\pi_1^{NRP} = \frac{t\Delta_1}{2\alpha}\left(1+3\left(\Delta_G\left(1-\lambda\right)+\lambda\Delta_0\right)-\Delta_1\right), \tag{19}$$

$$\pi_G^{NRP} = \frac{1-\lambda}{2\alpha}\left(1+\Delta_1-3\Delta_G\right)\left(3t\Delta_G-\gamma v\left(1-\theta\right)\right). \tag{20}$$

3.2 Reference pricing

Consider now the implementation of a reference pricing system. This implies that some drugs are aggregated into a cluster and are subject to the same reference price $\overline{p}$. The introduction of a reference pricing system involves the following decision-making. First, the regulator must decide which drugs to include in a cluster or reference group. In our model, this choice boils down to whether or not the new brand-name drug should be included. Inclusion of the horizontally differentiated new drug implies *therapeutic reference pricing* (TRP). On the other hand, if the reference group consists only of the old brand-name drug and its generic substitute, the reimbursement system is characterised as *generic reference pricing* (GRP).

Second, the regulator must decide on the reference price level. In most countries, this level is set at, or close to, the lowest drug price in the cluster. In the present analysis, we follow this practice by assuming that the lowest price in the reference group – i.e., the generic price – is chosen as the reference price level: $\overline{p} = p_G$.

3.2.1 Therapeutic reference pricing (TRP)

Under TRP, the reference group consists of all three drugs in the therapeutic market, also the horizontally differentiated drug 1. By the assumption of $\overline{p} = p_G$, the co-payments faced by patients under TRP are given by

$$c_i^{TRP} = \begin{cases} p_i^{TRP} - \left(1-\alpha\right)p_G^{TRP} & if \quad i = 0,1 \\ \alpha p_G^{TRP} & if \quad i = G \end{cases}. \tag{21}$$

The co-payments differ as compared to NRP, since the patients that are prescribed one of the original drugs are now also fully liable for the price difference with respect to the reference price.

As before, explicit expressions for the profit functions under the TRP-system are found by using (21) in (4)-(7), and the derivation of the equilibrium is similar to that under the NRP-system. We find equilibrium prices under TRP to be given by

$$p_i^{TRP} = \alpha p_i^{NRP}, \quad i = 0, 1, G. \tag{22}$$

Thus, compared with NRP, TRP implies that prices are set *as if* $\alpha = 1$. The reason is that, with TRP, the patients are fully liable for any price increase above the reference level. This also implies that equilibrium prices are independent of the co-payment rate. Furthermore, since equilibrium market shares are independent of α, both patient types are equally distorted under the two regimes.

Proposition 2 *In equilibrium, relative price differences and market shares are equal under NRP and TRP.*

Compared with the NRP-case, the (uniform) downward pressure on drug prices under TRP is also reflected in lower equilibrium profits, now given by

$$\pi_i^{TRP} = \alpha \pi_i^{NRP}, \quad i = 0, 1, G. \tag{23}$$

3.2.2 Generic reference pricing (GRP)

Under GRP, only generic substitutes are grouped into the same cluster as the original, off-patent drugs. Horizontally differentiated, but therapeutically equivalent drug versions are not included. In our model, co-payments faced by consumers under GRP are thus given by

$$c_i^{GRP} = \begin{cases} p_i^{GRP} - (1-\alpha)\, p_G^{GRP} & if \quad i = 0 \\ \alpha p_i^{GRP} & if \quad i = 1, G \end{cases}. \tag{24}$$

While only a fraction α of the drug price needs to be paid on drugs G and 1, patients that are prescribed the brand-name drug 0 must additionally pay the full price difference between the original drug and the generic substitute.

Equilibrium prices, derived in the same way as previously, are given by

$$p_0^{GRP} = \frac{\left(2 + \alpha - \sqrt{1-\lambda}\,(2 - \lambda - \alpha)\right)\Gamma}{\widetilde{\Delta}}, \tag{25}$$

$$p_1^{GRP} = \frac{t\overline{\Delta} + (1-\alpha)(1-\theta)\gamma v\left(\widehat{\Delta} - 2(2+\alpha)\right) - \sqrt{1-\lambda}\,(2\alpha - \lambda(\alpha+1))\,\Gamma}{\alpha\widetilde{\Delta}}, \tag{26}$$

$$p_G^{GRP} = \frac{3t\left(\alpha\lambda - 3\lambda + \lambda^2 + 4\right) - \gamma v(1-\theta)\,\widehat{\Delta} - (4-\lambda)\,\Gamma\sqrt{1-\lambda}}{\widetilde{\Delta}}, \tag{27}$$

where

$$\widehat{\Delta} := 4\alpha + 5\lambda - 2\alpha\lambda - 4\lambda^2 + \lambda^3 + \alpha\lambda^2 + 4 > 0, \tag{28}$$

$$\widetilde{\Delta} := 8\alpha + 8\lambda - 6\alpha\lambda - 5\lambda^2 + \lambda^3 + 2\alpha\lambda^2 + \alpha^2\lambda > 0, \tag{29}$$

$$\overline{\Delta} := 10\alpha + \lambda - 6\alpha\lambda + 2\lambda^2 - \lambda^3 + \alpha\lambda^2 + 2\alpha^2\lambda > 0, \tag{30}$$

$$\Gamma := 3t - \gamma v(1-\theta)(1-\alpha) > 0. \tag{31}$$

Using the equilibrium prices derived above, we can find the equilibrium market shares under GRP, characterised by the location of the indifferent patient in each patient-group:

$$\widetilde{x}_H^{GRP} = \frac{\Gamma\left[(2+\alpha) - (2-\lambda-\alpha)\sqrt{1-\lambda}\right]}{2t\widetilde{\Delta}}, \tag{32}$$

$$\widetilde{x}_L^{GRP} = \frac{\Gamma\left[\alpha(2-\lambda) + \lambda(3-\lambda) + (2\alpha+\lambda)\sqrt{1-\lambda}\right]}{2t\widetilde{\Delta}}. \tag{33}$$

Comparing with (16)-(17), it is also relatively straightforward to verify that

$$\widetilde{x}_j^{GRP} > \widetilde{x}_j^{TRP} = \widetilde{x}_j^{NRP}, \quad j = H, L, \tag{34}$$

implying that more patients choose one of the drugs included in the reference cluster under GRP – drug 0 and G.

In order to evaluate the ranking of equilibrium prices under GRP, we now make a rather weak assumption on the co-payment rate, namely that $\alpha < \frac{2}{3}$. We are then able to make the following characterisation of the pricing equilibrium under generic reference pricing:[19]

Proposition 3 *Assume that $\alpha < \frac{2}{3}$. Then, under GRP, the brand-name firm without a generic substitute always charges the highest price in equilibrium. Both patient groups are generally distorted; the L-types always consume more of the generic drug, while the H-types*

[19] For $\alpha \geq \frac{2}{3}$, the ranking of p_0^{GRP} and p_1^{GRP} is ambigious. It is possible to derive the exact condition, but the condition is rather messy and also hard to interpret, so we focus on the plausible case of $\alpha < \frac{2}{3}$. The exact condition can, however, be provided by the authors upon request.

consume more of the new patent-protected brand-name drug, if λ and/or t are sufficiently low, and more of the old off-patent product otherwise.

A proof is given in the Appendix.

We see that the ranking of equilibrium prices changes under a generic reference price system. The price is now higher for the brand-name drug without a generic substitute. The reason is simply that drug 1 is not included in the reference cluster. If a consumer chooses this drug, her co-payment is given by a share α on the *total* drug price. In contrast, if she chooses the off-patent drug 0, which is included in the reference cluster, she must pay the full price difference between the generic substitute and the brand-name drug. Thus, by not having its product included in the reference group, firm 1 faces a less elastic demand and will consequently charge a higher price in equilibrium.

In contrast to the NRP or TRP systems, the equilibrium price differences do not automatically translate into equivalent differences in equilibrium market shares. The reason is the asymmetry introduced by different co-payments for patients, depending on whether or not the demanded drug is subject to reference pricing. Consequently, even if firm 1 sets the highest drug price, it may not be the most expensive alternative for consumers, and consequently, this firm may have a higher market share in the H-segment. From Proposition 3, we see that this is the case, if λ and/or t are sufficiently low. In this case, the price of the on-patent drug is kept relatively low in order to capture a larger share of the L-segment (which is more important, the lower the level of λ) and/or due to fierce competition induced by a relatively low degree of horizontal differentiation.

On the other hand, the location of the indifferent L-type patient is always distorted towards drug 1, as before. In other words, due to the price difference between generic and brand-name drugs, a larger share of L-patients consume the generic drug G. Finally, it should be noted that even though the H-segment may be distorted 'both ways' under GRP, the L-segment is always more distorted towards drug 1. This can easily be verified from (32)-(33) by confirming that $\widetilde{x}_L^{GRP} > \widetilde{x}_H^{GRP}$.

Using the equilibrium prices reported in (25)-(27), we can derive equilibrium profits under GRP. These profit expressions are rather messy, and are therefore relegated to the Appendix.

3.3 Price comparison

As a next step, in order to evaluate how the reimbursement system affects drug prices, let us compare the equilibrium price levels for the same drugs across different regimes. Using the equilibrium prices reported for the different cases above, it is relatively straightforward to verify that

$$p_i^{NRP} > p_i^{GRP} > p_i^{TRP}, \quad i = 0, 1, G, \tag{35}$$

for all $t > \underline{t}$. In other words:

Proposition 4 *The price of every drug in the therapeutic market is highest under NRP and lowest under TRP.*

This result reflects and confirms the main rationale behind reference pricing. By introducing a reference pricing system, price competition is generally increased, since the price elasticity of drug demand increases for prices above the reference price level. Furthermore, this effect is stronger, if more drugs are included in the reference cluster, implying that drug prices are lower under TRP than under GRP. Since prices are strategic complements, the introduction of a reference price system of either kind puts a downward pressure on the prices of *all* drugs in the market. Compared with the NRP case, the introduction of generic reference pricing has a direct negative effect on the price level of drug 0, which in turn leads to a reduction also in the price of drug 1, even though this drug is not included in the reference cluster under GRP. Furthermore, by going from GRP to TRP, firm 1 gets a direct incentive to cut its drug prices, which then indirectly leads to a further price reduction also for drug 0. Finally, lower prices for brand-name drugs imply that the generic producer must also lower its price in order to stay in the market.

4 The market entry decision

Let us now turn to the question of market entry. When interpreting the market in question as a *country-specific* therapeutic market, demarcated by national regulation, we can realistically assume that firm 1 will enter this particular market (i.e., offer its newly developed product in this country) only if expected profits from sales in this market cover the market entry costs. When considering the costs and benefits of entry, the firm must take into account how

the reimbursement policy in a given country is likely to affect profits from drug sales in this country.

In our model, there is a clear-cut ranking of equilibrium profits for the potential entrant (firm 1) across the different reimbursement regimes:

Proposition 5 *Equilibrium profits of the patent-holding entrant are always highest under NRP and lowest under TRP.*

A proof is given in the Appendix.

The profit comparison between NRP and TRP is straightforward. Compared with the case of no reference pricing, the TRP system puts a downward pressure on drug prices, while keeping equilibrium market shares intact, implying that profits are unambiguously lower in the TRP equilibrium. NRP also outperforms GRP, from the viewpoint of firm 1, since prices *and* market shares are higher in the former case. A comparison between GRP and TRP, on the other hand, shows that in the former case prices are higher, but market shares lower. Nevertheless, equilibrium profits are always higher under generic reference pricing. The reason is that under GRP, firm 1 faces drug demand with a lower price elasticity, which enables this firm to charge a considerably higher price while suffering a moderate loss of market shares. All else equal, it follows that expected profits for a potential entrant are always lowest when entering a market that is subject to therapeutic reference pricing, and highest when entering a market with no reference pricing.

This result is not surprising and tallies well with popular concern about therapeutic reference pricing with respect to a potential erosion of patent rights, as discussed in the Introduction. However, it is worth noting that a patent-holding firm can be negatively affected by reference pricing even if on-patent drugs are exempted from this particular reimbursement system. In our model, firm 1's profits are lower under GRP, compared with no reference pricing, even though drug 1 is not included in the reference cluster. The reason is that firm 1 offers a drug that is an imperfect substitute to the drugs directly affected by the GRP system. Stronger price competition between firms 0 and G – induced by generic reference pricing – implies that firm 1 is also forced to lower the price of its on-patent drug in order to reduce the loss of market shares.

5 Welfare considerations

In this section we discuss how considerations for social welfare will influence the optimal choice of reimbursement scheme for pharmaceuticals. We naturally assume that a regulator has two main concerns: (i) aggregate mismatch costs and (ii) total drug expenditures. The former is a measure of total health risks to patients from drug consumption, which a benevolent regulator obviously wants to minimise. We assume that the regulator also wants to minimise total expenditures for drug consumption, but the weighting of these two objectives – in case of conflict – might depend on the characteristics of the country in question.

We can distinguish between two polar cases. In countries with a significant pharmaceutical industry, it is reasonable to assume that profits of pharmaceutical firms matter for the national regulator. In this case, the welfare costs of higher drug prices might be restricted to the efficiency costs of increased third-party funding for drug expenditures.[20] Naturally, a regulator will put relatively more emphasis on minimising aggregate mismatch costs from drug consumption in this case.[21] On the other hand, in countries with no pharmaceutical industry, it is reasonable to assume that drug expenditures are more important in terms of national welfare. Indeed, a stated desire behind the introduction of reference pricing in many countries is precisely to curb total outlays on pharmaceutical consumption.

In the subsequent analysis, we start out by examining the effect of different RP-systems on aggregate mismatch costs. Then, in the latter part of this section, we proceed to discuss the optimal choice of reimbursement system in the presence of three partly conflicting regulatory goals: minimising mismatch costs, keeping drug prices low, and stimulating market entry.[22]

5.1 Mismatch costs

Total mismatch costs under reimbursement system k, denoted by C_k, are given by

$$C_k = \lambda \left(\int_0^{\widetilde{x}_H^k} (st)\, ds + \int_{\widetilde{x}_H^k}^1 ((1-s)\, t)\, ds \right) + (1-\lambda) \left(\int_0^{\widetilde{x}_L^k} (st)\, ds + \int_{\widetilde{x}_L^k}^1 ((1-s)\, t)\, ds \right). \tag{36}$$

[20] In a model with unit demand, patient copayment for drugs is an efficient transfer from consumers to producers with no efficiency costs associated.

[21] This will also be the case if we take the perspective of *global* welfare.

[22] In our discussion of welfare and policy implications, we implicitly make the assumption that a regulator does not take into account the 'artificial' vertical differentiation between the branded and generic drugs, and attaches the same gross utility to objectively homogenous products. We think this is a reasonable (though not trivial) assumption.

Clearly, total mismatch costs are minimised if $\widetilde{x}_L^k = \widetilde{x}_H^k = \frac{1}{2}$. In other words, mismatch costs are minimised if all patients located at $x \leq \frac{1}{2}$ are prescribed either drug 0 or G, while all patients located at $x > \frac{1}{2}$ are prescribed drug 1. However, due to price differences, total mismatch costs will never be minimised in equilibrium. We have previously shown that $\widetilde{x}_j^k \neq \frac{1}{2}$ for at least one patient type in all three reimbursement regimes. We also know that equilibrium market shares are equal under NRP and TRP, implying that total mismatch costs must also be equal under these two regimes.

The explicit expression for total mismatch costs in each of the three different regimes, which are quite messy, are given in the Appendix. Based on these expressions, we are able to derive the following unambiguous ranking of reimbursement systems with respect to equilibrium mismatch costs:

$$C_{GRP} > C_{TRP} = C_{NRP}. \tag{37}$$

In other words:[23]

Proposition 6 *NRP and TRP yield equal mismatch costs in equilibrium, and these are always lower than under GRP.*

In order to explain this result, let us first consider the distortive effects of GRP on each of the two patient types. We know that $\widetilde{x}_L^{GRP} > \widetilde{x}_L^{TRP} = \widetilde{x}_L^{NRP} > \frac{1}{2}$, due to the larger price difference between the generic drug and the horizontally (and vertically) differentiated drug 1 under GRP. This implies that GRP always increases total mismatch costs in the L-segment. For H-types, on the other hand, we know that $\widetilde{x}_H^{TRP} = \widetilde{x}_H^{NRP} < \frac{1}{2}$ and $\widetilde{x}_H^{GRP} > \widetilde{x}_H^{TRP} = \widetilde{x}_H^{NRP}$. However, since $\widetilde{x}_H^{GRP} \lesseqgtr \frac{1}{2}$, it is possible that GRP reduces aggregate mismatch costs for the H-types, if $\widetilde{x}_H^{GRP}$ is sufficiently close to the midpoint of the line segment S. Nevertheless, a possible reduction in mismatch costs for H-types will always be more than outweighed by the increase in mismatch costs for L-types. The reason is twofold. First, mismatch costs are reduced for H-types only if λ – the fraction of H-types in the population – is sufficiently low (cf. Proposition 3), in which case the contribution of H-types to *total* mismatch costs is also relatively low. Second, since the location of the indifferent L-type is

[23] The proof, though conceptually straightforward, involves some extremely tedious and messy algebra and is thus not reported. However, just to give a brief sketch, it is possible to show that $C_{GRP} - C_{NRP} = \frac{\varphi_1}{\varphi_2}$, where $\varphi_2 > 0$ and φ_1 is a convex quadratic function of t which crosses zero from below at $t = \underline{t}$. Thus, $\varphi_1 > 0$ for $t > \underline{t}$. It follows that $C_{GRP} > C_{TRP} = C_{NRP}$ for $t > \underline{t}$.

further away from the midpoint of S in all regimes, the effect of a marginal relocation of the indifferent patient on total mismatch costs is – all else equal – larger in the L-segment.

The result stated in Proposition 6 is perhaps somewhat surprising. It certainly runs contrary to the popular concern about the discriminatory effects of therapeutic reference pricing, that this reimbursement system forces a larger number of patients to opt for a less suitable drug – thereby increasing mismatch costs – simply to avoid the extra co-payment. However, this is not the case in our model. True, therapeutic reference pricing will increase overall mismatch costs *for given prices*, if we use the NRP-case as a benchmark. But this argument ignores the fact that pharmaceutical firms will adjust their pricing policies according to the drug reimbursement system. In our specific model, we have seen that TRP will lead to a proportionally equal reduction in all drug prices, leaving patients' drug choices unaffected in equilibrium compared to NRP. Generic reference pricing, on the other hand, will lead to more distorted drug choices, due to larger equilibrium price differences within the therapeutic market. Since the on-patent drug is exempted from reference pricing under GRP, firm 1 faces a less price-elastic demand than its competitors and can thus charge a considerably higher price in equilibrium. This, in turn, induces more patients to choose the drugs that are included in the reference cluster, leading to higher overall mismatch costs.

5.2 Policy implications

If a regulator seeks to minimise overall mismatch costs, the above analysis suggests that generic reference pricing should never be implemented. Mismatch costs are minimised by choosing either NRP or TRP.

However, there are potentially two other considerations that might be taken into account. First, the price level of pharmaceutical drugs will play a role, if the regulator is concerned about curbing total outlays on pharmaceuticals. As previously discussed, the relative weighting of mismatch costs and prices in the welfare function is likely to depend on the relative importance of the pharmaceutical industry in the country in question. The more important the pharmaceutical industry is, the less concerned a regulator should be about pharmaceutical prices. In any case, as long as the regulator places any weight on pharmaceutical prices at all, the above analysis clearly suggests that a therapeutic reference price system should be implemented, as this reimbursement scheme minimises both mismatch costs and prices.

However, this conclusion is only valid if there is indeed an additional, horizontally differentiated, drug version that can be included in the therapeutic cluster. Since equilibrium profits are lowest under TRP (cf. Proposition 5), this reimbursement system makes market entry least likely for a given level of market entry costs. If the possibility of no market entry is taken into account, then the welfare considerations are no longer clearly in favour of TRP. First, no entry will lead to *maximal* mismatch costs, because only one treatment version (drug 0 and its generic substitute) is offered in the market. Second, the absence of competition from a horizontally differentiated drug will lead to increased drug prices under both NRP and GRP. In this scenario, the regulator must take into account how the choice of reimbursement system is likely to affect the probability of market entry for new drugs.

No clear-cut conclusions can be made about the optimal choice of reimbursement system. However, based on the above analysis, we can make the following classification of scenaria. *Therapeutic reference pricing* – which minimises both mismatch costs and drug prices – is clearly the socially favourable reimbursement system, if market entry costs are low with a corresponding low risk of no market entry for new drugs. However, if this is not the case, then either NRP or GRP might be necessary to stimulate market entry. There is then a case for *no reference pricing* – which minimises mismatch costs but maximises drug prices – in countries where drug prices do not play an important role for social welfare due to a dominant pharmaceutical industry. On the other hand, *generic reference pricing* might be the favoured reimbursement system in countries where the pharmaceutical industry is insignificant or non-existent, since GRP leads to lower drug prices than NRP.

6 Concluding remarks

We have analysed the effects of reference pricing systems for pharmaceuticals, focusing on a specific therapeutic market with potentially three pharmaceutical firms. Two of the firms offer horizontally differentiated brand-name drugs. One of these drugs is off-patent and faces competition from a generic version offered by a third firm. The other drug is on-patent, and will be introduced in the market, if the profits are sufficient to cover the entry costs.

This framework has allowed us to compare generic reference pricing (GRP) and therapeutic reference pricing (TRP), as well as the benchmark-case of no reference pricing (NRP). We have shown that TRP triggers competition most, resulting in lower equilibrium prices for

every drug in the therapeutic market. We have also shown that GRP distorts drug choices most, resulting in a higher level of patient health risks – measured in terms of aggregate mismatch costs – than the other two reimbursement systems. Thus, TRP is preferable from the perspective of both the purchaser (payer) and the patients.

Notably, the beneficial role of TRP crucially relies on the assumption that the new on-patent drug enters the market. If the market entry costs are sufficiently high, TRP may in fact result in a worse outcome than both GRP and NRP, as described above. It has, however, been argued that TRP may induce pharmaceutical firms to invest more in drastic innovations, which are not subject to reference pricing, rather than 'me-too' innovations, which very likely will be included in a reference group. The trade-off with respect to therapeutically similar me-too innovations is thus the following: while me-too innovations increase competition and reduce patients' mismatch costs by offering a different variant of treatment for the same illness, they might crowd out drastic innovations if they reduce the budget available for R&D. On the other hand, different drug versions are often innovated in so-called R&D-races, implying that me-too innovations are already in the 'pipeline' of innovations when the first drastic innovation enters the market. A thorough analysis of this issue requires an explicit model of drug innovations, which is outside the scope of the present paper. Thus, we leave this issue for further research.

A Derivation of the price equilibrium

In a vertically separating equilibrium, characterised by a price vector (p_0, p_1, p_G), the following conditions must hold:

Condition 1: $p_G \geq 0$.

Condition 2: $U_L(x, G) \geq U_L(x, 0)$.

Condition 3: $U_H(x, 0) \geq U_H(x, G)$.

Condition 4: $U_H(\widetilde{x}_H, 0) \geq 0$.

Condition 5: $U_L(\widetilde{x}_L, G) \geq 0$.

Condition 6: $\pi_0(p_0, p_1, p_G) \geq \pi_0(\widehat{p}_0, p_1, p_G)$, where $\widehat{p}_0$ solves $U_L(x, G) = U_L(x, 0)$.

Condition 7: $\pi_G(p_0, p_1, p_G) \geq \pi_G(p_0, p_1, \widehat{p}_G)$, where $\widehat{p}_G$ solves $U_H(x, 0) = U_H(x, G)$.

The first condition simply states that the generic price must be non-negative. Conditions 2-3 ensure that the equilibrium really separates, i.e., that H-types choose the brand-name drug 0, while L-types choose the generic substitute. Conditions 4 and 5 secure full market coverage, requiring that the indifferent patients obtain non-negative utility from purchasing and consuming either of the drugs. Finally, Condition 6 (7) ensures that Firm 0 (Firm G) has no incentive to deviate by reducing its price and serve the L-types (H-types).

In the following, we will derive the price equilibrium in detail for the NRP-case. For the two other cases – where the derivation of the equilibrium follows an identical procedure – we will just present the constraints that support the equilibrium.

A.1 No reference pricing (NRP)

Profit functions are given by (7), with $c_i = \alpha p_i$. Let us first confirm that unconstrained pricing by all three firms cannot constitute an equilibrium. Unconstrained maximisation of the firms' profit functions yields the following reaction functions:

$$p_0 = \frac{1}{2\alpha}(t + \alpha p_1), \tag{A1}$$

$$p_1 = \frac{1}{2\alpha}\left[t + (1-\lambda)(1-\theta)\gamma v + \alpha p_G (1-\lambda) + \alpha\lambda p_0\right], \tag{A2}$$

$$p_G = \frac{1}{2\alpha}\left[t + \alpha p_1 - \gamma v (1-\theta)\right], \tag{A3}$$

which yield the following candidate equilibrium prices:

$$p_0 = \frac{1}{\alpha}\left[t + \frac{1}{6}\gamma v (1-\theta)(1-\lambda)\right], \tag{A4}$$

$$p_1 = \frac{1}{\alpha}\left[t + \frac{1}{3}\gamma v (1-\theta)(1-\lambda)\right], \tag{A5}$$

$$p_G = \frac{1}{\alpha}\left[t - \frac{1}{6}\gamma v (1-\theta)(2+\lambda)\right]. \tag{A6}$$

We can show that this price vector always violates Condition 2. In the NRP-case, Condition 2 can be expressed as

$$p_G \leq p_0 - \frac{1}{\alpha}\gamma v (1-\theta). \tag{A7}$$

Using (A4) and (A6), this condition reduces to $1 \geq 2$, which is a contradiction. In other words, (A4)-(A6) cannot be an equilibrium, because p_G is too high to induce even the L-type patients to buy the generic drug. Consequently, we must look for an equilibrium where the generic drug is priced sufficiently low, so that not only the L-types are not induced to switch to drug 0, but firm 0 must also have no incentive to capture the L-types by lowering its price from the equilibrium level.

Using (A1)-(A2), we can express the profit of firm 0 as a function of p_G:

$$\pi_0 (p_G) = \frac{\lambda\left[3t + (1-\lambda)(\alpha p_G + (1-\theta)\gamma v)\right]^2}{2\alpha t (4-\lambda)^2}. \tag{A8}$$

Firm 0 can drive the generic competitor out of the market, and capture equal shares of the H- and L-types, by setting a price

$$\widehat{p}_0 = p_G + \frac{1}{\alpha}\gamma v (1-\theta), \tag{A9}$$

which yields a 'deviation' profit given by

$$\widehat{\pi}_0 (p_G) = \frac{\left[6t - (2+\lambda)(\alpha p_G + (1-\theta)\gamma v)\right](\alpha p_G + (1-\theta)\gamma v)}{2\alpha t (4-\lambda)}. \tag{A10}$$

The optimal strategy for firm G is thus to set a price p_G that is just low enough to make such a deviation unprofitable. This price is given by the solution to

$$\pi_0\left(p_G\right) = \widehat{\pi}_0\left(p_G\right). \tag{A11}$$

We can thus derive the price equilibrium by solving the three equations (A1), (A2) and (A11). The solution is presented as (9)-(11) in Section 3.

It remains to specify Conditions 1-7 for the NRP-case. By construction of the equilibrium, we know that Condition 6 is automatically satisfied. We can also show that Condition 2 is always satisfied. In the NRP-case, this condition is given by

$$\theta\gamma v - \alpha p_G^{NRP} \geq \gamma v - \alpha p_0^{NRP}, \tag{A12}$$

which, using (9) and (11), reduces to

$$\Delta_0 - \Delta_G \geq 0, \tag{A13}$$

which is true for all $\lambda \in (0,1)$. The remainder of the constraints can be expressed in the form of 4 different conditions on t. From (11), we see that a non-negative generic drug price – Condition 1 – is guaranteed if

$$t \geq t_1^{NRP} := \frac{(1-\theta)\gamma v}{3\Delta_G}. \tag{A14}$$

Furthermore, non-negative utility for the indifferent consumers of the H- and L-type, respectively, is guaranteed if

$$t \leq t_4^{NRP} := \frac{2v}{1+3\Delta_0+\Delta_1} \tag{A15}$$

and

$$t \leq t_5^{NRP} := \frac{2\gamma v}{1+\Delta_1+3\Delta_G}. \tag{A16}$$

The necessary Condition 7 is not analytically solvable. However, to simplify, we can find a *sufficient* condition on t that satisfies Conditions 3 and 7 simultaneously. By assuming that H-types always prefer drug 0 over drug G for the equilibrium price p_0^{NRP} and a zero-priced generic drug (i.e., $p_G = 0$), it must be true that H-types always prefer drug 0 in equilibrium

(for a non-negative generic drug price) *and* that price-undercutting by the generic firm in order to capture H-type consumers is not an option. Using p_0^{NRP} from (9), and setting $p_G = 0$, this condition is given by

$$t \leq t_7^{NRP} := \frac{v\,(1-\theta)}{3\Delta_0}. \tag{A17}$$

To sum up, a price equilibrium exists in the NRP-case, and is given by (9)-(11), when $t \in \left[\underline{t}, \overline{t}^{NRP}\right]$, where $\underline{t} := t_1^{NRP}$ and $\overline{t}^{NRP} := \min\left\{t_4^{NRP}, t_5^{NRP}, t_7^{NRP}\right\}$. In general, existence of the equilibrium requires that the share of L-types is relatively low, combined with a sufficiently large difference in gross valuations between the two types. To give an illustrative numerical example, assume that $v = 1$, $\lambda = 0.9$, $\theta = 0.8$ and $\gamma = 0.4$. In this case, $\underline{t} = 0.12$ and $\overline{t}^{NRP} = t_7^{NRP} = 0.20$. Note also that the equilibrium exists for an even wider range of mismatch costs, since the upper bound $\overline{t}^{NRP}$ in this case is a sufficient, but not necessary condition.

A.2 Therapeutic reference pricing (TRP)

The price equilibrium under TRP is derived similarly to the NRP-case and given by (22) in Section 3. As before, Condition 6 is automatically satisfied. Furthermore, Conditions 1 and 2 are identical under NRP and TRP. The remainder of the Conditions – 4, 5 and 3+7 – are given by, respectively,

$$t \leq t_4^{TRP} := \frac{2\,(1-\gamma\,(1-\theta)\,(1-\alpha))\,v}{1+3\Delta_0+\Delta_1-6\Delta_G\,(1-\alpha)}, \tag{A18}$$

$$t \leq t_5^{TRP} := \frac{2\,(\theta+\alpha\,(1-\theta))\,\gamma v}{1+\Delta_1-3\Delta_G\,(1-2\alpha)}, \tag{A19}$$

$$t \leq t_7^{TRP} := \frac{(1-\gamma\,(1-\alpha))\,(1-\theta)\,v}{3\,(\Delta_0-\Delta_G\,(1-\alpha))}. \tag{A20}$$

Thus, under TRP, an equilibrium exists, and is given by (22), when $t \in \left[\underline{t}, \overline{t}^{TRP}\right]$, where $\overline{t}^{TRP} := \min\left\{t_4^{TRP}, t_5^{TRP}, t_7^{TRP}\right\}$. It is worth noting that, due to lower equilibrium prices, the range of mismatch costs for which the equilibrium exists is generally wider under TRP. Using the same numerical example as in the NRP-case, with a 10 per cent co-payment rate ($\alpha = 0.1$), the lower and upper bounds on t are given by $\underline{t} = 0.12$ and $\overline{t}^{TRP} = t_7^{TRP} = 0.34$.

A.3 Generic reference pricing (GRP)

The price equilibrium under GRP is derived similarly to the NRP- and TRP-cases, and given by (25)-(27) in Section 3. As before, Condition 6 is automatically satisfied.

Using (25)-(27), we can derive the remainder of the conditions that support the equilibrium under GRP. Once more, it can be shown that Condition 1 is satisfied if $t \geq \underline{t}$, implying that Condition 1 is identical for all three regimes.

Condition 2 is given by

$$t \geq t_2^{GRP} := \frac{1}{3}(1-\alpha)(1-\theta)\gamma v. \tag{A21}$$

Since $t_1^{GRP} \geq (1-\theta)\gamma v$, it follows that $\underline{t} \geq t_2^{GRP}$. Thus, as long as Condition 1 is satisfied, Condition 2 is also automatically satisfied. Conditions 4 and 5 are given by, respectively,

$$t \leq t_4^{GRP} := \frac{2\widetilde{\Delta}v + (1-\alpha)(1-\theta)\gamma v\left(3(2+\alpha) + \varkappa - 2\widehat{\Delta}\right)}{\widetilde{\Delta} + \overline{\Delta} + 15\alpha - 3\lambda\alpha(4-\alpha-\lambda) - 3(1-\lambda)(2-\lambda) + 3\varkappa}, \tag{A22}$$

where

$$\varkappa := \sqrt{1-\lambda}\left[2 + \lambda - \alpha(5-2\lambda)\right],$$

and

$$t \leq t_5^{GRP} := \gamma v \frac{\widetilde{\Delta}(1+\theta) + (1-\theta)\left[(1-\alpha)\left[2(2+\alpha) + \varsigma\right] - \widehat{\Delta}(1-2\alpha)\right]}{\widetilde{\Delta} + \overline{\Delta} + 3\alpha\left[4 - \lambda(3-\alpha-\lambda)\right] + 3\varsigma}, \tag{A23}$$

where

$$\varsigma := \sqrt{1-\lambda}\left(\lambda(2\alpha+1) - 6\alpha\right).$$

Finally, the sufficient condition that simultaneously satisfies Condition 3 and Condition 7 is given by

$$t \leq t_7^{GRP} := \frac{(1-\theta)\left(\widetilde{\Delta}v + \gamma v(1-\alpha)\left(2 + \alpha + \sqrt{1-\lambda}(2-\alpha(3-\lambda)) - \widehat{\Delta}\right)\right)}{3\left(5\alpha + \lambda(1-\alpha)(3-\alpha-\lambda) + \sqrt{1-\lambda}(2-\alpha(3-\lambda)) - 2\right)}. \tag{A24}$$

Thus, under GRP, an equilibrium exists and is given by (25)-(27), when $t \in \left[\underline{t}, \overline{t}^{GRP}\right]$, where $\overline{t}^{GRP} := \min\left\{t_4^{GRP}, t_5^{GRP}, t_7^{GRP}\right\}$. Once more, due to the general price reducing effect of reference pricing, the range of mismatch costs for which the equilibrium exists is generally

wider under the GRP system compared to the NRP case. Using the same numerical example as previously, the lower and upper bounds on t are given by $\underline{t} = 0.12$ and $\overline{t}^{GRP} = t_7^{GRP} = 0.29$.

B Equilibrium profits under GRP

Equilibrium profits under generic reference pricing are given by

$$\pi_0^{GRP} = \frac{\left(2+\alpha-\sqrt{1-\lambda}\,(2-\lambda-\alpha)\right)^2\Gamma^2\lambda}{2t\widetilde{\Delta}^2}, \tag{B1}$$

$$\pi_1^{GRP} = \frac{(3t-\Gamma)\left(\Omega-2\sqrt{1-\lambda}\,(\lambda-2\alpha+\alpha\lambda)\,\Psi\right)+t^2\left(6\sqrt{1-\lambda}\,(\lambda-2\alpha+\alpha\lambda)\,\overline{\Delta}+\Phi\right)}{2t\alpha\widetilde{\Delta}^2}, \tag{B2}$$

$$\pi_G^{GRP} = \frac{\Gamma\left(\alpha\,(2-\lambda)+\lambda\,(3-\lambda)+\sqrt{1-\lambda}\,(2\alpha+\lambda)\right)(1-\lambda)\,\Theta}{2t\widetilde{\Delta}^2}, \tag{B3}$$

where

$$\Omega := 2t\omega_1+\gamma v\,(1-\alpha)\,(1-\theta)\,\omega_2,$$

$$\begin{aligned}\omega_1 \;:\; &= 64\alpha\lambda+8\alpha^2+2\lambda^2+9\lambda^3-12\lambda^4+6\lambda^5-\lambda^6\\ &-86\alpha\lambda^2-8\alpha^2\lambda+40\alpha\lambda^3+4\alpha^3\lambda-6\alpha\lambda^4+19\alpha^2\lambda^2\\ &-13\alpha^2\lambda^3-4\alpha^3\lambda^2+3\alpha^2\lambda^4+2\alpha^3\lambda^3,\end{aligned}$$

$$\begin{aligned}\omega_2 \;:\; &= 16\alpha\lambda+8\alpha^2+26\lambda^2-41\lambda^3+26\lambda^4-8\lambda^5+\lambda^6-30\alpha\lambda^2-16\alpha^2\lambda\\ &+28\alpha\lambda^3-12\alpha\lambda^4+2\alpha\lambda^5+13\alpha^2\lambda^2-5\alpha^2\lambda^3+\alpha^2\lambda^4,\end{aligned}$$

$$\begin{aligned}\Psi \;:\; &= \gamma v\,(1-\alpha)\,(1-\theta)\left(2\alpha+5\lambda-2\alpha\lambda-4\lambda^2+\lambda^3+\alpha\lambda^2\right)\\ &+2t\left(2\alpha-7\lambda+7\lambda^2-2\lambda^3-\alpha\lambda^2+\alpha^2\lambda\right),\end{aligned}$$

$$\begin{aligned}\Phi \;:\; &= 136\alpha^2-16\alpha\lambda+10\lambda^2-5\lambda^3+2\lambda^4-4\lambda^5+\lambda^6+82\alpha\lambda^2\\ &-192\alpha^2\lambda-60\alpha\lambda^3+40\alpha^3\lambda+16\alpha\lambda^4-2\alpha\lambda^5+105\alpha^2\lambda^2\\ &-13\alpha^2\lambda^3-24\alpha^3\lambda^2-3\alpha^2\lambda^4+4\alpha^3\lambda^3+4\alpha^4\lambda^2,\end{aligned}$$

$$\Theta := 3t\left(\alpha\lambda - 3\lambda + \lambda^2 + 4\right) - \gamma v\left(1-\theta\right)\widehat{\Delta} - \sqrt{1-\lambda}\left(4-\lambda\right)\Gamma.$$

C Equilibrium mismatch costs

Inserting the expressions for the locations of indifferent patients in the different reimbursement regimes – reported throughout Section 3 – into (36), equilibrium mismatch costs are given by

$$C_{NRP} = C_{TRP} = \frac{\left(\delta - 6\sqrt{1-\lambda}\left(5\lambda+4\right)\left(1-\lambda\right)^3\right)t}{4\left(3\lambda - 3\lambda^2 + \lambda^3 + 8\right)^2}, \tag{C1}$$

where

$$\delta := 104 + 6\lambda - 78\lambda^2 + 53\lambda^3 - 15\lambda^4 + 15\lambda^5 - 4\lambda^6,$$

and

$$C_{GRP} = \frac{\left(3t-\Gamma\right)\left[\left(3t-\Gamma\right)\left(2\sqrt{1-\lambda}\Upsilon - \Lambda\right) + 2t\left(\sqrt{1-\lambda}\mu - \eta\right)\right] + t^2\left(\digamma + 6\xi\sqrt{1-\lambda}\right)}{4t\widetilde{\Delta}^2}, \tag{C2}$$

where

$$\begin{aligned}
\xi \;:\; &= 16\alpha\lambda - 12\lambda - 4\alpha^2 + 23\lambda^2 - 17\lambda^3 + 4\lambda^4 - 18\alpha\lambda^2 + 5\alpha^2\lambda \\
&\quad + 4\alpha\lambda^3 - 2\alpha^3\lambda + \alpha\lambda^4 - 3\alpha^2\lambda^2 + 2\alpha^2\lambda^3 + \alpha^3\lambda^2,
\end{aligned}$$

$$\begin{aligned}
\digamma \;:\; &= 72\lambda + 64\alpha\lambda + 104\alpha^2 - 94\lambda^2 + 74\lambda^3 - 53\lambda^4 + 25\lambda^5 - 4\lambda^6 \\
&\quad - 150\alpha^2\lambda - 30\alpha\lambda^3 + 20\alpha^3\lambda + 44\alpha\lambda^4 - 10\alpha\lambda^5 + 66\alpha^2\lambda^2 \\
&\quad + 7\alpha^2\lambda^3 - 12\alpha^3\lambda^2 - 6\alpha^2\lambda^4 + 2\alpha^3\lambda^3 + 2\alpha^4\lambda^2 - 40\alpha\lambda^2,
\end{aligned}$$

$$\begin{aligned}
\Lambda \;:\; &= 12\lambda^3 - 16\alpha\lambda - 8\alpha^2 - 2\lambda^2 - 8\lambda - 7\lambda^4 + \lambda^5 + 24\alpha\lambda^2 \\
&\quad + 14\alpha^2\lambda - 14\alpha\lambda^3 + 2\alpha\lambda^4 - 8\alpha^2\lambda^2 + \alpha^2\lambda^3,
\end{aligned}$$

$$\Upsilon := 8\alpha\lambda - 4\lambda + 4\alpha^2 + 5\lambda^2 - 4\lambda^3 + \lambda^4 - 10\alpha\lambda^2 - 5\alpha^2\lambda + 3\alpha\lambda^3 + 2\alpha^2\lambda^2,$$

$$\begin{aligned}\mu \;\; : \;\; &= 24\lambda - 40\alpha\lambda - 8\alpha^2 - 38\lambda^2 + 29\lambda^3 - 7\lambda^4 + 48\alpha\lambda^2 + 10\alpha^2\lambda \\ &-13\alpha\lambda^3 + 2\alpha^3\lambda - \alpha\lambda^4 - 3\alpha^2\lambda^2 - 2\alpha^2\lambda^3 - \alpha^3\lambda^2,\end{aligned}$$

$$\begin{aligned}\eta \;\; : \;\; &= 24\lambda - 8\alpha\lambda + 8\alpha^2 - 34\lambda^2 + 21\lambda^3 - 12\lambda^4 + 6\lambda^5 - \lambda^6 \\ &+16\alpha\lambda^2 - 14\alpha^2\lambda - 20\alpha\lambda^3 - 2\alpha^3\lambda + 15\alpha\lambda^4 - 3\alpha\lambda^5 \\ &-5\alpha^2\lambda^2 + 11\alpha^2\lambda^3 + 2\alpha^3\lambda^2 - 3\alpha^2\lambda^4 - \alpha^3\lambda^3.\end{aligned}$$

D Proofs

Proof of Proposition 3

In equilibrium, the price difference between the two brand-name drugs is given by

$$p_1^{GRP} - p_0^{GRP} = \frac{\gamma v\,(1-\alpha)\,(1-\theta)\left[\widehat{\Delta} - 4 + \alpha^2 - \sqrt{1-\lambda}\left(\lambda - \alpha^2\right)\right] + t\sigma}{\alpha\widetilde{\Delta}}, \qquad \text{(D1)}$$

where

$$\sigma := 4\alpha + \lambda - 6\alpha\lambda - 3\alpha^2 + 2\lambda^2 - \lambda^3 + \alpha\lambda^2 + 2\alpha^2\lambda + 3\sqrt{1-\lambda}\left(\lambda - \alpha^2\right).$$

By the definition of $\widehat{\Delta}$, it can easily be verified that the sum of the four terms in the square brackets in the numerator in (D1) is positive for $\alpha \in (0,1)$ and $\lambda \in (0,1)$. The sign of the expression depends thus on the sign of σ. Once more, it is relatively straightforward to verify that $\sigma > 0$ for all $\lambda \in (0,1)$ if $\alpha < \frac{2}{3}$. Thus, $\alpha < \frac{2}{3}$ is a *sufficient* condition for $p_1^{GRP} > p_0^{GRP}$.

Regarding equilibrium market allocations, we derive from (33) that

$$\widetilde{x}_L^{GRP} > \frac{1}{2} \quad if \quad t > \gamma v\,(1-\theta)\,\beta,$$

where

$$\beta := (1-\alpha)\,\frac{\sqrt{1-\lambda}\,(2\alpha+\lambda) + 2\alpha + \lambda\,(3-\lambda-\alpha)}{3\sqrt{1-\lambda}\,(2\alpha+\lambda) - 2\alpha + \lambda + 3\alpha\lambda + 2\lambda^2 - \lambda^3 - 2\alpha\lambda^2 - \alpha^2\lambda}.$$

It is fairly straightforward to verify that $\beta < 1$ for $\alpha \in (0,1)$ and $\lambda \in (0,1)$. This implies that $t > \gamma v\,(1-\theta)\,\beta$ (and thus $\widetilde{x}_L^{GRP} > \frac{1}{2}$) as long as Condition 1 (non-negative generic price) is

satisfied.

Now consider the indifferent type-H patient. From (32) we can characterise $\widetilde{x}_H^{GRP}$ as a function of t in the following way:

$$\frac{\partial \widetilde{x}_H^{GRP}}{\partial t} > 0 \quad for \quad t \neq 0,$$

$$\lim_{t \to 0^+} \left(\widetilde{x}_H^{GRP}\right) \to -\infty,$$

and

$$\lim_{t \to -\infty} \left(\widetilde{x}_H^{GRP}\right) = \lim_{t \to \infty} \left(\widetilde{x}_H^{GRP}\right) = \vartheta,$$

where

$$\vartheta := \frac{3\left(2 + \alpha - \sqrt{1-\lambda}\,(2 - \lambda - \alpha)\right)}{2\widetilde{\Delta}}.$$

It follows that $\widetilde{x}_H^{GRP} < \frac{1}{2}$ for $t > 0$ if $\vartheta < \frac{1}{2}$ for $\alpha \in (0,1)$ and $\lambda \in (0,1)$. On the other hand, if $\vartheta > \frac{1}{2}$ for some combinations of λ and α, it must be that $\widetilde{x}_H^{GRP} > \frac{1}{2}$ if t is sufficiently high. Solving $\vartheta = \frac{1}{2}$ for α yields a function $\alpha^*(\lambda)$, such that $\vartheta < (>)\, \frac{1}{2}$ if $\alpha < (>)\, \alpha^*(\lambda)$. It is straightforward to verify that $\partial \alpha^* / \partial \lambda > 0$ and that $\alpha^* < 0$ for $\lambda < 0.54$. It follows that $\widetilde{x}_H^{GRP} < \frac{1}{2}$ if $\lambda < 0.54$, whereas, for $\lambda > 0.54$, $\widetilde{x}_H^{GRP} > \frac{1}{2}$ if λ and/or t are sufficiently high. By numerical simulations, it is also straightforward to verify that both cases, $\widetilde{x}_H^{GRP} < \frac{1}{2}$ and $\widetilde{x}_H^{GRP} > \frac{1}{2}$, can occur in equilibrium. *Q.E.D.*

Proof of Proposition 5

A direct analytical comparison of equilibrium profits for firm 1 under the three different regimes is infeasible, since the equilibrium profit expression under GRP is extremely messy. However, we can prove the proposition via a somewhat more subtle route, by considering how different reimbursement systems affect equilibrium prices and market shares. From Proposition 3 we know that there is a clear-cut ranking of equilibrium prices across the different regimes, where $p_i^{NRP} > p_i^{GRP} > p_i^{TRP}$, $i = 0, 1, G$. Regarding equilibrium market shares, we know that these are identical under NRP and TRP. Furthermore, we also know that $\widetilde{x}_j^{GRP} > \widetilde{x}_j^{TRP} = \widetilde{x}_j^{NRP}$, $j = H, L$. Thus, since $p_1^{NRP} > p_1^{GRP} > p_1^{TRP}$ and demand is at least as high under NRP than under any other reimbursement regime, it follows unambiguously that $\pi_1^{NRP} > \max\left\{\pi_1^{GRP}, \pi_1^{TRP}\right\}$. Regarding the comparison between GRP and TRP, it is not immediately obvious that firm 1 earns higher profits under GRP, since prices are higher,

but market shares are lower, compared with TRP. Note, however, that equilibrium prices are higher for *all* firms under GRP, compared with TRP. Furthermore, we know that, for given prices, $c_1^{GRP} < c_1^{TRP}$. Thus, if firm 1 unilaterally deviates from the GRP equilibrium by setting a price equal to the equilibrium price under TRP, this firm will increase its market shares, in both consumer segments, *beyond* its equilibrium market shares under TRP, and consequently earn higher profits than under TRP. Such a deviation is not profitable, so firm 1 must earn even higher profits in the GRP equilibrium, where $p_1^{GRP} > p_1^{TRP}$. *Q.E.D.*

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