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ABSTRACT

How Do Drug Prices Respond to a Change from External to Internal Reference Pricing? Evidence from a Danish Regulatory Reform^{*}

We study the effects of a change in the way patient reimbursements are calculated on the prices of pharmaceuticals using quasi-experimental data for Denmark which switched from external (where reimbursements are based on prices of similar products in foreign countries) to internal reference pricing (where they are based on the cheapest domestic substitute). We analyze three therapeutic classes with different treatment durations and show that the reform led to substantial price decreases for our lifelong treatment and to less substantial price reductions for our medium duration treatment while we do not find significant effects on our acute treatment. Moreover, the reform did only affect generics and did not impact original products or parallel imports.

NON-TECHNICAL SUMMARY

While it is widely accepted that reference price systems, where the amount of patient reimbursements for pharmaceuticals products is determined by a reference price, lead to price reductions and a decrease in health care expenditures, little is known about the design of such systems. A particularly important question is whether the reference price should be “externally” determined (via prices of similar products in other countries) or whether it should be “internally” determined by the price of the cheapest substitute.

We study the effect of a switch from external to internal reference pricing in Denmark that took place in April 2005. Our central finding is that there is a statistically and economically significant price decrease for anti-cholesterols only. For anti-ulcerants, which are taken for up to six months, we find statistically significant but economically much smaller effects. For antibiotics, which are prescribed for a few days only, there is no statistically significant effect at all. These findings highlight that for such a reform to matter, patients need to be experienced consumers and to be well informed about their substitution possibilities.

JEL Classification: I18, C23

Keywords: pharmaceutical markets, regulation, reference pricing, treatment duration

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1 Introduction

The use of reference pricing systems to calculate patients' reimbursement for prescription drugs constitutes a worldwide embraced tool to curb medical expenses (Berndt and Dubois 2012; Espín et al. 2011; López-Casasnovas and Puig-Junoy 2000). These systems aim at benefiting patients who prefer cheaper products over more expensive ones, thus targeting patients' price sensitivity and inducing competitive pressure on firms.

There exists a large body of empirical evidence that shows that such systems indeed are effective in curtailing drug prices (Aronsson et al. 2001; Brekke et al. 2007, 2009, 2011; Danzon and Liu 1998; Kanavos et al. 2008; Pavcnik 2002; Puig-Junoy 2007). Much less is known, however, about the consequences of the *design* of such systems on prices. One particularly important design feature is whether an internal or an external reference price system is used. Our paper studies the effects of a switch from external reference pricing to internal reference pricing that was implemented in Denmark in April 2005. Before the reform, the reference price was calculated as the average price of similar products in other European countries. After the reform, the reference price is set equal to the cheapest domestic price of a substitute product. The reform affected all prescription drugs in Denmark, independent of their patent status.

We empirically study the reform effects using a comprehensive panel set that covers three therapeutic markets over the time period 2003 to 2006. There are two main mechanisms through which the reform should drive down prices. First, it should create incentives for patients to buy the cheapest product within a set of substitutes since they else need to pay the full price difference out of their own pockets.¹ Second, before the reform, prices tended to cluster at the European average level since the external reference pricing system did not provide any incentives to set domestic prices below that level.

We speculate that the effects of the reform on prices vary with (i) the duration of a patients' medical condition, (ii) the type of the drug producer and (iii) the competitive situation. Regarding the duration of treatment, we separately consider anti-cholesterol drugs that are taken lifelong, antiulcerants that are taken between six weeks and six months and antibiotics whose treatments only lasts a few days. Our prior is that patients with more

¹This argument is formalized by Brekke et al. (2009, 2011)

chronic conditions are more price sensitive than patients with an acute condition. Apart from a chronic condition being associated with higher total expenditures, patients in longer treatments are likely to be more experienced and better informed about their substitution options and the (perceived) quality of the products. Regarding the type of producer, we differentiate original producers, generic producers and parallel importers.² Previous studies have found that original producers keep their prices high and are able to retain substantial market shares despite the rise of competition, e.g. after patent expiration. This behavior has been attributed to heterogeneity in consumer price sensitivity and brand-loyalty generated by first-mover advantages (Caves et al. 1991; Frank and Salkever 1997; Grabowski and Vernon 1992). Since our reform targets consumers' price sensitivity, we expect that the switch from external to internal reference pricing affects generics prices more than originals.³ Regarding market competition we, similarly to the seminal work of Pavcnik (2002) who studies a switch from price cap to external reference pricing in Germany, allow the reform effects to vary with product market competition. In the limiting case of a monopoly, the own price constitutes the reference price and producers are hence not affected by competition or external reference prices. By contrast, if competition within the set of substitutes is intense, each competitor has incentives to lower prices in order to secure market shares. We therefore expect the reform effects to be stronger in markets with more available substitutes.

Apart from Pavcnik (2002), whose findings suggest that producers substantially reduced prices after the German reform, other relevant work includes Brekke et al. (2009, 2011) as well as Kaiser et al. (2014). Like Pavcnik (2002), Brekke et al. (2009, 2011) study a switch from price cap to reference price regulation in Norway, showing that the reform effectively

²Original producers engage in R&D using intellectual property rights to protect their innovations. Generic firms produce drugs that are bioequivalent copies of original products and may only legally enter the market after the respective patents have expired. Parallel importers do not engage in manufacturing and instead buy products in low-price countries, repackage, relabel, and resell them in high-price countries. Parallel importing is legal within the European Union and in Denmark it is permitted for both on-patent and off-patent pharmaceuticals. Méndez (2014) offers a thorough analysis of the market for parallel imports in Denmark.

³In addition, we expect parallel imports to react more similarly to originals than compared to generics since a substantially higher share of parallel imported products are originals.

reduced consumer prices for both original and generic products. In Kaiser et al. (2014), we conduct a welfare analysis of the Danish change from external to internal reference pricing. Our previous analysis focuses on anti-cholesterol products only and shows that the reform effects are stronger for generics than for branded drugs. The present analysis extends our earlier work by additionally analyzing treatments for semi-chronic and acute conditions.

We find that the switch from external to internal reference pricing primarily affected generic drugs while prices for parallel imports and originals have remained unchanged. The negative price effect for generics is larger the longer the treatment lasts — the effects are both statistically and economically most significant for anti-cholesterols, economically much smaller for anti-ulcerants and statistically insignificant for antibiotics. Stronger competition reinforces the reform effects for anti-cholesterols only while there are no such effects for the other two treatments.

2 Institutional Background

In Denmark, producers of pharmaceuticals are free to set prices. They must, however, fortnightly report them to the Danish Medicines Agency (DKMA). DKMA makes them publicly available online under URL <http://medicinpriser.dk> which also constitutes the source of our data. The number and location of pharmacies as well as their markups are regulated by the government. Danish pharmacists are required to offer the cheapest product, usually a generic, among available substitutes but patients may opt for a more expensive substitute. In that case, they have to pay the price difference out of their own pockets. The level of patients copayments is calculated on the basis of a patient's own annual expenditures and the reference price. In particular, a patient's co-payment p^c is the difference between the pharmacy retail price (list price, p^l) and the product of the reimbursement rate ρ and the reference price, $p^c = p^l - \rho p^r$. Consumers in chronic treatments get as much as 80 percent of their expenses reimbursed, while patients with an acute condition obtain only around 40 percent refund.

The reference price reform took effect on April 1, 2005. Before the reform, the reference price for a given product was defined as the pharmacy retail price of the chosen product up to the average price of the same product in the EU-15 member states, excluding Greece,

Luxembourg, Spain, and Portugal. Once the retail price exceeded the EU average price, the reference price was set equal to the EU average price. After the reform, the reference price was set to be equal to the cheapest domestic price among available substitutes. Substitution groups are defined by the Danish Medicines Agency on the basis of active substance, administration form, strength and package size.

Our analysis focuses on a base period during which no information about prospective changes in the regulatory system was available. This period lasted from September 15, 2003 to June 7, 2004. Our treatment period covers the time span between April 1, 2005, when the reform took effect, and September 25, 2006, when a new regulatory measure was introduced.

3 Data

Our data set contains fortnightly prices and other characteristics of pharmaceutical products in three therapeutical markets: 228 anti-cholesterols, 251 antiulcerants, and 152 antibiotics that we observe for 59 fortnightly time periods. This amounts to a total of 21,895 observations on 631 unique products. We normalize prices using the World Health Organization defined daily dosages (DDD) to make products of different strengths and package sizes comparable.

The Appendix displays descriptive statistics of our variables. The table shows that one DDD of antibiotics costs on average more than one DDD of statins or antiulcerants. Average reference prices are higher than average pharmacy purchase prices since the latter do not include prescription fees or taxes. The average number of products and the average number of producers is relatively stable between the two time periods. The average number of substitution groups and the average number of products in a substitution group differs substantially across markets with antibiotics having around 80 different substitution groups with around two products each and anti-cholesterols less than 40 substitution groups and each with around six products. Antiulcerants constitute an intermediate case. The table also shows that the share of generics in the chronic and semi-chronic conditions is higher than the share of original products. Parallel imports are also well represented in these groups. This is different for antibiotics where originals dominate.

4 Empirical Approach

Our dependent variable pharmacy purchase price in DDD is skewed and non-negative which implies that log-linear regression is not advisable as it leads to inconsistent estimates in the presence of heteroskedasticity. We therefore follow a suggestion by Santos Silva and Tenreyro (2006) and use a Poisson pseudo-maximum-likelihood estimator instead. The coefficients in this model are semi-elasticities which makes them directly interpretable. Following Pavcnik (2002), our regression equation takes the following form:

$$\exp(p_{jt}^f) = \rho R_t + \alpha_1 R_t * d_{jt}^{op} + \alpha_2 R_t * d_{jt}^{pi} + \gamma_1 z_{jt} + \gamma_2 R_t * z_{jt} + \mathbf{X}_{jt} + \mu_j + \epsilon_{jt}, \quad (1)$$

where R_t denotes a dummy variable that is coded one in the treatment period and zero otherwise. The terms d^{op} and d^{pi} constitute dummy variables that indicate if the product is an original (“op”) or if it is a parallel import (“pi”) respectively. We interact these dummy variables with the reform dummy to allow for different reform effects for different types of producers. The variable z_{jt} denotes the number of products in a substitution group that measures the current competitive situation of product j at time t . We interact z_{jt} with the reform dummy to allow competition for having different effects on prices before and after the reform. The term μ_j lumps together all product-specific time-invariant characteristics of product j like strength, active ingredient, package size and substitution group. We hence do not need to separately account for them. The variables included in vector \mathbf{X}_{jt} are a dummy indicating if the product belongs to the prescription (combination of strength and package size) with highest sales in period t and a set of time dummies. The “common dosage” dummy constitutes another measure of a product’s competitive situation and captures learning by physicians and patients as new drugs become available or as older drugs’ patents expire. The term ϵ_{jt} is an iid normal distributed error term.

5 Results

Table ?? displays our estimation results. Our most parsimonious model, shown in columns (1) includes a dummy variable for the reform only. The associated coefficient is to be interpreted as a 46 percent decrease in prices for anti-cholesterols. There are no statistically

significant effects for anti-ulcerants and antibiotics. The other specifications, displayed in columns (2) to (5), additionally include a set of time and product name dummies. Including these almost halves the reform effect on anti-cholesterols and leaves the results for the two other drug types unaffected as shown in columns (2).

In columns (3), we allow the reform effects to differ between different types of drug producers. The reform dummy is now to be interpreted as the effect of the reform on generics, while the sum of the coefficient on the reform dummy and the coefficients on the interactions $reform \times OP$ and $reform \times P$ constitutes the reform effect on originals and parallel imports, respectively. The coefficients on the interaction variables alone are to be interpreted as the percentage deviation from the reform effect on generics. Column (3) in Table ?? shows that the reform induced a price reduction of generic anti-cholesterols by 61 percent. The effect on parallel imports is -27.1 percent (-61 percent+33.9 percent) and statistically weakly significant as shown on the bottom of the table. By contrast, the effect is statistically insignificant for original products. While we neither find statistically significant effects on generic or original anti-ulcerants, we do find statistically significant negative effects on parallel imports. Our results for antibiotics are qualitatively similar to the ones for anti-cholesterols but economically substantially smaller. The reform effect on generics is estimated to be -4.6 percent and is weakly significant. For parallel imports, it is -29.7 percent. The latter results is to be interpreted with caution since there are only two parallel imported drugs in the antibiotics market.

Specification (4) additionally controls for the number of substitutes a product is facing competition from as well as its interaction with the reform dummy. The coefficient on the interaction term is statistically significantly negative for anti-cholesterols only while it is statistically insignificant for the other two treatments. This may indicate that consumers are better aware of their substitution possibilities in life-long treatments compared to treatments of shorter duration which makes them more willing to switch to cheaper substitutes once the reference pricing system changes. The effect of the number of substitutes before the reform is negative and statistically significant for antiulcerants and antibiotics, but not for anti-cholesterols. We attribute the latter effect to the importance of brand loyalty in this market.⁴ Controlling for competition reduces the coefficient on the reform dummy

⁴Running the same specification for anti-cholesterols leaving out the name dummies results in a negative

variable for anti-cholesterol generics to -33.2. The reform effect rises with the number of competitors; it is -52.7 percent for the average number of competitors in a substitution group. Controlling for competition makes the reform effect on parallel imported drugs statistically insignificant. Similarly, the effect on parallel imported anti-ulcerants becomes statistically insignificant while the results now show that it entailed statistically weakly significant price reductions of 3.2 percent for generic anti-ulcerants. Our estimation results for antibiotics are qualitatively and quantitatively similar to the ones that did not control for competition.

Finally, columns (5) additionally include common dosages. This additional control variable does not affect any of the results we already discussed and is statistically significant and negative only for statins and antiulcerants.

6 Conclusion

While reference price systems constitute widely embraced cost containment tools, little is known about their design. Using data on a reference price reform in Denmark, we study how effective internal reference pricing is compared to external reference pricing in bringing down prices for prescription drugs. Our analysis also studies what difference it makes (i) how long a medical treatment with a particular drug lasts, (ii) if the drug is a generic, a parallel import or an original and (iii) what role competition plays. We show that the switch from external to internal reference pricing lead to substantial price reduction for anti-cholesterol generics and much less substantial reductions for anti-ulcerants generics. By contrast, prices of original products and, by and large, parallel imports, have remained unchanged. In addition, we only find statistically significant and economically substantial effects for longer treatments while the reform did not affect prices for antibiotics. Finally, competition statistically and economically moderates the reform effects for anti-cholesterols only while it does not have a statistically significant additional effects on the two treatments of shorter duration.

Overall, our findings suggest that internal reference pricing is likely to only drive down and significant sign which corresponds well with the “generic competition paradox” (Grabowski and Vernon, 1992) where original producers increase prices when faced by more intense competition.

prices of drugs for treatments of long duration. They also underscore how important it is that consumers are well informed about their substitution options for any competition-enforcing reform to have any statistically and economically significant effect.

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Appendix: descriptive statistics

Table 2: **Summary statistics**

Type of treatment	Variable	Before reform		After reform	
		Mean	Std. Dev.	Mean	Std. Dev.
Anti-cholesterol	Pharmacy purchase price p^f	6.18	4.48	3.90	4.33
	Reference price p^r	7.38	5.51	4.35	5.36
	Number of products	125.72	4.50	123.00	12.97
	Number of firms	19.00	0.46	21.89	2.36
	Number of substitution groups	39.90	0.64	38.95	0.98
	Products in substitution group	6.94	4.56	5.01	2.57
	Original product (=1 if original)	0.30	0.46	0.28	0.45
	Generic product (=1 if generic)	0.43	0.50	0.56	0.50
	Parallel import (=1 if pi)	0.27	0.45	0.16	0.37
	Total Observations	2,511		4,617	
Antiulcerants	Pharmacy purchase price p^f	6.70	7.01	6.43	6.84
	Reference price p^r	10.37	11.56	9.43	10.71
	Number of products	130.35	2.43	145.55	15.50
	Number of firms	22.65	0.49	21.33	0.93
	Number of substitution groups	69.30	1.81	60.59	1.25
	Products in substitution group	3.01	2.10	3.58	1.96
	Original product (=1 if original)	0.32	0.47	0.18	0.39
	Generic product (=1 if generic)	0.55	0.50	0.59	0.49
	Parallel import (=1 if pi)	0.13	0.34	0.23	0.42
	Total Observations	2,606		5,610	
Antibiotics	Pharmacy purchase price p^f	7.54	9.81	7.53	16.74
	Reference price p^r	13.95	17.99	13.45	24.48
	Number of products	124.45	2.55	104.29	3.50
	Number of firms	11.75	0.79	10.87	0.61
	Number of substitution groups	84.05	1.61	76.64	2.19
	Products in substitution group	2.00	1.24	1.68	0.86
	Original product (=1 if original)	0.61	0.49	0.59	0.49
	Generic product (=1 if generic)	0.38	0.48	0.39	0.49
	Parallel import (=1 if pi)	0.02	0.13	0.02	0.14
Total Observations	2,488		4,759		

Notes: The Appendix reports summary statistics for all variables in each therapeutic group. Prices are fortnightly averages for a defined daily dose in Danish kroner. All figures deflated using consumer prices index with June 2005 as basis. Exchange rates in June 2005: DKK 1 = \$ 0.1634 = €0.1343.