Identifying Industry Margins with Unobserved Price Constraints: Structural Estimation on Pharmaceuticals

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Abstract

This paper develops a structural model to investigate the effects of pharmaceutical price regulation on demand and on manufacturers' price-setting behavior in France. We estimate price-cost margins in a regulated market with unknown price constraints and infer whether these constraints are binding. Once the shape of demand is recovered, the identification strategy exploits cost restrictions across drugs, which come from observing the same drugs in potentially price constrained markets (France) and in markets where prices are unregulated (the US and Germany). Using data on the anti-ulcer market from 2003 to 2013, we find that some drugs are significantly constrained by regulation. Counterfactual simulations suggest that price constraints generated some modest savings (approximately 3% of total expenses) and increased consumer surplus, relative to a free pricing scenario. These effects come from shifting consumption towards branded drugs at the expense of generics. On the contrary, a policy defining price caps by average prices in other countries (external reference pricing) would increase generic penetration and generate additional savings and consumer surplus, by reducing all prices, particularly those of generics.

Key words: empirical IO, price constraints, Bertrand competition, regulation, pharmaceuticals, anti-ulcer drugs.

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1 Introduction

Understanding the role played by regulatory constraints is of major importance in an industry such as pharmaceuticals, where regulation is pervasive throughout all stages of drug development and commercialization. However, the extent of regulation once a drug has been marketed differs across countries. Some countries make commercialization of prescription drugs subject to price negotiations with the national health care system, while others allow manufacturers to freely choose prices. In the US, prices are not regulated once drugs are approved by the Food and Drug Administration (FDA); on the contrary, France has traditionally been very active in regulating the pricing of pharmaceuticals covered by public health insurance. Due to rising drug expenditures in the 1990s, French pharmaceutical regulation underwent a process of reform in the 2000s, resulting in major changes. These include a cap on reimbursements for branded drugs after generic entry and stricter requirements on price levels and their evolution over time. These regulatory changes targeted both demand and supply, by affecting the drug choices of prescribers, pharmacists, and patients and the pricing decisions of firms. They may have squeezed pharmaceutical manufacturers' margins. Our difference-in-difference evidence on the effects of the price cuts introduced in 2006 suggests that prices declined significantly as a consequence of this reform, on average by 30% for the drugs subject to this policy.

This paper develops a structural model to investigate the effects of price regulation in France. We estimate price-cost margins in a regulated market with unknown price constraints and infer whether these constraints are binding. Once the shape of demand is recovered, the identification strategy relies on assumptions on the price competition game played by firms and the knowledge that some markets are not price constrained, which allows for the use of cost restrictions across drugs and markets. We investigate whether the current price-setting regulation in France imposes binding constraints on the prices of anti-ulcer drugs, using US and Germany as the unconstrained markets. With IMS data on drug sales from 2003 to 2013, we evaluate the counterfactual free pricing equilibrium and a different regulated equilibrium based on external reference pricing, a policy that was recently implemented in France. These comparisons allow us to quantify changes

in prices, demand, and spending due to price regulation. Estimating demand is the first step of our analysis and requires a flexible yet tractable model able to capture the differentiation and substitution patterns among anti-ulcer drugs. Moreover, we expect considerable heterogeneity in demand parameters that must be taken into account in the estimation (Ching, 2010a and 2010b). Following demand estimation in empirical IO (Berry, 1994; Berry, Levinsohn and Pakes, 1995 (BLP); Nevo, 2000 and 2001), we use a random coefficient logit model to allow for heterogeneity in preferences over drug characteristics and for price disutilities. Björnerstedt and Verboven (2016) use this approach to examine the demand for pain-killers in a Swedish merger analysis. Other works have applied random coefficient logit to individual-level data to explore the role of drug quality and innovation in determining welfare (Dunn, 2012; Yin, 2012). Our demand specification accounts for quality, by including quality-related drug characteristics, and for advertising (primarily in the form of detailing, the practice of sending pharmaceutical sales representatives to physicians, because direct-to-consumer advertising (DTCA) for prescription drugs is forbidden in Europe). The literature has shown that detailing is the form of marketing most effective at increasing sales (Berndt, Bui, Railey and Urban, 1996; Azoulay, 2002; Berndt, Pindyck and Azoulay, 2003; Arcidiacono, Ellickson, Landry and Ridley, 2013, for anti-ulcer drugs) and at decreasing price elasticity (Rizzo, 1999; Donohue and Berndt, 2004). However, different forms of advertising (detailing, DTCA) and scientific information can be complementary under uncertainty over drug quality and if information is complex (Ching and Ishihara, 2010; Ching, Clark, Horstmann and Lim, 2016). In addition to directing sales towards certain brands (business stealing), advertising may increase sales for the whole market (Shapiro, 2016), if it conveys information rather than being merely persuasive (Leffler, 1981; Ching and Ishihara, 2012; Anderson, Ciliberto and Lyaukonyte, 2013, 2016). In line with the literature on pharmaceutical demand, we find that demand is price elastic and that advertising affects sales. Even after controlling for advertising, brand-name drugs are preferred to generics, although there is significant heterogeneity in preferences. Consistent with medical knowledge, we find that anti-ulcer drugs are highly differentiated and that substitution occurs mostly at the level of the molecule or subclass.

Once we have identified demand and substitution patterns, we explore the impact of regulation on prices and margins, in a setting where firms strategically choose prices given the constraints imposed by the regulator. We expect the regulation of pharmaceutical prices to affect behavior in the industry. For example, price controls have been found to render generic competition ineffective or even counterproductive (Danzon and Chao, 2000) and to affect drug entry decisions beyond the role of market size and firm characteristics (Scott-Morton, 1999; Kyle, 2006). Price regulation may discourage or delay drug introduction (Kyle, 2007; Danzon, Wang, and Wang, 2005; Danzon and Epstein, 2008), leading to large welfare losses at a global scale (Filson, 2012). However, price controls may be welfare-improving when used to counterbalance the welfare losses from other regulatory measures (Chaudhuri, Goldberg, and Jia, 2006, on TRIPS product patents in India). However, price caps are not always the best regulations. For example, policies that impose additional copayments on patients demanding high-priced branded drugs can be more effective than price caps in lowering drug prices and provide incentives for pharmacists to promote generic sales (Brekke, Grasdal and Holmås, 2009; Brekke, Holmås and Straume, 2011 and 2013, on Norway).

Regulation in France can impose price constraints on pharmaceutical companies. As prices must be approved by the regulator, it can arbitrarily impose some price caps that are unknown to the econometrician and may or may not be binding for pharmaceutical companies. Thus, the magnitude of these price ceilings and whether they are binding for firms is unknown. Since 2004, the regulator has also been able to define maximum reimbursement prices for drugs once generics have entered the market. Our modelling and identification strategies allow price constraints to be unknown and to change across drugs and periods. Under the assumption of a model of competition across firms *à la* Bertrand, the strategy is based on the presence of unconstrained markets (the US and Germany) and on certain restrictions on the costs of drugs across markets, which allows us to recover such constraints. In a similar vein, Goldberg (1995) studies the car industry and the role of trade policy, such as voluntary export restraints, that imposed a quota on Japanese cars in the US market in the 1980s. The Lagrange multipliers associated with the quantity constraints on imported cars are identified by exploiting observations from the truck market, which was not

subject to the same quota constraints. In Goldberg (1995), quantity constraints are observed and explicitly incorporated into the first-order conditions, while we do not necessarily observe the implicit price caps imposed by the regulator. Salvo (2010) addresses a similar problem in estimating market power in the Brazilian cement industry, where firms are constrained in price setting due to the threat of entry by foreign producers, which poses an observable ceiling for the price that domestic competitors can set. Salvo (2010) predicts the price ceiling based on observed costs, while we do not need such an assumption. Brenkers and Verboven (2006) study how constraints on international markup differentials introduced after liberalizing the distribution of cars in Europe affect the market equilibrium. After estimating the demand for cars before liberalization and thus without price constraints, they simulate a new price equilibrium by imposing a given maximum difference of markups across countries. We use instead the variation across countries to generate the cost restrictions needed for identification. Our identification strategy could thus be used in the context of markets where prices may be affected by inequality constraints on markups across markets.

We find that some but not all drugs are significantly constrained. Regulation creates spillover effects on drugs not directly subject to price cuts, as prices chosen by manufacturers are affected by the regulatory constraints on their closest substitutes through the equilibrium conditions. Counterfactual simulations suggest that regulatory rules reduced prices relative to a free pricing scenario, especially in years in which price cuts were introduced. Such declines in prices, especially for high-quality drugs, shifted consumption towards branded drugs at the expense of generics, which experienced a smaller decrease in price, in both absolute and percentage terms. Once the difference between the branded and the generic price is reduced, the preference for the branded drug (as captured by our demand estimates) leads to substantial losses for generic manufacturers, as profits would be 72% higher in a free pricing scenario, compared to an increase of only 18% for branded firms. Nevertheless, price constraints generate some modest savings, approximately 3% of total expenses, on average, over the 11 years of data and increase consumer surplus, due to the greater utilization of cheaper and preferred branded drugs. To avoid the increased consumption

of branded drugs, other simulations suggest that the regulator could instead constrain prices using price caps defined by prices in other countries, so-called external reference pricing. Under such a rule, introduced in France for other drugs in 2004, prices would decline by even more and demand would increase but less than proportionally, leading to additional savings. Contrary to the regulation in place for anti-ulcer drugs during the period 2003-2013, generic penetration would increase (one of the objectives of the French regulator), due to the significant reductions of generic prices and margins. However, while in the short run consumer surplus would be higher than under the current regulatory setting, we should be cautious because of possible negative effects on the survival of generics in the long run.

In the following, Section 2 describes the market for anti-ulcer drugs and the data used; it also illustrates how price regulation operates in France and provides difference-in-difference evidence of its impact on prices. Section 3 presents our identification of price-cost margins in an oligopoly model when demand is known, provided that both constrained and unconstrained markets are observed. Thereafter, Section 4 explains the particular demand model estimated as a first step of the supply-side estimation. The results are discussed in Section 5. Section 6 reports counterfactual price equilibrium and savings calculations in the absence of the price setting regulation in France (Section 6.1) or with external reference pricing (Section 6.2). Finally, Section 7 concludes.

2 Market, Data, Regulation and Difference-in-Difference Evidence

2.1 Regulatory Framework in France

The consumption of pharmaceuticals in France has historically been high, driven primarily by brand-name drugs at the expense of generic equivalents, which have long been considered inferior or even unsafe substitutes. The reason for such behavior is manyfold. First, the generous French welfare system, covering nearly the entire French population, has long reimbursed a large part of the price of prescription drugs, branded and generic alike. In addition, more than 90% of the population has complementary health insurance, which formerly covered the entire price (Nguyen-Kim, Oz, Paris and Sermet, 2005). Furthermore, the late introduction of generic substitutability at the pharmacy (only in 1999) encouraged the perpetuation of a strongly brand-oriented system

of prescription and purchase. All of these factors have contributed to a low demand elasticity with respect to price. Nevertheless, French drug prices have long remained below the level displayed in other comparable European markets, especially Germany and the UK (Nguyen-Kim et al., 2005).

To be commercialized in France, a drug must be granted authorization for market entry by the Agency for the Safety of Health Products (*Agence Française de Sécurité Sanitaire des Produits de Santé*, AFSSAPS). To be covered by public insurance, prescription drugs must undergo an additional evaluation, to determine the coverage level and subsequently the price, which is regulated. Drugs that are covered must be included on a so-called *positive list* by the Ministry of Health, after considering the advice from the "Transparency Commission". Evaluation by this commission, which has since 2004 been part of the High Authority of Health (*Haute Autorité de la Santé*, HAS), is based on two indices of the drug's therapeutic value, evaluated at the market entry of a drug and revised every 5 years. The first index (called *SMR* for *Service Médical Rendu*) measures the absolute medical benefit of the drug and is based on both drug and disease class characteristics. The second index (*ASMR* for *Amélioration du Service Médical Rendu*) refers to the improvement in medical benefit of the drug in terms of higher efficacy, fewer side effects and ease of use as compared to existing products in its class. If the SMR awarded by the "Transparency Commission" is deemed sufficient, the drug is included on the positive list and reimbursement is set at 15%, 35%, 65% or 100%, depending on the SMR level (on a 1-5 scale). Since 2004, a major role in the decision on the reimbursement rate has been played by UNCAM (National Union of Sickness Insurance Funds). Once the reimbursement rate is set, the Economic Committee for Health Products (CEPS - *Comité Economique des Produits de Santé*) sets the price based on the ASMR level, the anticipated sales volume and the price of comparable drugs present on the list. Further details on the price setting and negotiation are reported in Section 3.2 below.

In the early 2000s, pharmaceutical expenses in France doubled with respect to the previous decade (reaching 30 billion euros in 2004), increasing more rapidly than anywhere else in Europe (Nguyen-Kim et al., 2005). This situation accelerated a project to reform the pharmaceutical

regulatory system that was intended to reduce public expenditures on drugs, which represented one-fifth of total public expenditures on health in France. The reform started in 2003 and introduced a number of major changes to the system of drug reimbursement and price setting. A maximum reimbursement price system was introduced ("TFR" for *Tarif Forfaitaire de Responsabilité*) when generic penetration does not reach a certain threshold defined by the Ministry of Health. In such a case, coverage for these drugs is only up to the TFR price, which is set by the CEPS and based on generic prices[1]. Manufacturers can keep the price above this TFR price, but the difference is paid out of pocket by the patient. In 2004, external referencing was introduced as an additional criterion in the drug pricing decision and included the stipulation that they need to be in line with prices in four neighboring countries (Italy, Germany, the UK and Spain). In 2006, a change was introduced that allowed imposing price cuts on all drugs based on the same molecule when generics become available or when they have been on the market for at least 24 months. The rule for price cuts has evolved over time (both in terms of the percentage of the price to be cut and time since generic entry) but can still be applied to markets not subject to TFR (TFR and price cuts being mutually exclusive). The reform also promoted the use of generics, both as a tool to reduce public expenses and as a major goal in itself as recommended by the European Commission (2009). Generic usage was encouraged through public campaigns to increase awareness and convey the idea that generics are safe equivalents of branded drugs. In addition, to stimulate generic substitution at the pharmacy, introduced in 1999 but of limited success, financial incentives were offered to pharmacists (see additional details in Section 4.1). In 2001, physicians formally agreed to start prescribing using the molecule (the INN, International Nonproprietary Name) rather than the brand name of the drug. However, only 8.5% of all prescriptions used the INN by 2006 (Grandfils and Sermet, 2006), forcing the Ministry of Health to urge physicians to prescribe primarily drugs for which generic alternatives are available.

[1] The regulator decides which molecules are subject to TFR based on the rate of generic penetration. In general, TFR can be introduced when the market share of generics for a molecule is below 60% after 18 months or 65% after 2 years since generic entry. These percentages and timing have changed slightly over time and unexpectedly, and the regulator total power over this issue, meaning that it can make exceptions and unilaterally decide to define a TFR.

Table 1 summarizes the regulatory changes between 2003 and 2013 that affected the demand side and the supply side of the anti-ulcer market in France.

Table 1: Regulatory Changes Affecting the Anti-ulcer Market in France since 2003

Regulatory changes affecting the Demand side	
Date	Description
September 2003	Introduction of maximum reimbursement price (TFR) for presentations of Cimetidine (Tagamet) and Ranitidine (Zantac and Raniplex)
March 2004	Revision of TFR: decrease of 0.02-0.04 € per box for Cimetidine and Ranitidine
April 2005	Revision of TFR: decrease of 0.5 € for Ranitidine
January 2006	Revision of TFR: decrease for Cimetidine and Ranitidine Introduction of TFR on Famotidine (Pepcidine)
December 2007	Introduction of TFR for another presentation of Cimetidine
January 2012	Revision of TFR for Cimetidine, Ranitidine, and Famotidine
Regulatory changes affecting the Supply side	
Date	Description
January 2006	Price cut of all drugs in a class if generics enter or have been available for 24 months - Omeprazole (Losec) and Lansoprazole (Takepron, Lanzor)
January 2008	Price cut for branded drugs if enough sales of generics of the same or close substitute molecules - Esomeprazole (Nexium)
January 2009	Revision of the price cut rule (18 months instead of 24) for Omeprazole, Lansoprazole, and Pantoprazole (Pantozol)
January 2012	Revision of the price cut rule at generic entry for Omeprazole, Lansoprazole, Pantoprazole, and Rabeprazole (Pariet)

Note: A presentation of a drug is a combination of its therapeutic form, dosage, and package size.
Price cuts in 2006, 2009, 2012 are of different percentages.

2.2 The Anti-ulcer Drugs Market

We define the anti-ulcer prescription drugs market using the A02B category of the international WHO ATC classification. The absence of real substitutes for these drugs (hospitalization and surgery target different conditions) make the market easily identifiable in the A02B class, without having to include drugs from other therapeutic classes among competitors (Crawford and Shum, 2005). The market comprises three subclasses that can be regarded as three different generations of drugs treating ulcer and ulcer-related conditions. The subclass of histamine antagonists (H2) includes anti-ulcer treatments of the first generation, introduced in the 1970s and 1980s, which treat ulcer symptoms by blocking the action of histamine in the stomach. H2 drugs are based on a number of molecules, the most common of which are Cimetidine (brand name: Tagamet), Famotidine (brand name: Pepcidine), Ranitidine (brand names: Zantac and Raniplex) and Nizatidine (brand

name: Panaxid). H2 had considerable success in many countries, driven by SmithKline's Tagamet (Cimetidine) and Glaxo's Zantac (Ranitidine); they remained top sellers until the late 1980s, when a new generation of ulcer treatments was introduced, the proton-pump inhibitors (PPI). These drugs, instead of blocking the reception of histamine, act at the source of acid secretion, inhibiting it for a longer time. This subclass includes several derivatives of benzimidazole: Omeprazole (brand name: Losec), Esomeprazole (brand name: Nexium), Lansoprazole (brand names: Lanzor and Takepron), Pantoprazole (brand name: Pantozol), and Rabeprazole (brand name: Pariet). These molecules are considered superior to H2 and other existing drugs. AstraZeneca's Omeprazole-based drug, Losec (Prilosec in the US), was the world's top-selling drug for several years. Finally, the third subclass is a residual category, which includes Prostaglandins, which are used primarily for the prevention and treatment of peptic ulcer in the elderly (Misoprostol, brand name: Cytotec).

The anti-ulcer market has long been one of the top-selling therapeutic classes worldwide (leading from 1990 to 2003). This was driven by the presence of blockbusters and competition based on subsequent innovations. Anti-ulcer drugs are manufactured by several of the most important pharmaceutical players: AstraZeneca (Losec and Nexium), GlaxoSmithKline (Zantac), Takeda (Takepron and Pantozol), Pfizer (Cytotec), Sanofi (Lanzor), Johnson&Johnson (Pariet), Merck (Pepcidine), Abbott (Raniplex), Aptalis (Tagamet), Norgine (Panaxid), and Forest (Pylera). In addition, the market experienced patent expiration for major drugs in the early 2000s, and several entry waves of generics started populating the French market.

2.3 Data and Descriptive Statistics

We use data from IMS Health covering all wholesale transactions in the retail sector (revenues and quantities sold for each drug in a country-year) for the period 2003-2013. We also use advertising data from IMS Health Global Promotional Track for France, Germany and the US. We have data on advertising expenditures for each drug specialty by media at the country level for France, Germany and the US. Descriptive statistics on the advertising by market are presented in Table A1 in Appendix A.4 and report the yearly average of total advertising expenditures for branded drugs or generics by country and the part of these advertising that correspond to detailing expenses. We

can see that in France most expenses are in the form of detailing, with the rest being in journal publications, meetings and other. Advertising of generics is also much lower than for branded drugs, and this is also true in the US but not in Germany, where the ratio of advertising expenses over total revenue is much higher for generics than in France or the US. We also observe the number of advertising units in detailing, which will be useful for computing an average price per detailing unit in each year and country. In the quantity sales data, one observation (the drug-country-year triplet) is uniquely identified by detailed information on the name of the drug, its manufacturer, its molecule, its therapeutic form, and its brand type (originator, licensed or generic drug). We compute an average wholesale price per standard unit from the figures on quantities (where standard units are defined as the smallest unit of the drug standardized across dosage and therapeutic form) and revenues per year (in constant $US). The data were aggregated at the therapeutic form level to avoid distinguishing the different methods of administration of exactly the same drug (tablet and effervescent capsules, for instance). We use these IMS data for both quantities and revenues for France, Germany and the US but also use the average wholesale prices in Italy, Spain and the UK as instrumental variables (see section 5 below). We also use the website *www.theriaque.org* (approved by the regulatory agency HAS) to gather additional information on the indications and side effects of each drug, the medical benefit indices (SMR and ASMR) for each indication, and the date of introduction and level of TFR.

Between 2003 and 2013, a total of 103 different drugs were sold in France by 29 different companies: among them, 13 are branded firms, and the remaining 16 are generic manufacturers. The majority of the drugs (77) belong to the PPI subclass (A02B-C), which represents the bulk of sales, followed by H2 (A02B-A), with 24 products; Prostaglandins (A02B-B) are present with only one drug (Pfizer's Cytotec); and a combination of an anti-ulcer and antibiotic drug completes the list. French anti-ulcer drugs in this period are based on 11 active ingredients: five PPI (Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole and Rabeprazole), four H2 (Cimetidine, Famotidine, Nizatidine and Ranitidine), one Prostaglandin (Misoprostol) and one combination (Bismuth and

antibiotic). For eight of these, generics were or became available during the sample period: Misoprostol, Nizatidine, and the combination drug were sold only as brand names. In Germany and the US, the number of drugs is higher than in France in some periods, but all drugs sold in France are always sold in these two other countries.

The medical benefit of these drugs, as measured by the SMR, is classified as important (level 2) for most of the years in the sample. As a result, all drugs are covered at the 65% rate, except for some older H2 drugs, the reimbursement for which has been reduced to 35% since 2007, following the revision of their SMR. The improvement in medical benefit delivered by these drugs, as measured by the ASMR, is considered insufficient (level 5) in most cases, except for AstraZeneca's Losec (Omeprazole) and Nexium (Esomeprazole). Additional measures of drug quality, beyond ASMR, are the number of therapeutic forms (between 1 and 4 in the data), indications and side effects. A higher number of therapeutic forms makes it possible to better suit the needs of heterogeneous patients. Generic drugs offer at most two different forms. The number of indications and side effects differs significantly across drugs, from a minimum of two to a maximum of nine indications (Losec and Nexium) and eight side effects (Nexium's peculiarity).

Table 2: Summary Statistics for France

	Number of drugs			Quantity	Market Share		Wholesale Price		Expenses
Year	All	Branded	Generics	(1,000 std units)	Branded	Generics	($US/std unit)	(€/std unit)	(1,000 $US)
2003	25	12	13	1 131 140	98%	2%	0.75	0.55	1 414 127
2004	39	12	27	1 233 735	86%	14%	0.78	0.57	1 455 683
2005	40	12	28	1 334 331	77%	23%	0.70	0.51	1 423 278
2006	42	12	30	1 444 926	73%	27%	0.63	0.46	1 404 320
2007	51	12	39	1 508 936	70%	30%	0.60	0.44	1 364 369
2008	49	12	37	1 535 426	61%	39%	0.56	0.41	1 240 799
2009	59	12	47	1 596 513	55%	45%	0.52	0.38	1 183 251
2010	62	12	50	1 669 252	50%	50%	0.46	0.33	1 069 219
2011	74	12	62	1 732 595	39%	61%	0.43	0.31	974 594
2012	86	12	74	1 820 351	29%	71%	0.39	0.28	853 985
2013	94	11	83	1 890 575	18%	82%	0.32	0.23	619 035

Notes: Price is the average price per standard unit across all drugs in $US or in €(constant exchange rate for 2014Q2 from ECB: €/$US=1.3772).

Expenses is the total manufacturer-level revenue of the class. Wholesale prices are at the manufacturer level.

Here, the market shares are relative to the total sales of anti-ulcer drugs (no outside good as in the model).

Table 2 shows that there is a steady and significant increase in the number of drugs marketed, from 25 in 2003 to 94 in 2013, due to the entry of generics, the market share of which rose significantly during the period. In the early 2000s, several Ranitidine- and Cimetidine-equivalents entered the market (Zantac and Tagamet lost patent protection in the 1990s), but generics still represented a residual category in terms of volumes and revenues. In 2004, a second entry wave took place in the form of generics of the world's top-selling drug, Losec (AstraZeneca's Omeprazole), followed by many others at the patent expiration of other PPI molecules during the later years of the sample period. By 2011, generic sales constituted more than half of the class volume, representing the vast majority at the end of the sample period. These figures are similar in Germany and the US, with the former reaching even higher levels of generic penetration (see Tables A2 and A3 in Appendix A.4). Interestingly, in France, the market for anti-ulcer drugs expanded at the same time as generic penetration, meaning that the sales of branded versions did not decline dramatically. Actually, aggregate quantity increased by approximately 50% during the period. However, revenues also declined, leading to a decreasing average price per standard unit, in line with generics being cheaper (the price of generics is capped at a fixed percentage of the price of their brand-name counterpart) and to the increased pressure imposed by the reform on the regulated prices of brand-name drugs.

2.4 Difference-in-Difference Evidence of the Effect of Regulation on Prices

As reported in Table 1, there are several regulatory rules that may affect demand or supply in France during the period of study. Before turning to the structural modelling of demand and supply, we use the known regulatory events to test whether these have had any effect on prices. Table 1 shows that the regulator can impose some price cuts on branded drugs since 2006. It also shows that reimbursement rules changed over time and affected some drugs with a maximum reimbursement price through the TFR rules explained above. Before showing how one can structurally identify and estimate the impact of these regulations on prices, demand, and expenditures, we provide difference-in-difference evidence on the effects of these events on prices. The TFR rule, which imposes a maximum reimbursement price, was introduced in France at the end of 2003 and caps the reimbursement level of branded drugs and applies also to their generics. In 2004 and 2005, three

anti-ulcer drugs were subject to this rule: Tagamet (Cimetidine), Zantac and Raniplex (Ranitidine); a fourth was added in 2006, Pepcidine (Famotidine). Moreover, since 2006, for drugs not subject to TFR, price were reduced after generic drugs entered or when such drugs have been on the market for at least 24 months, whether they are based on the same molecule or on different ones considered close substitutes. This affected the PPI anti-ulcer drugs Losec (Omeprazole), Lanzor and Takepron (Lansoprazole) since late 2006, Nexium (Esomeprazole) since 2008, Pantozol (Pantoprazole) since 2009, and Pariet (Rabeprazole) since 2012.

Using the data from France, Germany and the US, we test the effects of these events on the prices of drugs using triple difference regressions within this class across markets. To do this, we define the group of drugs denoted "TFR" as those drugs that have been subject to the maximum reimbursement price in France rule since 2004, and we denote by "Price Cut" the dummy variable for the group of drugs subject to that rule in France. Of course these two rules are supposed to have affected the price of drugs in France only and not in Germany and the US, but these drugs could also be different from other drugs within the anti-ulcer market, hence the use of interaction with country dummies.

Table 3 reports the results of the regression of the log price of drugs on drug characteristics, on the drug group dummies "TFR" and "Price Cut", on the interaction between these group dummies and the dummy for whether the time period is after the regulatory event (i.e., when the TFR or price cut was introduced for each affected drug), and on the interaction between the dummy variable for France after the start of the regulatory event and these group dummies. The coefficients of these last interactions can be interpreted as the effect of the regulatory event in France on prices. In column (1), adding country fixed effects, molecule fixed effects, and year fixed effects, we find that the drugs in the "Price Cut" and "TFR" groups are slightly more expensive (although the effect is not significant) and that their prices have increased slightly (albeit not significantly). However, the interaction of each group dummy with the regulatory period dummy "After" and the interaction with the French dummy shows that in France these drugs became cheaper when each of these regulations was implemented. The effect is significant for both "Price Cut" and "TFR" (except for

the last two specifications for "Price Cut"). With different country and year fixed effects or country and molecule fixed effects in columns (2), (3) and (4), the results are similar, but the significance is weaker in the fourth specification. Remark that in column (4), we have country-molecule-year fixed effects, meaning that the effects of drug characteristics and regulation are identified from variations within a molecule-country-year triplet. Table 3 also shows that branded drugs are more expensive, whereas drugs with more side effects or with the NSAID indication are cheaper (the results are similar with price as the dependent variable).

Table 3: Triple Difference Regression of Log Prices

Variables	(1) Log Price	(2) Log Price	(3) Log Price	(4) Log Price
Drug Characteristics				
Branded	1.943***	1.891***	2.011***	2.038***
	(0.444)	(0.423)	(0.444)	(0.484)
Nb. Side Effects	-0.489***	-0.485***	-0.406***	-0.136***
	(0.0648)	(0.0682)	(0.0679)	(0.0502)
Formats	0.0943	0.0844	-0.0248	-0.108
	(0.119)	(0.128)	(0.155)	(0.135)
Helicobacter Indication	3.431***	3.594***	2.612***	0.719***
	(0.301)	(0.340)	(0.184)	(0.204)
NSAID Indication	-0.838***	-0.780**	1.008***	0.133
	(0.278)	(0.328)	(0.241)	(0.222)
Drug Group Dummies				
Group "TFR"	0.300	0.229	-0.197	0.147
	(0.231)	(0.287)	(0.285)	(0.273)
Group "Price Cut"	0.174	0.0610	-0.283	-0.337
	(0.216)	(0.225)	(0.227)	(0.315)
Drug Group Dummies * After				
"TFR" * After	0.147	0.197	0.181	-0.0257
	(0.284)	(0.339)	(0.400)	(0.303)
"Price Cut" * After	0.000941	0.137	0.102	-0.0105
	(0.145)	(0.117)	(0.113)	(0.185)
Regulatory Event in France				
"TFR" * After * France	-0.602**	-0.803***	-1.174**	-0.815*
	(0.265)	(0.301)	(0.472)	(0.475)
"Price Cut" * After * France	-0.457**	-0.680***	-0.421	-0.303
	(0.207)	(0.220)	(0.254)	(0.205)
Country FE	Yes			
Molecule FE	Yes	Yes		
Year FE	Yes			
Country*Year FE		Yes	Yes	
Country*Molecule FE			Yes	
Molecule*country FE			Yes	
Country*Molecule*Year FE				Yes
Observations	4,339	4,339	4,339	4,339
R-squared	0.403	0.422	0.493	0.459

Notes: Standard errors are clustered by country-molecule. *, **, and *** indicate significance at the 10%, 5% and 1% levels. Dependent variable is price in $US. Data for France, Germany, and the US from 2003 to 2013.

This difference-in-difference evidence seems to confirm that these regulatory events did reduce prices; however, this is conditional on counterfactual prices having been similar. It is indeed possible that demand changed during these years due to country-specific changes, leading to lower prices, or that specific cost shocks also affected the equilibrium pricing. A structural estimation will allow us

to interpret those results and test whether regulation actually constrained prices or observed price changes are simply due to demand or supply conditions. We illustrate our structural model in the next two sections.

3 Supply Model and Identification of Margins

Assuming that the shape of demand for pharmaceuticals is known, the modelling and estimation of which is deferred to the next section, we first present our model of the effect of regulation on the supply side.

We consider an oligopoly model with a given market structure, taking entry decisions as exogenous. Pharmaceutical innovation involves long R&D delays, decided many years in advance, and generic entry is constrained by patent protection. Kyle (2007), Danzon et al. (2005), and Danzon and Epstein (2008) have shown that delays in entry can be strategic, but we leave to future research the modelling of pricing and regulation in a fully dynamic setting. Moreover, all but one entry in our data are due to generics, and thus, they will not be affected by anticipation in the pricing decisions for branded drugs. We thus focus on pricing with an exogenously given market structure.

Let us consider the problem of price regulation of pharmaceuticals in France. The prices of drugs must be agreed upon by the regulator (CEPS) and are not determined with some fully binding regulatory rules. Thus, it is possible that pharmaceutical companies obtain prices that do maximize profits. Lobbying and negotiations between the regulator and companies may lead to a price equilibrium not far from profit maximization equilibria (Grandfils, 2008): it is known that the price approved by the regulator is often that proposed by the manufacturer in the first place through a procedure called "depôt de prix" (Grandfils and Sermet, 2006). This seems to signal that, despite regulation, the price remains a decision taken primarily by the company. However, companies may anticipate price constraints imposed by the regulator that are not observed by us.

3.1 Free Pricing Equilibrium

In the case of free price setting, which is the most relevant model for the US and Germany but could also be the equilibrium outcome for France, it is well known how profit maximizing prices

should be set and how marginal costs can be identified if the shape of demand is known (BLP, 1995; Nevo, 2001) and a model of conduct of firms is assumed.

Denote by Π_{ft} the variable profit of multi-product firm f in market t, where a market will be defined as a country-year. As fixed costs and other R&D costs are not affecting pricing decisions, a firm f selling all of the products in set F_f will maximize

$$\Pi_{ft} = \sum\nolimits_{j \in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t, \mathbf{a}_t) - a_{jt}$$

where p_{jt} is the price of drug j, a_{jt} is the advertising expense for drug j, c_{jt} is the constant marginal cost of product j, and $q_{jt}(\mathbf{p}_t, \mathbf{a}_t)$ is the quantity of drug j demanded given the vector $\mathbf{p}_t$ of all drug prices and the vector of advertising expenditures $\mathbf{a}_t$ for all J products.

As assumptions on firms' advertising choices are not necessary to identify marginal costs, we only consider the firms' profit-maximizing conditions in prices and assume that they compete in price *à la* Bertrand. Assuming that a pure-strategy Bertrand-Nash equilibrium in prices exists, the price of any product j sold by firm f must satisfy the first-order conditions

$$q_{jt} + \sum\nolimits_{k \in F_f} (p_{kt} - c_{kt}) \frac{\partial q_{kt}\left(\mathbf{p}_t, \mathbf{a}_t\right)}{\partial p_{jt}} = 0$$

Then, with the following matrix and vector notations (with $\mathbf{1}_{\{j \in F_f\}} = 1$ if $j \in F_f$ and 0 otherwise)

$$D_f = \begin{bmatrix} \mathbf{1}_{\{1 \in F_f\}} & 0 & 0 \\ 0 & \ddots & 0 \\ 0 & 0 & \mathbf{1}_{\{J \in F_f\}} \end{bmatrix}, \quad Q_{p_t} = \begin{bmatrix} \frac{\partial q_{1t}(\mathbf{p}_t, \mathbf{a}_t)}{\partial p_{1t}} & \dots & \frac{\partial q_{Jt}(\mathbf{p}_t, \mathbf{a}_t)}{\partial p_{1t}} \\ \cdot & \cdot & \cdot \\ \frac{\partial q_{1t}(\mathbf{p}_t, \mathbf{a}_t)}{\partial p_{Jt}} & \cdot & \frac{\partial q_{Jt}(\mathbf{p}_t, \mathbf{a}_t)}{\partial p_{Jt}} \end{bmatrix}$$

and $\mathbf{q}_t = (q_{1t}, ., q_{Jt})'$, $\mathbf{p}_t = (p_{1t}, ., p_{Jt})'$, $\mathbf{c}_t = (c_{1t}, ., c_{Jt})'$, we obtain the usual formula for all firms f :

$$D_f\left(\mathbf{p}_t - \mathbf{c}_t\right) = -\left[D_f Q_{p_t} D_f\right]^{-1} D_f \mathbf{q}_t \tag{1}$$

Thus, given demand estimates and the observation of prices, one can obtain price-cost margins per product and per year by solving the system of first-order conditions obtained above. This is the usual identification result of price-cost margins[2].

[2]Remark that if we assume that advertising is optimally chosen by firms in a static Bertrand-Nash equilibrium jointly with prices, first-order conditions in advertising lead to a full set of constraints between the matrix of advertising elasticities of demand, that of the price elasticity of demand and the ratio of advertising expenditures to revenue. We will not use these additional constraints in the estimation because we do not need them to identify marginal costs. Using only the optimal pricing strategy allows us to identify marginal costs and is robust to the modelling of the supply side determination of advertising.

An alternative strategy to identify the marginal costs of drugs is to use the long-term price equilibrium of drugs after the entry of generics under the assumption that margins are almost zero for those drugs. In this case, the marginal cost of a molecule can be thought of as the lowest price of its generic version (Grabowski and Vernon, 1992). This approach is very robust in cases in which marginal costs are "constant" over time, as it does not rely on any demand specification, and when the lowest price of generics by molecule has converged, which does not seem to be the case for anti-ulcer molecules, where some generics have entered only recently.

3.2 Price-Constrained Profit Maximization Equilibrium

Let us now consider the effects of price regulation on the pricing equilibrium. In France, regulation amounts to implicitly imposing some price ceiling on branded or generic drugs, either because of explicit constraints on prices (as in the case of the price cut rules after 2006) or because of implicit constraints imposed by the regulator to the industry. For simplicity, let us consider a market t (that can represent a country and year) in which firms are potentially price constrained such that each price p_{jt} must belong to a set Ω_{jt}.

For branded drugs in France, some price ceiling may be imposed by the regulator when the drug is first authorized and revised over time. In such cases, if the only constraint is that the price p_{jt} must be lower than $\overline{p}_{jt}$ chosen by the regulator, then $\Omega_{jt} = [0, \overline{p}_{jt}]$.

For generic drugs, French regulation also imposes a price ceiling that depends on the price of the originator drug and is a specific proportion of the price of the branded version. If for a generic drug j we denote by $b(j)$ the index of the branded version of the same molecule, the price constraint can then be written as $p_{jt} \leq \tau_{b(j)t} p_{b(j)t}$, where $\tau_{b(j)t}$ is a year-specific factor set by the regulator (sometimes molecule-specific); then, $\Omega_{jt} = [0, \tau_{b(j)t} p_{b(j)t}]$. Until 2005, at entry, the generic price could not exceed 55% of the branded regulated price. This share was reduced to 50% in 2006, 45% in 2009, and 40% in 2012. However, the percentage may be higher in specific cases approved by the regulator and molecule-specific (high production costs, late or difficult entry for generic manufacturers, low price of the branded drug), as long as the difference between the brand-name and the generic price is at least 10%.

Then, removing advertising arguments in demand to simplify notation, firm f's constrained price maximization, given other firms' pricing strategies, is

$$\begin{array}{rcl} \max\limits_{\{p_{jt}\}_{j\in F_f}} \Pi_{ft} & = & \sum\nolimits_{j\in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t) \\ s.t. \quad p_{jt} & \in & \Omega_{jt} \end{array}$$

Assuming that a pure-strategy Bertrand-Nash equilibrium in prices exists, the necessary first-order conditions of the above problem are[3]

$$q_{jt} + \sum\nolimits_{k\in F_f} (p_{kt} - c_{kt}) \frac{\partial q_{kt}(\mathbf{p}_t)}{\partial p_{jt}} = \lambda_{jt} \qquad \forall j \in F_f, \forall f$$

In the current regulatory framework in France, denoting by $\tilde{\lambda}_{jt}$ the Lagrange multiplier of the price cap constraint that may implicitly or explicitly be imposed by the regulator on branded drugs ($p_{jt} \leq \overline{p}_{jt}$) and on generic drugs ($p_{jt} \leq \tau_{b(j)t} p_{b(j)t}$) and denoting by $g(j)$ the index of the generic version of the branded drug j, we can express λ_{jt} as a function of the "true" Lagrange multipliers, as $\lambda_{jt} = \tilde{\lambda}_{jt}$ if j is a generic and $\lambda_{jt} = \tilde{\lambda}_{jt} - \tilde{\lambda}_{g(j)t}/\tau_{jt}$ if j is a branded drug and its manufacturer also owns the generic drug $g(j)$[4]; otherwise, $\lambda_{jt} = \tilde{\lambda}_{jt}$.

In all cases, the first-order conditions of firm f can be written in matrix form as

$$D_f(\mathbf{p}_t - \mathbf{c}_t) = -\left[D_f Q_p(\mathbf{p}_t) D_f\right]^{-1} D_f(\mathbf{q}_t - \boldsymbol{\lambda}_t)$$

where the elements of $\boldsymbol{\lambda}_t = (\lambda_{1t}, .., \lambda_{Jt})$ are unknown (J_t allows the total number of products to vary with t).

Thus, with $\boldsymbol{\lambda}_t$ being unknown, even with known demand and prices, one cannot identify price-cost margins without further assumptions. Theoretically, the net effects of regulation on prices are ambiguous and will depend on all own- and cross-price elasticities of demand. A price reduction

[3] This is always possible provided that there exist N_j functions Ψ^n_{jt} such that

$$p_{jt} \in \Omega_{jt} \Leftrightarrow \Psi^n_{jt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t) \leq 0 \text{ for } n = 1, .., N_j$$

which is the case as soon as the set Ω_{jt} is the union of a finite number of intervals. Then, the first-order conditions are valid and we have

$$\lambda_{jt} = \sum\nolimits_{k\in F_f} \sum\nolimits_{n=1}^{N_j} \Lambda^n_{kt} \frac{\partial \Psi^n_{kt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t)}{\partial p_{jt}}$$

where Λ^n_{kt} is the Lagrange multiplier of the price constraint $\Psi^n_{jt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t) \leq 0$.

[4] This is the case only for the manufacturer Sanofi, which owns the branded drug Lanzor and several generic versions.

for one drug can affect other drugs that are not constrained because of cross-price elasticities of demand. Using first-order conditions, for each vector $\boldsymbol{\lambda}_t$, we have price-cost margins or marginal cost $c_{jt}(\boldsymbol{\lambda}_t)$ as a known function of $\boldsymbol{\lambda}_t$ (depending on demand and prices). Using the super-script f for the vector in which the elements corresponding to products not belonging to firm f are replaced by zeros, the first-order conditions can also be written as

$$\mathbf{c}_t^f(\boldsymbol{\lambda}_t^f) = \mathbf{p}_t^f + Q_p^f(\mathbf{p}_t)^{-1}(\mathbf{q}_t^f - \boldsymbol{\lambda}_t^f) \tag{2}$$

Thus, we cannot identify marginal costs without restrictions on $\boldsymbol{\lambda}_t^f$. Moreover, price constraints have spillover effects across drugs because the marginal cost of product i of firm f depends on the constraint of price j of firm f through $\boldsymbol{\lambda}_{jt}^f$ according to

$$\frac{\partial c_{it}^f(\boldsymbol{\lambda}_t^f)}{\partial \boldsymbol{\lambda}_{jt}^f} = -\left[Q_p^f(\mathbf{p}_t)^{-1}\right]_{i,j} \text{ for } i,j \in F_f$$

where $[.]_{i,j}$ stands for the row i column j term of the matrix in the brackets.

However, adding some cost restrictions may allow for identification. Our approach is similar to that of Goldberg (1995), who uses observations not subject to quotas in the car market to identify the effect of quantity constraints on exports.

Let us first make the following assumption that some unconstrained markets are observed:

Assumption U_S: There are markets S that are not price constrained, that is

$$\boldsymbol{\lambda}_t = 0 \text{ for any } t \in S$$

If we add the very simple cost restriction that the marginal costs of drugs should be the same across markets, whether price constrained or not, then we can easily identify the costs of drugs using only observations from unconstrained markets, provided that the drugs in constrained markets are also present and observed in other markets in which prices are freely chosen by firms.

Assuming such cost equality across markets is of course too strong, but a similar idea can be applied and used for identification with more flexible cost restrictions across markets. We can thus consider the following restriction:

Assumption C_S: For any $t \in S$, there exists a vector of observed variables $\mathbf{z}$ such that, for all

$t_0 \notin S$, the marginal costs c_{jt} satisfy

$$c_{jt} - c_{jt_0} = (\mathbf{z}_{jt} - \mathbf{z}_{jt_0})' \delta + \omega_{jt}$$

for all products j, with

$$E(\omega_{jt} | \mathbf{z}_{jt} - \mathbf{z}_{jt_0}) = 0$$

Assumption C_S means that cost differences between markets in the set S and other markets satisfy the cost restriction above, such that the difference in costs across markets depends linearly on a set of observable differences $\mathbf{z}_{jt} - \mathbf{z}_{jt_0}$ and on unobserved, market-specific, additive mean independent shocks ω_{jt}.

Then, we can state the following proposition that allows us to identify the marginal costs for potentially constrained markets (see the proof in Appendix A.1):

Proposition: With assumptions C_S and U_S and a market $t_0 \notin S$, marginal costs $\mathbf{c}_{t_0}$ are

$$\mathbf{c}_{t_0} = \mathbf{p}_{t_0} + Q_p^f(\mathbf{p}_{t_0})^{-1}(\mathbf{q}_{t_0} - \boldsymbol{\lambda}_{t_0})$$

where $\boldsymbol{\lambda}_{t_0}$ is identified using the following moment condition:

$$E(\boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})) = 0 \tag{3}$$

with vector $\boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})$ defined by

$$\boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0}) = \left[\mathbf{p}_t - \mathbf{p}_{t_0} + Q_p(\mathbf{p}_t)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0}\right] + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} - (\mathbf{z}_t - \mathbf{z}_{t_0})'\delta$$

provided that the matrix $E\left[(\mathbf{z}_t - \mathbf{z}_{t_0})', Q_p(\mathbf{p}_{t_0})^{-1}\right]$ has full rank.

The proposition shows that identification is obtained when all prices are potentially constrained in market t_0, provided that the rank condition is satisfied: this intuitively means that there are enough goods markets that are unconstrained ($\sum_{t \in S} J_t$ is sufficiently large) and that the observable factors $\mathbf{z}$ that explain marginal cost differences are not collinear with the columns of the inverse of the price derivatives of demand or, equivalently, with the columns of the transpose of the matrix of cofactors of the price derivatives of demand. In a two-product case, this would mean that observable

factors z are not in the space spanned by the vectors of the absolute values of own- and cross-price elasticities of the other product[5].

Assumption C_S makes use of restrictions on marginal costs across markets. The identification power in our application will come from the fact that there can be relevant and robust cost restrictions across markets and products with constrained and unconstrained prices. As all drugs in France are potentially price constrained, our identification will come from restrictions on the marginal costs of the same drug across countries, some regulated (France) and others not price constrained (US or Germany). Restrictions across drugs within countries can also be used if one can identify years and products where prices should not be constrained, as in Lasio (2015), who exploits the removal from coverage and price regulation that happened in a different drug class in France.

In Appendix A.2, we provide further details on the empirical estimation counterparts of the moment condition (3) used for the estimation of parameters $\boldsymbol{\lambda}_t$ and thus of the marginal costs. In our application, we use a log-cost restriction based on drug-specific effects and costs in the US and Germany. This is justified by the fact that the marginal costs are likely to have some market-specific component because they include packaging costs and transportation costs for each country. Denoting in the vector $\mathbf{z}_t$ the set of all these explanatory variables, we show in Appendix A.2 that we obtain estimates of the vector $\boldsymbol{\lambda}_t$ as the solution of a Non-linear Least Squares problem:

$$\boldsymbol{\lambda}_t = \arg\min_{\boldsymbol{\lambda} \geq \mathbf{0}} \left\| \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] \log(\mathbf{c}_t \left(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t \right)) \right\| \tag{4}$$

In Appendix A.2, we show that this problem has a closed-form solution when the cost restriction is in levels instead of logs.

4 Demand Model

To identify the shape of demand for pharmaceuticals in each market, we estimate a random utility discrete choice model, which has the advantage of being flexible enough to capture any substitution patterns among differentiated products as in Björnerstedt and Verboven (2016). The literature

[5] In the 2×2 matrix case, the vectors $\mathbf{z}$ must not be in the space spanned by vectors $(q_2(1-q_2), q_1 q_2)'$ and $(q_1 q_2, q_1(1-q_1))'$.

on pharmaceuticals has employed many different approaches to demand estimation, from log-log models (as in Berndt et al., 1996; Berndt, Kyle and Ling, 2003; Rizzo, 1999), to AIDS and multi-stage budgeting (for instance, Ellison, Cockburn, Griliches and Hausman, 1997, to estimate the elasticity between branded and generic versions of four antibiotics (cephalosporins), and Chaudhuri et al., 2006, for demand for antibiotics in India). Closer to our approach, Azoulay (2002), Berndt et al. (2003), and Crawford and Shum (2005) use logit models to study the market for prescription anti-ulcer drugs. Donohue and Berndt (2004) and Stern (1996) use nested logit demand models. Arcidiacono et al. (2013) extend the nested logit by allowing for unobserved preferences to be correlated across nests, thus generating more reasonable substitution patterns than the simpler nested logit. Ching (2010a and 2010b) explicitly accounts for heterogeneity in price sensitivity and incorporates consumer learning. Although we think learning is important when we consider the choice of treatment for individual patients (Crawford and Shum, 2005), it seems to be much less of a first order concern when looking at aggregate demand at the year level. Moreover, we believe that the uncertainty over drug quality for this market in this period is small, as all branded drugs entered before 2003 and the diffusion of generics was already quite high (different from Ching, 2010a and 2010b). For this reason, we use a static model and leave for future research a dynamic structural model.

4.1 Random Utility Model

Anti-ulcer drugs are highly differentiated. They can be partitioned into three subclasses, which refer to different generations of products. Older H2 drugs are still widely used, even if PPI are considered superior products, while Prostaglandins are mainly prescribed for elderly patients. Differences also emerge within a subclass, at the molecule level. For instance, H2 anti-ulcer drugs are easily substitutable among one another, but there exist differences between, say, Cimetidine and Ranitidine. These levels of differentiation stem from objective differences that make one drug more appropriate to treat one condition or more suitable for one type of patient. Given a molecule, there is also product differentiation between branded and generic drugs. This is not justified by a difference in their curative effects, as both have the same molecule and are thus therapeutically

equivalent. However, despite being (nearly) perfect substitutes (other than potential differences in the inert components, shape and color of the drug that do not compromise efficacy or curative effects for most patients), patients have historically perceived vertical differentiation.

We will start by specifying the utility of using drug $j \in \{1, .., J_t\}$ for patient i in period t as

$$u_{ijt} = \sum\nolimits_k \alpha_i^k x_{jt}^k - \beta_i^0 p_{jt} 1_{\{p_{jt} \leq \bar{p}_{jt}\}} - \beta_i^1 p_{jt} 1_{\{p_{jt} > \bar{p}_{jt}\}} + \zeta_{jt} + \varepsilon_{ijt} \tag{5}$$

where x_{jt}^k are k drug characteristics including advertising a_{jt}, p_{jt} is the price of the drug, $\bar{p}_{jt}$ is the maximum reimbursement price of the drug (coming from the TFR rule), which by convention will be equal to $+\infty$ for drugs that are not subject to TFR reimbursement rules, ζ_{jt} are drug-period-specific effects, and ε_{ijt} is consumer i's deviation from the mean utility of taking drug j in period t. The preference parameters α_i^k, β_i^0, β_i^1 are allowed to vary across users i. β_i^0 can be interpreted as the price sensitivity for all drugs not subject to the maximum reimbursement price or with prices below the maximum reimbursed level, while β_i^1 is the price sensitivity of drugs subject to the TFR reimbursement rules when the price is above the reference price, meaning that the reimbursement rate is lower for patients who have to pay the difference out of pocket.

The model is completed by the inclusion of an outside good, which corresponds to not choosing any of the J_t products, with a normalized indirect utility $u_{i0t} = \varepsilon_{i0t}$. This option includes not taking any drug or using milder, OTC heartburn medications.

We assume that each user chooses an element in the choice set $\{0, 1, .., J_t\}$ according to maximum utility (5). This modelling of choices can be seen as a reduced form of a more complex mechanism by which patients, prescribers and pharmacists interact. It is thus important that the preference parameters be heterogenous across users i, because of unobserved variation in price-sensitivity that may be driven by the patient's choices and their reimbursement scheme; by the prescriber's choice, which may follow the insurance system's recommendation to prescribe cheaper drugs; and by the pharmacist, who also influences the choice of brand-name versus generic drugs. In particular, in France, the pharmacist's margins are regulated such that pharmacists have a preference for generic drugs. Indeed, pharmacists' margins decrease stepwise in the price of the drug (26.1% of the retail price if below 22.9€, 10% between 22.9€ and 150€, and 6% above 150€) and are larger in relative

terms for generic than branded drugs (because the absolute margins of generics are equal to those of the branded drug), which may influence their effort in generic substitution when facing the purchaser. Heterogeneity in the preference parameters $\left(\alpha_i^k, \beta_i^0, \beta_i^1\right)$ across decision makers in this demand model is thus crucial to capture the aggregate shape of demand resulting from these heterogeneous situations.

We specify random coefficients $\left(\alpha_i^k, \beta_i^0, \beta_i^1\right) = (\alpha^k + \sigma_\alpha^k \nu_i^k, \beta^0 + \sigma_{\beta^0} \nu_i^{\beta_0}, \beta^1 + \sigma_{\beta^1} \nu_i^{\beta_1})$, where ν_i^k, $\nu_i^{\beta_0}$, $\nu_i^{\beta_1}$ summarize all the unobserved consumer characteristics, and $(\sigma_\alpha^k, \sigma_{\beta^0}, \sigma_{\beta^1})$ characterize how consumer tastes vary according to these unobserved characteristics. Indirect utility can then be redefined as $u_{ijt} = \delta_{jt} + \mu_{ijt} + \varepsilon_{ijt}$ with mean utility $\delta_{jt} = \sum_k \alpha^k x_{jt}^k - \beta_i^0 p_{jt} 1_{\{p_{jt} \leq \bar{p}_{jt}\}} - \beta_i^1 p_{jt} 1_{\{p_{jt} > \bar{p}_{jt}\}} + \zeta_{jt}$ and deviation $\mu_{ijt} = \sum_k \sigma_\alpha^k x_{jt}^k \nu_i^k - \sigma_\beta p_{jt} \nu_i^p$.

Under the assumption that ε_{ijt} is independently and identically distributed according to Gumbel (extreme value type I) distribution, the choice probability of alternative j by consumer i is

$$s_{ijt}\left(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t\right) = \frac{\exp\left(\delta_{jt} + \mu_{ijt}\right)}{1 + \sum_k \exp\left(\delta_{kt} + \mu_{ikt}\right)}$$

Assuming that $\nu_i = \left(\nu_i^1, .\nu_i^k, ., \nu_i^K, \nu_i^p\right)$ is distributed with p.d.f. φ, the market share of product j, s_{jt}, is given by

$$s_{jt}\left(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t\right) = \int s_{ijt}\left(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t\right) \varphi\left(\nu_i\right) d\nu_i$$

and own- and cross-price elasticities follow the classical formulas in a random coefficient logit.

As the data allow us to observe quantities and not market shares, we approximate the aggregate yearly market size denoted by M_t using a fixed coefficient logit version of this model with a non-linear least squares calibration procedure similar to that in Huang and Rojas (2013, 2014). The details are provided in Appendix A.3. The market sizes are such that the outside good's market share declines from 38% in 2003 to 17% in 2010 and then remains stable until 2013.

4.2 Identification and Estimation

Identification of this random coefficient logit model can be obtained with aggregate data using moment conditions between constructed demand shock variables ζ_{jt} and some instrumental variables (Berry, 1994; BLP, 1995). As in the simple logit demand models, one has to take into account the

problem of endogeneity of prices correlated with unobserved demand factors ζ_{jt}. Previous estimation of demand models in pharmaceuticals has used instrumental variables regularly proposed in empirical IO, such as measures of the degree of competition (Stern, 1996), of costs (Azoulay, 2002), or prices for different markets or segments (Hausman instrumental variables, used for example in Azoulay, 2002, and Berndt et al., 2003). Other approaches use the characteristics of competing products (BLP, 1995). Then, the estimation can be performed on aggregate data with GMM using the moment condition

$$E\left[\zeta_{jt}\left(\theta\right)|\mathbf{x}_t, \mathbf{w}_t\right] \tag{6}$$

where $\theta = (\alpha^k, \beta, \sigma_\alpha^k, \sigma_\beta)$ is the vector of parameters and $\mathbf{w}_t$ are instrumental variables, for example cost shifters as in Nevo (2000). Instruments are crucial for the consistency and robustness of the estimates (Knittel and Metaxoglou, 2014).

Using data from the hospital segment and from other countries, we define Hausman-style instrumental variables to instrument prices in the retail sector. For France, we use prices of anti-ulcer drugs sold in French and foreign hospitals (Germany, Italy, Spain, the UK, and the US). However, the validity of such instruments relies on the fact that prices across markets are correlated because of common cost shocks and not because of common unobserved demand shifters (such as changes in scientific knowledge). Thus, we regress those prices on molecule dummies and country and year fixed effects and use the residuals as instrumental variables for the price in France. Controlling for country and time effects, we isolate the quality of each drug proxied by molecule dummies, which is the part of the price more likely to be correlated with demand unobservables: what remains is supposed to be correlated with the marginal cost of each drug. As additional instruments, we use the predictions from a regression of prices on interactions between firm dummies and exchange rates between $US and, separately, Euros, UK Pounds and Swiss Francs (which are the currencies of most drug-producing countries). Finally, we include industry price indices and wages in each

country[6]. Those instruments for prices can also be assumed to instrument for advertising (detailing) expenses, as advertising benefits will clearly depend on the marginal cost of drugs. However, we also add instruments that should affect advertising independent of the costs of drugs: we use the average price of detailing per drug and its square. We obtain this average price using the advertising dataset that reports advertising expenses and the quantity of detailing "units" measured at the brand level in each country.

Following Berry et al. (1999) and Reynaert and Verboven (2014), we use approximations of optimal instrumental variables (Chamberlain, 1987) which are $E\left[\frac{\partial \zeta_{jt}(\theta)}{\partial \theta'}|\mathbf{x}_t, \mathbf{w}_t\right]$, to improve the efficiency of our estimation. Reynaert and Verboven (2014) show that in the case in which price equals marginal cost (perfect competition), we can approximate these optimal instrumental variables by using the predicted price $\hat{p}_{jt}$ from the regression $p_{jt} = \mathbf{x}_{jt}\gamma_x + \mathbf{w}_{jt}\gamma_w + \varepsilon_{jt}$ (where $\mathbf{w}_{jt}$ are country-specific cost shifters) and derivatives of the mean utility with respect to variance coefficients $\frac{\partial \delta_{jt}}{\partial \sigma_\alpha^k}$, $\frac{\partial \delta_{jt}}{\partial \sigma_\beta}$ (approximated by taking derivatives at the mean instead of the mean of derivatives). These non-linear functions of exogenous variables and cost shifters are only approximations of optimal instruments in the case of perfect competition but prove to be quite informative even in the case of imperfect competition. Reynaert and Verboven (2014) also show that there are small gains from estimating the demand model jointly with a non-competitive supply side and that the simplifying assumption of perfect competition does not lead to meaningful bias in the demand estimates.

[6] The producer price index for all pharmaceuticals in France, for anti-secretory/anti-spasmodics in the US, and for pharmaceutical preparations in Germany and wages in the manufacturing industry for France, in the manufacturing of basic pharmaceutical products and preparations for Germany, and in the pharmaceutical manufacturing industry for the US. The sources are the French National Statistical Institute INSEE for France, the US Bureau of Labor Statistics for the US, and Eurostat for Germany.

5 Estimation Results

5.1 Demand Estimation Results

The results of the random coefficient logit (BLP) demand model are reported in Table 4[7]. The drug-specific variables used in the demand specification include the brand type (branded or generic), molecule dummies, the number of side effects and the number of formats. We also include a dummy for the indication for the eradication of helicobacter pylori (the major bacterial cause of ulcer), for GERD (gastroesophageal reflux disease), and for co-prescription with non-steroidal anti-inflammatory drugs (NSAID). Interactions between the branded dummy and the number of formats or the number of side effects are also used in the demand model. These variables capture the most important product characteristics that influence demand and are the result of a specification search allowing for more interactions. Year and molecule dummies were included in the estimation but are not reported in Table 4. Most molecule dummies are significant and their sign reflects perceived quality, higher for PPIs, lower for drugs based on older molecules. Branded drugs are preferred over generics in all three countries, although the effect is not significant in the US. As expected, in line with findings in the literature (Berndt et al., 1996, Azoulay, 2002, Berndt et al., 2003, and Arcidiacono et al., 2013), advertising (detailing) positively affects demand, although not significantly for the US. This result for the US may be due to the large effect of being branded and its heterogeneity, which may be capturing some of the effects of advertising. Having an indication for the eradication of helicobacter pylori (the major bacterial cause of ulcer) or for co-prescription with non-steroidal anti-inflammatory drugs (NSAID) is more valuable (except for Germany), while being indicated to treat gastroesophageal reflux (GERD) is less. The other measures of quality,

[7] Several robustness checks were performed. Coefficients were estimated through the simulated method of moments. The simulations were used to compute the predicted aggregated market shares using 500 normalized Halton draws. We chose Halton draws over the more commonly used (pseudo-)random draws due to their superior performance: Train (2003) shows how the results are similar with 100 Halton draws to using 1000 random draws but the standard errors are lower. Knittel and Metaxoglou (2014) and Dubé, Fox and Su (2012) emphasize some numerical problems in the nested fixed point (NFP) algorithm used to estimate this model. We checked the robustness of the estimates across different sets of starting values, tight convergence criteria, and minimization algorithms, following the suggestions in those papers. We approximate optimal instrumental variables as suggested by Berry, Levinsohn and Pakes (1999) and Reynaert and Verboven (2014). As in Reynaert and Verboven (2014), our estimates are very robust to starting values and simulation draws once we use the optimal instrumental variables approximation.

namely the number of available therapeutic forms (formats) and the number of side effects, have the expected sign when they are significant.

Estimates of the heterogeneity coefficients are reported in columns denoted "sigma". We allow random coefficients for the price and for the branded dummy. Consumers are heterogeneous in their price sensitivity in the three countries (although the variance estimate is not very precise in the case of Germany), less so in their preference for branded drugs, except in the US where there is substantial and significant heterogeneity. In France, the price sensitivity is much larger when the price is above the reimbursement price, called the "TFR" price (denoted $\bar{p}_{jt}^{tfr}$): in this case, the out-of-pocket cost of the drug for the patient is increased by the difference between the price and the TFR price; thus, it is understandable that patients are much more price sensitive. The heterogeneity in price sensitivity is however similar across the different reimbursement regimes (that for drugs with a price higher than the TFR and that for all other drugs), as suggested by the similar magnitude of the sigmas associated with the two price coefficients.

Table 4: Estimation Results of Random Coefficient Logit Model

Random Coefficient Logit	France		Germany		US	
	mean	sigma	mean	sigma	mean	sigma
Price			-5.50***	3.00	-4.06***	2.97**
			(1.50)	(1.87)	(1.36)	(1.52)
Price below TFR ($p_{jt} \times 1_{\{p_{jt} \leq \bar{p}_{jt}^{tfr}\}}$)	-6.95***	6.62**				
	(2.70)	(3.25)				
Price above TFR ($p_{jt} \times 1_{\{p_{jt} > \bar{p}_{jt}^{tfr}\}}$)	-18.73***	6.83***				
	(6.24)	(1.38)				
Advertising	0.27**		0.17***		0.05	
	(0.11)		(0.04)		(0.14)	
Branded	2.44*	1.07	2.81**	0.27	6.31	3.10**
	(1.37)	(3.17)	(1.39)	(0.80)	(4.91)	(1.55)
Nb. formats	0.49*		0.38		1.40***	
	(0.30)		(0.25)		(0.55)	
Generic*nb. formats	1.90***		1.48***		0.02	
	(0.48)		(0.29)		(0.99)	
Nb. side effects	-0.25***		0.02		-0.39***	
	(0.07)		(0.19)		(0.14)	
Generic*nb. side effects	-0.05		-0.22		0.57	
	(0.19)		(0.19)		(0.79)	
Helicobacter indication	1.36***		1.73***		3.58***	
	(0.26)		(0.42)		(0.78)	
NSAID indication	0.61**		0.46***		0.18	
	(0.29)		(0.16)		(0.35)	
GERD indication	-1.44***		-1.52***		-1.58***	
	(0.35)		(0.25)		(0.42)	
Year fixed effects	Yes		Yes		Yes	
Molecule fixed effects	Yes		Yes		Yes	

Notes: Standard errors in parentheses under each coefficient. *, **, and *** indicate significance at the 10%, 5% and 1% levels.

The mean column reports the mean of random coefficients and the estimates of fixed coefficients.

The column sigma reports the estimates of the standard deviation of random coefficients.

Once the BLP demand model is estimated, one can obtain demand elasticities with flexible substitution patterns. Mean own-price elasticity across products and years for France is -3.6 and ranges from -13 to -1 across products. Overall, generics show lower own-price elasticities than branded drugs (-2.9 versus -5.7): this can be interpreted as a consequence of the incentive for generic substitution for pharmacists. Indeed, all pharmacies in France are independent, and pharmacists' returns to capital thus depend on the ratio of the margin to the price of the drug that they have to store. The pharmacists' margins on each drug are regulated as a percentage of the price of the branded drug and the margin is required to be the same in absolute terms for the generic and

branded versions. As a consequence, the pharmacist's returns, which depend on the ratio of margin to price, are higher for generics than for branded drugs. As a result, pharmacists earn higher returns on generics, and the difference between the return on generics and the branded version increases with the price of the drug. This may explain why the own-price elasticity of branded drugs can be larger in absolute value than the own-price elasticity of the generic. Table 5 displays own-price elasticities for a sample of major branded drugs in four years in France. Price elasticity tends to be higher for drugs subject to the TFR rule with a price above the maximum reimbursement price (Tagamet, Zantac, and Pepcidine after 2006), which comes from the additional copayments for patients in this case. Elasticities also change over time. Elasticities for higher quality and more recent branded drugs (in the PPI subclass) tend to decrease gradually over time. Older drugs (H2 and Prostaglandins) display increasing or fairly stable own-price elasticities. Elasticities for recent branded drugs such as Nexium, Lanzor and Takepron decrease after their introduction and then stabilize. Conversely, older drugs such as Cytotec have more stable own-price elasticities at a lower absolute level.

Table 5: Own-Price elasticities of main branded drugs (France)

Drug	Subclass	2003	2006	2009	2012
Losec	PPI	-5.97	-7.86	-5.48	-6.86
Nexium	PPI	-10.94	-6.40	-3.90	-4.66
Lanzor	PPI	-7.78	-6.51	-5.47	-4.85
Takepron	PPI	-7.83	-6.47	-5.25	-4.02
Pantozol	PPI	-7.56	-5.41	-4.91	-5.05
Pariet	PPI	-7.89	-6.05	-4.94	-4.63
Tagamet	H2	-2.74	-7.19	-6.97	-8.88
Zantac	H2	-4.88	-6.76	-5.63	-7.56
Pepcidine	H2	-6.27	-12.81	-12.94	-15.87
Cytotec	Prost.	-2.10	-1.98	-2.45	-2.09

Notes: PPI: Proton Pump Inhibitors. H2: H_2 receptor antagonist. Prost.: Prostaglandins.

Table 6 reports own- and cross-price elasticities for the main drugs in France in 2009. Consistent with medical evidence, anti-ulcer drugs are highly differentiated (low cross-price elasticities) and are mostly substitutable within subclasses (H2, PPI, Prostaglandins). This is clear from the magnitude of the sales gained by drugs in each class if same-class competitors raise prices (Zantac-Tagamet, Nexium-Losec-Takepron). PPI branded drugs are those that usually have the largest cross-price

elasticities with other drugs, showing that the branded and even generic PPI drugs are close substitutes, but they also have quite significant cross-price elasticities with H2 drugs. However, the substitutability relationships go beyond ATC subclass or molecule: patients are willing to switch to the best-seller Nexium if the price of Zantac increases, instead of buying the closest alternative, i.e., one of its generics, such as Mylan's Ranitidine.

Table 6: Own- and Cross-Price elasticities for main drugs, 2009 (France)

Sub-Class	H2	H2	PPI	PPI	PPI	Prost.	H2	PPI
Branded/Generic	Branded	Branded	Branded	Branded	Branded	Branded	Generic	Generic
Company	Aptalis	Glaxo	AstraZ	AstraZ	Takeda	Pfizer	Mylan	Mylan
Molecule	Cimet.	Ranit.	Omep.	Esom.	Lanso.	Miso.	Ranit.	Omep.
Drug Name	Tagamet	Zantac	Losec	Nexium	Takepron	Cytotec	Generic	Generic
Tagamet	-6.96	2.84	0.003	0.23	0.05	0.01	0.02	0.14
Zantac	0.71	-5.62	0.002	0.19	0.04	0.01	0.02	0.13
Losec	0.00	0.00	-5.48	1.64	0.16	0.00	0.003	0.05
Nexium	0.00	0.00	0.19	-3.90	0.25	0.005	0.01	0.14
Takepron	0.00	0.00	0.13	1.73	-5.24	0.01	0.01	0.16
Cytotec	0.002	0.01	0.01	0.81	0.17	-2.45	0.02	0.16
Ranit. Mylan	0.001	0.003	0.02	0.68	0.13	0.01	-3.00	0.23
Omep. Mylan	0.001	0.002	0.04	0.91	0.16	0.01	0.03	-3.68

Notes: Each column is the price elasticity of demand for the drug in the first row with respect to the drug named in the first column.

Company names: Glaxo is GlaxoSmithKline. AstraZ is AstraZeneca.

Molecules: Ranit. is Ranitidine, Omep. is Omeprazole, Esom. is Esomeprazole, Lanso. is Lansoprazole. Miso. is Misoprostol.

5.2 Structural Estimation of Margins and Costs

As reported in Table 1, several regulatory rules may have imposed price cuts on both branded and generic drugs since 2006. Table 1 lists the drugs that were potentially affected by these constraints. Moreover, even before 2006, prices were subject to regulation, as they are set by the regulator (CEPS). However, a potential price cap may not be binding if the counterfactual price decision of a firm not subject to such a constraint could have led to the same choice. Our identification method allows us to determine whether constraints are binding. Once demand is estimated, we use our supply-side model to obtain price-cost margins and marginal costs and test whether price constraints are actually binding.

Using the structural supply model presented in Sections 3.1 and 3.2, we can estimate price-cost margins under free pricing (Section 3.1) and under a price constrained profit maximization (Section

3.2). We assume that firms' pricing is not constrained in the US or in Germany. In France, we allow prices to be possibly constrained at any time, but several regulatory events likely increased the constraints on the price setting of drugs. For example, the anti-ulcer drugs Losec, Lanzor, and Takepron fall under the potential price cut rule after 2006, either because of generic entry in the corresponding subclass (Lansoprazole for Lanzor and Takepron) or because generics had been on the market for long enough (Omeprazole generics for Losec). Given these regulatory rules, it is interesting to check whether estimates of constraints show that the prices of these drugs were indeed more downward constrained after 2006. As explained in Section 3.2, we assume that the log marginal cost of drugs in France is the sum of a time-invariant drug effect and a drug-specific additive linear function of the log costs in the US and Germany, plus an uncorrelated additive deviation.

Following the minimization in equation (4), Table 7 below reports the non-linear least squares (NLLS) estimates of the λ_{jt} parameters for all products j in France from 2003 to 2013. With this method, the inference on all λ_{jt} in France for all periods relies on the large number of products in other countries. We report the yearly means and mean standard errors of the λ_{jt} estimates that are significantly different from zero. Columns 2 and 3 of Table 7 report the total number of branded and generic products in France, while columns 4 and 5 report the corresponding number of products with λ_{jt} significantly different from zero. Columns 6 and 7 display the mean estimates of λ_{jt} and the mean standard errors. Column 8 shows the mean market share of the corresponding products with λ_{jt} significantly different from zero. The last column reports the sum of market shares of products with a corresponding λ_{jt} that is significantly different from zero ($\sum_{j|\lambda_{jt}>0} s_{jt}$).

The results show that not all products are significantly constrained by regulation and in particular that many more products have a significant λ_{jt} estimate starting in 2010. Furthermore, there are more products with significant λ_{jt} in more recent years, and they represent a larger total market share, due to more generic products having entered the market and potentially because more molecules became subject to price cuts, following the entry of generics in the PPI subclass. Further inspection of the significant λ_{jt} shows that the drugs that have a significant λ_{jt} are branded

PPI and Prostaglandins but never H2 branded drugs, and mostly H2 generics until 2009 and then mostly PPI generics. Remark that products that have λ_{jt} not significantly different from zero are still directly constrained by regulation if one product owned by the same firm has a λ_{jt} that is significantly different from zero. Furthermore, even if none of the λ_{jt} is significantly different from zero for all the products j of a firm, the prices chosen by this firm are affected indirectly by the regulatory constraints on other products through the equilibrium conditions. The magnitude of the λ_{jt} estimates is between one-fourth and one-half of the market share of the corresponding product, suggesting that they should have an economically significant impact on equilibrium prices. Counterfactuals will confirm that the regulatory constraints on prices are economically significant.

Table 7: NLLS Estimates of λ_{jt}

	All products		Products with λ_{jt} significantly positive					
	Nb. of products		Nb. of products		λ_{jt}		s_{jt}	
Year	Branded	Generics	Branded	Generics	Mean	Std err	Mean	Sum
2003	12	11	2	4	0.0025	0.0012	0.0089	0.0534
2004	12	27	2	10	0.0026	0.0008	0.0072	0.0864
2005	12	28	3	2	0.0094	0.0033	0.0248	0.1240
2006	12	30	0	8	0.0002	0.0000	0.0006	0.0048
2007	12	37	1	6	0.0003	0.0001	0.0014	0.0098
2008	12	36	1	6	0.0020	0.0007	0.0064	0.0448
2009	12	47	1	10	0.0004	0.0001	0.0018	0.0198
2010	12	50	1	16	0.0008	0.0002	0.0029	0.0493
2011	12	62	0	27	0.0015	0.0002	0.0056	0.1512
2012	12	74	1	38	0.0019	0.0003	0.0067	0.2613
2013	11	83	3	48	0.0027	0.0005	0.0091	0.4641

Notes: The standard error column for λ_{jt} is the mean of each individual standard error.

We now turn to the corresponding marginal cost estimates $c_{jt}(\boldsymbol{\lambda}_t)$ using equation (2). As a matter of comparison, we also estimate the marginal costs we would obtain under the assumption that there are no regulatory constraints that correspond to estimates $c_{jt}(\mathbf{0})$. The evolution of price-cost margins and the differences obtained using the two models should shed some light on the actual role played by regulation in the price-setting decisions of the firms. Table 8 displays the annual averages of the estimated price-cost margins (as a percentage of price) for the constrained model and the free pricing model. The average price-cost margin is 6 to 8 percentage points lower when taking into account the price constraints until 2009 and 10 to 15 percentage points lower from

2010 to 2013. This difference is larger for generics than for branded drugs. The average margins for branded drugs are smaller as a percentage of the price than for generics.

Table 8: Average price-cost margins (France)

Year	All Drugs		Branded		Generic	
	Free	Constr.	Free	Constr.	Free	Constr.
2003	27%	21%	21%	16%	33%	26%
2004	28%	20%	23%	16%	30%	21%
2005	27%	20%	23%	16%	28%	22%
2006	30%	22%	21%	15%	33%	24%
2007	27%	21%	21%	16%	28%	23%
2008	29%	23%	20%	15%	32%	26%
2009	31%	24%	22%	16%	33%	26%
2010	38%	28%	20%	15%	42%	31%
2011	40%	30%	22%	16%	43%	33%
2012	44%	33%	21%	17%	47%	35%
2013	53%	38%	29%	21%	56%	40%

Notes: Free and Constr. stand for free and constrained price equilibrium.

Margins as a percentage of price.

Table 9 reports average price-cost margins by molecule. It shows the estimated margins under the free pricing model and the price constrained model. Margins are between 9% and 37% for branded drugs and 23% to 47% for generics. The generics Cimetidine and Rabeprazole show much higher margins than their corresponding branded versions. This is not surprising: it is common wisdom in the industry that generic firms display lower marginal costs than branded manufacturers, and this is especially true for older molecules, such as Cimetidine (Arcidiacono et al., 2013). Markups also vary substantially across molecules. Examining margins drug by drug also uncovers interesting variation across drugs: the difference is important for Losec for the full period (between 7 and 12 percentage points) but not as much for Takepron and Pantozol. For Lanzor and Pariet, the difference is small in 2003 but grows over time for Lanzor and more importantly for Pariet, showing that constraints mattered more over time and consistent with explicit price cuts introduced in 2006 and 2012 for these molecules.

Table 9: Average price-cost margins by molecule (France)

		All Drugs		Branded Drugs		Generic Drugs	
Sub-Class	Molecule	Free	Constr.	Free	Constr.	Free	Constr.
H2	Cimetidine	52%	41%	15%	14%	62%	47%
	Ranitidine	30%	23%	24%	19%	32%	24%
	Famotidine	28%	20%	10%	9%	36%	26%
	Nizatidine	18%	14%	18%	14%		
PPI	Omeprazole	29%	22%	22%	14%	30%	23%
	Esomeprazole	43%	31%	24%	15%	50%	37%
	Lansoprazole	39%	29%	20%	14%	45%	34%
	Pantoprazole	43%	33%	20%	14%	47%	36%
	Rabeprazole	45%	33%	18%	13%	60%	43%
Prost.	Misoprostol	47%	37%	47%	37%		
Combi.	Bismuth/Antibiotic	27%	21%	27%	21%		

Notes: Margins as a percentage of price. Empty cells indicate that there is no generic version of the molecule named in corresponding row.

Unsurprisingly, the estimates of λ_{jt} are often larger and (more) significant in the years when the price cuts were introduced for each molecule. This translates into larger differences between constrained and unconstrained margins. This effect is especially clear for Nexium in 2009 and Pantozol in 2008, although it seems to persist for Nexium, while it fades out for Pantozol: this does not mean that prices increased but, instead, that the regulated prices are closer to what the unregulated prices for these drugs in those years would have been, presumably due to stronger competition from other drugs. The spillover effects of regulation on drugs not directly subject to price cuts are salient in the case of Cytotec: this old Prostaglandin drug displays constrained markups up to 16 percentage points lower than unconstrained markups, showing how the prices chosen by its manufacturer are affected by the regulatory constraints on its closest PPI substitutes (mainly Nexium and Takepron) through the equilibrium conditions. A similar although less-striking pattern is estimated for Zantac. However, this is not true for all drugs: there does not seem to be such an effect on Tagamet or Pepcidine, the constrained and unconstrained margins of which are almost identical after 2004-2005. The effect on drugs in the H2 subclass seems to prevail in the beginning of the period, when Cimetidine and Ranitidine became subject to the demand-side regulation of TFR, which determines the maximum reimbursement that a patient can obtain. Our demand estimates show that the TFR regulation affected the shape of demand, and these results suggest that the CEPS may have placed some additional pressure on prices for these drugs when introducing the maximum reimbursement price with the TFR rule.

These comparisons show how much one would overestimate margins, or underestimate costs, when not taking into account price constraints. However, they do not show what the counterfactual price difference would be if there were no pricing regulation (Table B1 in Appendix B.1 shows that Tagamet's counterfactual prices would have been much higher and thus its margins much higher under free pricing). It is certainly possible that margins under the two models are not estimated to be very different given the observed equilibrium prices, while the counterfactual free pricing margins would be very different because the prices of substitute drugs would change. We turn to the counterfactual analysis in the next section.

6 Counterfactuals

In this section, we analyze counterfactual scenarios in which we change the regulatory environment of drug price setting in France. Holding the shape of demand unchanged, we first study the case in which drug prices would no longer be constrained by the regulator but freely chosen by firms. We expect prices to increase, as we found that price constraints are sometimes binding. However, the magnitude of the effect on prices, demand, and expenses is unknown and ambiguous. As the results in the previous section suggest, by no means are all prices directly constrained by regulation, as many potential constraints on prices are found to be non-binding, but equilibrium prices are all likely to change. Then, we investigate a counterfactual in which the regulator would set price caps through an external reference pricing policy. In both counterfactuals, not only can we evaluate the changes in prices, demand, and expenses, but we can also compute the consumer surplus as evaluated by the revealed preferences identified in our demand model. Of course, as patients' revealed preferences are affected by the health insurance system, this measured surplus may not represent the true benefit for society, whose willingness to pay for drugs is mis-measured by the prescriber/patient's price sensitivity. We however report this surplus change, which is obtained with the standard formula for random coefficient logit models.

6.1 Counterfactuals of Free Pricing in France

Using marginal costs estimated when allowing regulatory constraints on prices, we assess the impact of price constraints on prices and quantities by simulating the counterfactual market equilibrium of free pricing. Specifically, we estimate the price equilibrium with free pricing for branded drugs and maintain the current regulatory price cap rules for generics that cap the price of generics as a fixed proportion of the price of the corresponding branded drug (which, on average across drugs and years, results in generics having approximately half the price of their branded version)[8]. We thus solve the following pricing equilibrium in which all firms f choose prices such that

$$\begin{aligned} \max_{\{p_{jt}\}_{j\in F_f}} \Pi_{ft} &= \sum\nolimits_{j\in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t) \\ s.t. \quad p_{jt} &\leq \tau_{b(j)t} p_{b(j)t} \text{ if } j \text{ is a generic} \end{aligned}$$

Imposing that all prices are larger than marginal costs ($p_{jt} \geq c_{jt}$), we solve for the Bertrand-Nash equilibrium.

Comparing the difference between observed and counterfactual prices for branded and generic drugs, by molecule for all years, Tables 10 and 11 show that branded drugs are cheaper than in the absence of price regulation: this is true for Cimetidine and Misoprostol for the full period and for all drugs after 2010 (negative changes mean that observed prices are lower than the counterfactual prices). The price decline for generics due to regulation is always smaller as a percentage of the price and thus even smaller in absolute terms, as generics are cheaper than their branded versions. This shows that the regulation of drug prices in France has a larger effect on the prices of branded drugs than on those of generics.

Consistent with the pattern of λ_{jt} estimates described in the previous section, observed and counterfactual prices begin to diverge more in the year when the price cuts were introduced. This is true for all PPI-based drugs, which show fairly close observed and counterfactual prices in 2003 but larger differences subsequently. For example, the gap is already substantial in 2006

[8] This percentage evolved over time: until 2005, at entry, the generic price could not exceed 55% of the branded regulated price. The share was reduced in later years: 50% in 2006, 45% in 2009, and 40% in 2012. However, the percentage may be higher in specific cases (high production costs, late or difficult entry for generic manufacturers, or low price of the branded drug), as long as the difference between the brand-name and the generic price is at least 10%.

for Losec and tends to increase once its closest competitors also become subject to the price cuts. Similarly, if manufacturers could freely choose prices, Pantozol (Pantoprazole molecule) and Pariet (Rabeprazole molecule) would be substantially more expensive since 2009 and 2012, respectively. Tagamet (Cimetidine molecule) is clearly cheaper because of the price regulation but more so towards the end of our period. The results by brand in Table B1 in Appendix B.1 show that Zantac (Ranitidine molecule) is almost unaffected and Raniplex (also the Ranitidine molecule) is, but only starting in 2012, being only 4 cents cheaper than it would be with free pricing. The price reduction policy implemented in 2006 appears to have been effective in lowering prices even more for Tagamet. PPI drugs are only very slightly cheaper in 2003 but become more affected by the regulatory constraints starting in 2006, especially for Losec, when the first price cut rule was introduced for Omeprazole and Lansoprazole. This shows that the price-reducing effect of regulatory constraints on H2 drugs also affected Losec in equilibrium. The price-reduction constraints introduced in 2006 on PPI drugs had larger price-reduction effects starting in 2009, except for Takepron. Table B2 in Appendix B.1 reports the observed and counterfactual prices for generics (in the interest of space, we report results every three years).

Table 10: Average Price Change for Branded Drugs
from Free Pricing to Current Regulation

Subclass			H2				PPI			Prost.	Combi.	
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	-11%	-3%	-2%	-2%	-2%	-2%	-3%	-2%	-2%	-11%		-4%
2004	-18%	-6%	-4%	-3%	-8%	-3%	-4%	-2%	-3%	-12%		-6%
2005	-15%	-8%	-5%	-3%	-7%	-3%	-4%	-3%	-3%	-14%		-6%
2006	-17%	-5%	-4%	-3%	-7%	-3%	-4%	-3%	-3%	-13%		-6%
2007	-20%	-4%	-4%	-3%	-10%	-6%	-4%	-3%	-3%	-11%		-6%
2008	-24%	-3%	-3%	-2%	-7%	-6%	-4%	-4%	-3%	-9%		-6%
2009	-19%	-3%	-4%	-3%	-11%	-6%	-10%	-4%	-3%	-8%		-7%
2010	-12%	-3%	-3%	-2%	-9%	-8%	-9%	-5%	-2%	-11%		-6%
2011	-14%	-4%	-3%	-3%	-11%	-10%	-14%	-12%	-3%	-11%		-8%
2012	-28%	-4%	-5%	-3%	-11%	-12%	-18%	-18%	-24%	-11%		-12%
2013		-10%		-9%	-23%	-19%	-27%	-27%	-28%	-16%	-11%	-18%

Notes: Percent changes are computed as (counterfactual price - observed price)/counterfactual price.

Empty cells when branded molecules had not entered yet or had exited. Column "Total": unweighted average of average changes by molecule.

Brands are Pylera for molecule Combi. (Bismuth/Antibiotic), Tagamet for Cimetidine, Nexium for Esomeprazole,

Pepcidine for Famotidine, Lanzor and Takepron for Lansoprazole, Cytotec for Misoprostol, Panaxid for Nizatidine,

Losec for Omeprazole, Pantozol for Pantoprazole, Pariet for Rabeprazole, Zantac and Raniplex for Ranitidine.

Comparing those counterfactual effects on price with the triple difference effects estimated in Table 3, we see that the difference-in-difference estimates of price cuts on the prices of drugs in France would strongly overestimate the impact of this regulation on prices, as we find estimates of -30% (column 4 of Table 3) on the prices of the "price cut" regulatory rule. Evaluating the average counterfactual price change due to regulation on the set of drugs subject to the "price cut" rule (Losec, Lanzor, and Takepron since 2006; Nexium since 2008; Pantozol since 2009; and Pariet since 2012), we find instead an 11.5% lower price due to the price constraints, ranging from a 4% decline in 2006 up to a 24% decline in 2013, when all PPI molecules became subject to the regulation.

Table 11: Average Price Change for Generics
From Free Pricing to Current Regulation

Subclass		H2				PPI			
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Total
2003	-8%	-4%							-5%
2004	-4%	-6%	-5%	-2%					-4%
2005	-3%	-5%	-4%	-1%					-3%
2006	-7%	-6%	-4%	-3%					-5%
2007	-2%	-5%	-1%	-1%	-3%				-2%
2008	-5%	-6%	-3%	-3%	-5%				-4%
2009	0%	-6%	-2%	-2%	-4%	-4%			-3%
2010	-2%	-6%	-4%	-4%	-7%	-6%			-5%
2011	-2%	-6%	-4%	-4%	-7%	-6%	-5%		-5%
2012	-6%	-6%	-2%	-5%	-9%	-8%	-7%	-5%	-7%
2013	-14%	-8%	24%	-11%	-12%	-11%	-10%	-12%	-10%

Notes: Percent changes are calculated as (counterfactual price - observed price)/counterfactual price.

Empty cells when the generics had not entered yet. Column "Total": unweighted average of average changes by molecule.

Regarding the effects on total equilibrium quantities (reported in Tables B3 and B4 in Appendix B.1), we can see that regulatory constraints on prices had a positive overall effect on quantities consumed, albeit a relatively modest one at the end of our period of study. The effect arises primarily from an increase in branded drug consumption compared to generic consumption. Price effects are thus not encouraging generic use (and even decrease it towards the end of our period of study in 2013) but are instead increasing the consumption of branded drugs. Price cuts are also steering consumption towards certain drugs. The higher counterfactual free prices would result in lower sales for most PPI drugs in later years, in favour of cheaper, older H2 drugs, especially those based on Ranitidine (Zantac and Raniplex). However, the blockbuster Losec, despite a higher counterfactual

price, would benefit from the higher prices of its closest competitors (Nexium and Takepron) and sell even more than under the regulated lower price.

In terms of total expenses, Table B5 and B6 in Appendix B.1 show that the price regulation has small effects until 2010, and then 5 to 6% decreases in 2011 and 2012 and up to 10% in 2013, when the large price-reducing effect of regulatory constraints made it possible to reduce total expenditures on anti-ulcer drugs.

One can then compute savings in expenditures on drugs due to the policy. Table 12 shows the different results in terms of savings compared to the counterfactual situation of free pricing. Negative savings mean that expenses would have been lower under the counterfactual free pricing and thus that regulation increases expenses. Overall, aggregated savings of the current regulatory situation compared to the free pricing equilibrium represent 261 million dollars for the anti-ulcer market in France over the period 2003-2013, i.e., approximately 3% of total expenditures for this market. The savings are due primarily to the last years, as they were very small until 2009 and much larger afterwards, and come from the PPI subclass. Regulation had small and even negative effects on total expenses on H2 drugs, with a particular increase in expenses for Ranitidine due to considerably higher sales. Savings on PPI derive primarily from Omeprazole and especially Rabeprazole in the last years of the period. Without additional policy changes in the regulation of prices, the free pricing of drugs would lead to an increase in drug expenditures.

Table 12: Counterfactual Savings and Surplus from Free Pricing

		2003	2006	2009	2012	2003-2013
Sub-Class	Molecule					
H2	Cimetidine	-787	-200	199	128	-623
	Ranitidine	-705	-474	-310	711	-3,597
	Famotidine	-3	18	41	50	196
	Nizatidine	3	1	2	2	22
Sub-total H2		-1,492	-654	-70	891	-4,003
PPI	Omeprazole	5,501	10,353	11,142	10,827	177,005
	Lansoprazole	486	53	72	4,488	8,535
	Pantoprazole	-457	-854	3,704	2,139	18,856
	Esomeprazole	2,479	-1,469	-248	1,887	27,088
	Rabeprazole	635	161	-2,233	46,305	34,888
Sub-total PPI		8,643	8,244	12,436	65,645	266,373
Prost.	Misoprostol	-208	-154	-44	36	-1,076
Combi.	Bismuth/Antibiotic					54
Total		6,943	7,436	12,323	66,572	261,348
Sub-total	Branded	7,098	7,138	8,829	39,792	95,325
	Generics	-155	298	3,494	26,779	166,023
Consumer Surplus Change		+2%	+3%	+4%	+13%	+15%

Notes: Savings are in 1,000 $US. Negative numbers indicate increased expenditures compared to observed.

Surplus change is in percentage of counterfactual estimated surplus.

Finally, we can assess the impact of these regulatory rules on welfare, by computing the change in consumer surplus compared to the counterfactual free pricing scenario. We find that consumer surplus is higher under the constrained price equilibrium. Table 12 shows that the increase is 2% in 2003, 3% in 2006, 4% in 2009 and 13% in 2012, primarily and unsurprisingly due to greater utilization of sometimes cheaper drugs and of preferred branded drugs.

Hence, while reducing prices on high-quality PPI drugs encourages their consumption at the expense of older and less-effective H2 drugs, it is doing so at the expense of their generic versions, which also see their prices reduced but less in absolute and percentage terms. Generic manufacturers are substantially harmed by price cuts, as profits would be 72% higher in a free pricing scenario, compared to an increase of only 18% for branded firms. The regulation of prices thus reduces one layer of differentiation between branded and generic drugs, the difference in price. Without this wedge, the preference for the branded drugs prevails (as captured by our demand estimates) and generics lose sales in favour of the now cheaper – yet still more expensive – branded versions. The mechanism is similar to the segmentation identified in previous research (Frank and Salkever, 1997;

Ching, 2010b), with the price difference between the branded and the generic drug acting as a differentiation device that regulation reduces.

It is interesting to compare the previous results to those obtained in a fully free pricing equilibrium, in which even the constraint on the price of the generics is lifted and generics are no longer subject to a cap on their price in the form of a percentage of the branded price. A summary of the results is reported in Appendix B.3. As we expected, the average difference between observed and counterfactual generic prices is larger than in the regulated setting, with all generics increasing their prices, but with molecule variation (especially Cimetidine, Famotidine, and Rabeprazole). More interestingly, branded manufacturers respond by setting lower prices than in the scenario with free branded price but regulated generics, with prices being closer to those observed under the current price cut regulation. This is because even if on average there is a preference for branded versions in France, it is not particularly strong and is highly heterogeneous. We interpret this lower preference for brands than in other countries (everything else being equal) as a possible effect of the strong incentives for pharmacists to substitute generic drugs for branded ones when the prescription does not prevent substitution, despite the likely preference of patients for branded drugs. As a consequence, demand shifts from generic to branded drugs, while the aggregate effects on expenditures are similar to those obtained under the cap on generics. Ultimately, allowing generics to freely set their prices seems to lead to a larger shift in sales to branded drugs.

6.2 Counterfactuals of External Reference Pricing in France

External reference pricing was introduced in France in 2004 as one criterion used by the CEPS in setting the price of new drugs. It only applies to some drugs that entered the French market after this date and none in our sample on the anti-ulcer market until 2013. Under this policy, the entry price of innovative drugs (i.e., those with an ASMR of 1, 2 or 3) must be consistent with prices observed in the reference countries, which are Germany, Italy, Spain and the UK. For non-innovative drugs (i.e., with an ASMR of 4 or 5), the main criterion used is the possibility of providing savings with respect to an appropriate comparator drug. For these drugs, external reference pricing may be used by the CEPS to restrict prices.

We thus perform counterfactual simulations with an explicit cap on prices $\bar{p}_{jt}^{ref}$ for drug j in year t that is defined as the average price excluding the lowest price across the four reference countries for two innovative drugs, Losec and Nexium (ASMR 2 and 3), and the average prices across the four countries for other branded drugs. For generics, we maintain the current regulation that caps their price as a percentage of the branded drug (as described in Section 6.1). We thus solve the following external reference pricing equilibrium in which all firms f choose prices such that

$$\begin{aligned} \max_{\{p_{jt}\}_{j\in F_f}} \Pi_{ft} &= \sum\nolimits_{j\in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t) \\ s.t. \quad p_{jt} &\leq \bar{p}_{jt}^{ref} \qquad \text{if } j \text{ is a branded drug} \\ p_{jt} &\leq \tau_{b(j)t} p_{b(j)t} \quad \text{if } j \text{ is a generic} \end{aligned}$$

We also require all prices to exceed marginal costs ($p_{jt} \geq c_{jt}$), and we solve for the Bertrand-Nash equilibrium. We perform an additional counterfactual (reported in Appendix B.4) in which we remove this additional constraint on generics and allow generic manufacturers to have the same external reference cap as their branded versions.

Before examining the counterfactuals, let us mention that this definition of external reference prices implies that observed prices tend to be, on average, higher than this external reference price from 2003 to 2005 but lower after 2006, which is when the French regulator introduced price cut rules.

Tables 13 and 14 report the average price changes from the current observed prices to the equilibrium prices under the external reference pricing caps, as a percentage of counterfactual prices. On average, the counterfactual prices under the external reference pricing rule are lower (and in some years significantly so) than observed prices under the current regulation, and the difference increases over time (see column "Total" of Tables 13 and 14). Hence, despite the introduction of price cuts in France, which lowered prices with respect to a free pricing scenario, external reference prices as defined above would further reduce prices. However, the differences across drugs are substantial. H2 and Prostaglandin drugs would be forced to set a lower price in all years, although the difference with the observed price is sometimes small. In the PPI subclass, Losec and Nexium, the innovative drugs (with a price cap significantly higher than the observed price), would set a

higher price (but usually lower than the reference cap) except in 2013. Other PPI drugs seem to benefit from these higher prices for the two best-selling drugs and are also able to increase their prices, although not always.

Table 13: Average Price Change for Branded Drugs
From Current Regulation to External Reference Caps

Subclass			H2				PPI			Prost.	Combi.	
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	-10%	-12%	-4%	-10%	3%	2%	3%	3%	2%	-21%		-4%
2004	-7%	-4%	-5%	-9%	3%	3%	5%	2%	4%	-23%		-3%
2005	-6%	-21%	-10%	-9%	2%	1%	0%	3%	3%	-24%		-7%
2006	-8%	-2%	-3%	-8%	2%	3%	3%	3%	4%	-26%		-2%
2007	-6%	0%	-3%	-9%	3%	2%	2%	5%	2%	-31%		-3%
2008	-1%	-1%	-3%	-8%	3%	4%	-6%	6%	-5%	-36%		-4%
2009	-6%	-1%	-3%	-8%	0%	0%	-6%	9%	-4%	-38%		-5%
2010	-4%	-8%	-3%	-8%	3%	5%	-7%	15%	-5%	-32%		-4%
2011	-3%	-16%	-2%	-12%	3%	5%	-8%	17%	4%	-34%		-5%
2012	-5%	-4%	-2%	-11%	2%	-7%	8%	20%	8%	-38%		-3%
2013		-3%		-8%	-9%	-10%	-11%	-14%	-15%	-31%	-15%	-12%

Notes: Percent changes are calculated as (counterfactual price - observed price)/counterfactual price.

Empty cells when branded molecules had not entered yet or had exited. Column "Total": unweighted average of average changes by molecule.

Brands are Pylera for molecule Combi. (Bismuth/Antibiotic), Tagamet for Cimetidine, Nexium for Esomeprazole,

Pepcidine for Famotidine, Lanzor and Takepron for Lansoprazole, Cytotec for Misoprostol, Panaxid for Nizatidine,

Losec for Omeprazole, Pantozol for Pantoprazole, Pariet for Rabeprazole, Zantac and Raniplex for Ranitidine.

Table 14 shows the results for generics. The downward effect on the prices of generic drugs under this counterfactual regulation is consistent across all molecules and years and often very substantial, with observed prices sometimes being more than twice the counterfactual prices. Regarding the effects on demand in Tables B9 and B10 in Appendix B.2, demand, on average, increases in all years, but the substitution of sales seems to go towards much cheaper H2 drugs at the expense of more innovative and more effective PPI drugs, with Nexium and Losec limiting their losses in some years despite their higher prices thanks to their recognized superior quality. Other PPI drugs such as Lanzor, Takepron, and Pariet lose substantial market share. On the contrary, H2 and Prostaglandins sell much more in early years. Unsurprisingly, given their much lower price, the big winners from external reference pricing are generics, the sales of which increase substantially in all years for all molecules (with the exception of Famotidine and Ranitidine, when their branded version exits the market in 2013).

Table 14: Average Price Change for Generics
From Current Regulation to External Reference Caps

Subclass		H2				PPI			
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Total
2003	-62%	-19%							-35%
2004	-77%	-21%	-23%	-7%					-26%
2005	-96%	-23%	-24%	-10%					-29%
2006	-102%	-27%	-31%	-13%					-31%
2007	-120%	-30%	-32%	-14%	-25%				-33%
2008	-136%	-28%	-32%	-17%	-29%				-37%
2009	-126%	-30%	-33%	-20%	-34%	-32%			-35%
2010	-128%	-27%	-31%	-30%	-54%	-43%			-44%
2011	-132%	-29%	-31%	-34%	-64%	-58%	-37%		-50%
2012	-151%	-31%	-41%	-36%	-69%	-67%	-60%	-91%	-61%
2013	-125%	-22%	-28%	-60%	-77%	-84%	-81%	-83%	-63%

Notes: Percent changes are calculated as (counterfactual price - observed price)/counterfactual price.

Empty cells when the generics had not entered yet. Column "Total": unweighted average of average changes by molecule.

As shown in Tables B11, B12 and B13 in Appendix B.2, despite the much lower price level, on average, expenditures under external reference pricing regulation would not differ substantially from those observed under the current regulatory rules in early years: the increased demand would slightly outweigh the effect of lower prices until 2009. After this year, however, external reference pricing would lead to savings, with total expenditures declining by up to 50% at the end of the period. In later years, the savings are generated by all drugs, the majority coming from PPI. Between 2003 and 2008, expenditures would be higher for H2 and Omeprazole. Moreover, in this counterfactual scenario, expenditures on generics are higher, except in 2011-2013, when demand increases but the price is so low that it generates savings relative to current price regulation. As a result, Table 15 shows that the counterfactual consumer surplus would be much larger than the observed one and would increase over time.

These counterfactual simulations suggest that different regulatory rules may lead to different equilibrium levels of demand and prices but that they may also determine winners and losers. The drugs that are generally harmed by external reference pricing regulation are branded PPI drugs, which can set a higher price in early years but sell less, to the benefit of H2 drugs. Subsequently, when PPI generics become available, demand generally switches to generics. Thus, this rule seems to encourage generic sales, but it entails strong pressure on their margins (for some, the price is

estimated to decrease to the marginal cost). Therefore, it would fulfil one of the objectives of the French regulator, to increase generic penetration, but it is unclear what the long-run effects might be if generics were priced at the level of marginal costs. To assess these long-run effects on the entry and exit of drugs, however, we would need a dynamic model, something which is outside the scope of our paper.

Table 15: Counterfactual Savings and Surplus with External Reference Caps

			2003	2006	2009	2012	2003-2013
Sub-Class	Molecule						
H2	Cimetidine		-1,216	-511	-233	385	-3,659
	Ranitidine		-10,370	-1,809	-913	5,221	-19,995
	Famotidine		-576	-98	100	-71	-2,087
	Nizatidine		-239	-43	11	36	-452
Sub-total H2			-12,400	-2,462	-1,206	5,743	-26,193
PPI	Omeprazole		-5,855	-18,328	-7,054	48,410	6,571
	Lansoprazole		4,588	5,565	-3,376	19,016	85,067
	Pantoprazole		3,923	7,757	3,680	20,486	105,880
	Esomeprazole		-701	-953	3,583	28,559	78,939
	Rabeprazole		1,846	4,300	11,117	2,077	124,195
Sub-total PPI			3,800	-1,659	7,950	118,548	400,653
Prost.	Misoprostol		-526	-339	-264	461	-1,752
Combi.	Bismuth/Antibiotic						539
Total			-9,126	-4,460	6,480	124,751	373,246
Sub-total		Branded	-7,205	16,401	27,282	30,564	261,753
		Generics	-1,921	-20,861	-20,802	94,187	111,493
Consumer Surplus Change			+3%	+9%	+26%	+47%	+37%

Notes: Savings are in 1,000 $US. Negative numbers indicate increased expenditures relative to observed.

Surplus change is as a percentage of the counterfactual estimated surplus.

In Appendix B.4, we present tables of results when we allow generic prices to be capped at the same external reference price level as their branded versions, i.e., we remove the requirement that generic prices are capped at a fixed percentage of their branded versions. Our simulations suggest that the removal of this rule would eliminate the effect we reported in the previous paragraph, leading instead to generic prices being very close to and sometimes higher than the observed values. Branded prices would be similar to those estimated in the previous counterfactual, except for a downward pressure that these more expensive generics seem to be placing on some PPI branded drugs at their entry on the market, especially on Nexium after 2008 and Pariet and Pantozol since 2012. Thus, in this scenario, generics would enjoy a larger markup but to the detriment of their sales. However, the effect does not seem to be simply a transfer from generics to branded, as total

demand declines, expenditures increase and consumer surplus is estimated to be lower than the observed value, and this is the case to a larger extent in the last four years of the period considered.

7 Conclusion

We develop a structural model of demand and supply to study the impact of the price regulation of anti-ulcer drugs in France. Using IMS Health data on retail sales of anti-ulcer drugs for the period 2003-2013, we first estimate demand for France, the US and Germany, using a flexible model that accommodates the consumer heterogeneity prevalent in this market. The results confirm that anti-ulcer drugs are strongly differentiated and that consumers are highly heterogeneous in their price sensitivity. Consistent with the previous literature, brand-name drugs are preferred to their generic versions, and advertising increases demand. We use these demand estimates to investigate the effect of price regulations on firms' pricing behavior. We model the pricing decisions of firms as being potentially constrained by these regulatory rules in the form of price caps. Identification relies on observing the same products in a regulated market (France) and in markets under free pricing (the US and Germany) and uses cost restrictions for the same drugs across markets. The results show that not all products are significantly constrained by regulation and that, unsurprisingly, this is more common in the years when the French regulator (CEPS) introduced price cuts for branded drugs based on the availability of generics, which directly affected six anti-ulcer drugs in our sample after 2006.

To quantify the effects of regulation, we perform a counterfactual simulation of the equilibrium without any price regulation for branded drugs, with generics still subject to the cap based on the price of their branded versions. We find that recent regulation was effective in reducing prices, especially for high-quality drugs, and this encouraged their consumption. However, it did so at the expense of their generic versions, which also experienced a decline in price but one less in both absolute and percentage terms. With a smaller wedge between the branded and generic prices, the preference for the branded drugs captured by our demand estimates shifts demand from generics to the now cheaper – yet still more expensive – branded versions. Nevertheless, price constraints generate some modest savings, on average 3% of total expenses for the full 11-year

period. Counterfactuals also show that consumer surplus increases thanks to regulation, due to greater utilization of cheaper and preferred branded drugs.

We simulate a second counterfactual equilibrium under an external reference pricing policy (similar to that introduced in France but never used for the drugs in our sample), which caps the price in France with a reference depending on the average price of the same drug in Italy, Germany, the UK and Spain. We find that prices would decline even more and demand would increase but less than proportionally, leading to additional savings. Furthermore, generic penetration would increase (one of the objectives of the French regulator), driven by very small generic margins. While this short-run effect would increase consumer surplus, it is unclear what the long run effects on the entry and exit of generics could be.

Our work demonstrates the importance of accounting for regulation in estimating market power or welfare and raises concerns about the ability of regulators to predict ex ante the equilibrium effects generated by different regulatory rules. While we believe that this may be a general message and not something that is induced by the specific setting that we study, we are aware of some limitations of our work. For example, the results produced by our static model do not take into account dynamics in demand, such as learning effects or dynamics in supply, and only provide a short-term evaluation of the effects of the policy. An evaluation of the long-run effects of a regulation should take into account its effects on research and development and the entry of drugs, both branded and generic, topics that we leave for future research.

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A Appendix

A.1 Proof of Proposition

With assumption C_S and U_S, $\mathbf{c}_t$ is identified using price-cost margins solutions (1) in all unconstrained markets S. Then, using (2) and

$$\mathbf{c}_{t_0} = \mathbf{p}_{t_0} + Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0} - Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0}$$

we have

$$\begin{aligned}\mathbf{c}_t - \mathbf{c}_{t_0} &= \mathbf{p}_t - \mathbf{p}_{t_0} + Q_p\left(\mathbf{p}_t\right)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0} + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} \\ &= \left(z_t - z_{t_0}\right)'\delta + \boldsymbol{\omega}_t\end{aligned}$$

Denoting

$$\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right) = \left[\mathbf{p}_t - \mathbf{p}_{t_0} + Q_p\left(\mathbf{p}_t\right)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0}\right] + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} - \left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)'\delta$$

using C_S, the true $\boldsymbol{\lambda}_{t_0}$ should satisfy the moment condition for all $t \in S$

$$E\left(\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right)\right) = 0$$

The identification rank condition is that the matrix $E\left[\frac{\partial \boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})}{\partial \delta}, \frac{\partial \boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})}{\partial \boldsymbol{\lambda}_{t_0}}\right] = \left[\left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)', Q_p^{-1}(\mathbf{p}_{t_0})\right]$ has full rank $J_{t_0} + \dim(\delta)$. As J_t is the number of goods in market t, and the expectation of the moment condition is over goods and markets $t \in S$, we also need that $J_{t_0} + \dim(\delta) \leq \sum_{t \in S} J_t$ which will be often the case.□

A.2 Estimation of Constrained Marginal Costs

Given the demand estimates that determine the demand shape $Q_p\left(\mathbf{p}_t\right)$, given a vector $\boldsymbol{\lambda}_t$, the marginal cost vector is

$$\mathbf{c}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t\right) = \mathbf{p}_t + A\left(\mathbf{p}_t\right)\left(\mathbf{q}_t - \boldsymbol{\lambda}_t\right)$$

where $A\left(\mathbf{p}_t\right) = \sum_f Q_p^f\left(\mathbf{p}_t\right)^{-1}$ is composed of block of the inverse demand derivatives by firm $Q_p^f\left(\mathbf{p}_t\right)$ ($Q_p^f\left(\mathbf{p}_t\right)$ is the matrix on demand derivatives $Q_p\left(\mathbf{p}_t\right)$ where all rows and columns not corresponding to firm f products are replaced by zeros). Remark that the cost vector $\mathbf{c}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t\right)$ implicitly depends on demand estimates through the estimated $A\left(\mathbf{p}_t\right)$.

We impose a cost restriction that can be written with a given vector of observable variables $\mathbf{z}_t$, wit a known transformation $f(.)$, as

$$f(\mathbf{c}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t\right)) = \mathbf{z}_t\gamma + \boldsymbol{\omega}_t$$

with

$$E\left[\boldsymbol{\omega}_t | \mathbf{z}_t\right] = 0$$

We thus look for $(\boldsymbol{\lambda}_t, \gamma)$ that satisfy this moment condition whose empirical counterpart leads us to the following minimization problem

$$\min_{(\boldsymbol{\lambda}_t, \gamma)} \left\| f(\mathbf{c}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t\right)) - \mathbf{z}_t\gamma \right\|$$

using the usual L_2 norm, which leads to the following solution

$$\boldsymbol{\lambda}_t = \arg\min_{\boldsymbol{\lambda}} \left\| \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] f(\mathbf{c}_t \left(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t \right)) \right\|$$

where we replaced γ by the OLS estimates of the projection of $f(\mathbf{c}_t \left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t \right))$ on $\mathbf{z}_t$. $\boldsymbol{\lambda}_t$ will be the solution of the same problem with a minimization over $\lambda \geq 0$ if the constraint is known to be of the form $p_{jt} \leq \overline{p}_{jt}$.

In the particular case where $f(.)$ is the identity, we obtain a closed form solution for $\boldsymbol{\lambda}_t$ as is shown below.

As the residual $\boldsymbol{\omega}_t$ of the orthogonal projection of $\mathbf{c}_t$ on $\mathbf{z}_t$ is

$$\begin{aligned} \boldsymbol{\omega}_t \left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right) &= \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] \mathbf{c}_t \left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t \right) \\ &= \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] \left(\mathbf{p}_t + A \left(\mathbf{p}_t \right) \mathbf{q}_t \right) - \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] A \left(\mathbf{p}_t \right) \boldsymbol{\lambda}_t \\ &= \tilde{\boldsymbol{\omega}}_t \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right) - B \left(\mathbf{p}_t, \mathbf{z}_t \right) \boldsymbol{\lambda}_t \end{aligned}$$

where $\tilde{\boldsymbol{\omega}}_t$ is the residual of the orthogonal projection of $\left(\mathbf{p}_t + A \left(\mathbf{p}_t \right) \mathbf{q}_t \right)$ on $\mathbf{z}_t$ and $B \left(\mathbf{p}_t, \mathbf{z}_t \right)$ the residual of the orthogonal projection of $A \left(\mathbf{p}_t \right)$ on $\mathbf{z}_t$:

$$\begin{aligned} \tilde{\boldsymbol{\omega}}_t \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right) &= \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] \left(\mathbf{p}_t + A \left(\mathbf{p}_t \right) \mathbf{q}_t \right) \\ B \left(\mathbf{p}_t, \mathbf{z}_t \right) &= \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] A \left(\mathbf{p}_t \right) \end{aligned}$$

The problem is thus

$$\min_{\boldsymbol{\lambda}_t} \boldsymbol{\omega}_t \left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right)' \boldsymbol{\omega}_t \left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right)$$

whose first order condition leads to

$$-\tilde{\boldsymbol{\omega}}_t' \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right) B \left(\mathbf{p}_t, \mathbf{z}_t \right) + \boldsymbol{\lambda}_t' B \left(\mathbf{p}_t, \mathbf{z}_t \right)' B \left(\mathbf{p}_t, \mathbf{z}_t \right) = 0$$

and thus the following solution

$$\boldsymbol{\lambda}_t = \left[B \left(\mathbf{p}_t, \mathbf{z}_t \right)' B \left(\mathbf{p}_t, \mathbf{z}_t \right) \right]^{-1} B \left(\mathbf{p}_t, \mathbf{z}_t \right)_t' \tilde{\boldsymbol{\omega}} \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right)$$

which exists and is unique if $B \left(\mathbf{p}_t, \mathbf{z}_t \right)' B \left(\mathbf{p}_t, \mathbf{z}_t \right)$ is invertible. $\boldsymbol{\lambda}_t$ is thus the OLS coefficient of the projection of $\tilde{\boldsymbol{\omega}} \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right)$ on $B \left(\mathbf{p}_t, \mathbf{z}_t \right)$.

Remark also that if the price constraint is known to be a price ceiling as $p_{jt} \leq \overline{p}_{jt}$ then we know that λ_{jt} is the Lagrange multiplier associated with this constraint and should be non negative. In this case $\boldsymbol{\lambda}_t = \arg\min_{\boldsymbol{\lambda} \geq \mathbf{0}} \left\| \left[I - \left(\mathbf{z}_t' \mathbf{z}_t \right)^{-1} \mathbf{z}_t' \right] f(\mathbf{c}_t \left(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t \right)) \right\|$ which has also a closed form solution if $f(.)$ is linear. Actually when $f(.)$ is the identity,

$$\boldsymbol{\lambda}_t = \left[\left[B \left(\mathbf{p}_t, \mathbf{z}_t \right)' B \left(\mathbf{p}_t, \mathbf{z}_t \right) \right]^{-1} B \left(\mathbf{p}_t, \mathbf{z}_t \right)_t' \tilde{\boldsymbol{\omega}} \left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t \right) \right]_+$$

where $[.]_+$ means that each non positive element of the vector is replaced by zero.

A.3 Market Size Approximation

In our demand model we normalize the utility of the outside good and model the aggregate market share of each drug as a function of different characteristics. As usual, one needs to take a stand on the potential market size, in order to use observed sales quantities q_{jt} and market size M_t to obtain measures of market shares as $s_{jt} = q_{jt}/M_t$. As the market size is not observed and we do not have an obvious definition of the potential market for antiulcer drugs, we approximate market size per year using the insights of Huang and Rojas (2013, 2014) in the simple case of the fixed coefficient logit version of our model. In the logit case, we can simply use the market share equations of the logit to obtain, by difference between two goods j and j',

$$\ln q_{jt} - \ln q_{j't} = \sum\nolimits_k \alpha^k (x_{jt}^k - x_{j't}^k) - \beta (p_{jt} - p_{j't}) + \zeta_{jt} - \zeta_{j't}$$

which does not depend on any market size assumption and allows to identify α^k, β, by two stage least squares with the usual instrumental variables. In a second stage we estimate the market sizes M_t that minimize

$$\min_{M_t} \sum\nolimits_t \left(\sum\nolimits_k \left[\hat{\alpha}^k \left(M_t \right) - \hat{\alpha}^k \right]^2 + \left[\hat{\beta} \left(M_t \right) - \hat{\beta} \right]^2 \right)$$

where $\hat{\alpha}^k \left(M_t \right)$ and $\hat{\beta} \left(M_t \right)$ are the 2SLS coefficient estimates of the following equation

$$\ln q_{jt} - \ln(M_t - \sum\nolimits_{k=1}^{J} q_{kt}) = \sum\nolimits_k \alpha^k x_{jt}^k + \beta p_{jt} + \zeta_{jt}$$

A.4 Additional Tables

Table A1: Descriptive Statistics on Advertising Expenses per Year

Country	Drugs	Advertising Expenses	Detailing Expenses	Total Std Units	Total Revenue	Mean Number of Molecules
France	Generics	30,732	23,960	661,180	261,695	7.7
	Branded	88,735,165	78,650,392	468,729	510,157	11.5
Germany	Generics	33,127,671	30,787,284	1,183,946	451,724	10.7
	Branded	77,203,416	75,382,398	228,744	258,760	15.1
US	Generics	742,622	58,330	872,036	297,256	12.0
	Branded	933,106,598	572,960,477	665,647	2,166,961	16.0

Notes: All expenses are in 1,000 $US per year.

Table A2: Summary Statistics for the US

	Number of drugs			Quantity	Market Share		Price	Revenue
Year	All	Branded	Generics	(1,000 std units)	Branded	Generics	($US/std unit)	(1,000 $US)
2003	66	15	51	2 025 452	67%	33%	0.88	4 034 679
2004	70	17	53	1 875 573	64%	36%	1.10	4 091 029
2005	71	17	54	1 795 266	63%	33%	1.14	4 113 685
2006	72	16	56	1 894 541	62%	38%	0.97	4 329 421
2007	73	17	56	1 925 183	59%	41%	1.08	4 437 844
2008	76	16	60	1 845 887	51%	49%	1.01	4 264 548
2009	84	17	67	1 919 050	45%	55%	1.12	4 116 476
2010	88	16	72	1 956 464	35%	65%	1.40	3 841 758
2011	95	16	79	2 013 497	29%	71%	1.31	3 414 379
2012	100	17	83	1 788 713	28%	72%	1.34	3 111 634
2013	112	16	96	1 757 347	25%	75%	1.67	3 014 056

Notes: Price is the average price per standard unit in $US across all drugs. Revenue is total revenue of the class.

Table A3: Summary Statistics for Germany

	Number of drugs			Quantity	Market Share		Price	Revenue
Year	All	Branded	Generics	(1,000 std units)	Branded	Generics	($US/std unit)	(1,000 $US)
2003	90	18	72	922 774	40%	60%	1.63	1 024 096
2004	83	15	68	963 578	44%	56%	1.75	1 153 481
2005	90	15	75	1 118 165	49%	51%	1.65	1 225 519
2006	92	15	77	1 222 855	43%	57%	1.56	1 087 547
2007	86	15	71	1 413 689	32%	68%	1.56	1 040 938
2008	90	13	77	1 611 532	29%	71%	1.49	1 079 989
2009	113	12	101	1 791 422	17%	83%	1.25	953 712
2010	116	12	104	1 979 180	10%	90%	1.26	800 048
2011	109	13	96	2 176 575	5%	95%	2.02	662 924
2012	111	13	98	2 377 741	4%	96%	1.97	643 147
2013	106	13	93	2 541 186	3%	97%	2.01	591 608

Notes: Price is the average price per standard unit in $US across all drugs. Revenue is total revenue of the class.

B ONLINE APPENDIX

B.1 Additional Tables on Counterfactual Free Pricing

Table B1: Observed and counterfactual (free pricing) prices for branded drugs

Sub-Class	Molecule	Drug	Price	2003	2006	2009	2012
H2	Cimetidine	Tagamet	observed	0.39	0.41	0.44	0.56
			counterfactual	0.43	0.48	0.52	0.72
	Ranitidine	Zantac	observed	0.65	0.46	0.49	0.53
			counterfactual	0.67	0.46	0.49	0.53
	Ranitidine	Raniplex	observed	0.74	0.44	0.46	0.46
			counterfactual	0.76	0.48	0.48	0.50
	Famotidine	Pepcidine	observed	0.79	0.77	0.73	0.97
			counterfactual	0.81	0.80	0.76	1.01
	Nizatidine	Panaxid	observed	0.81	0.83	0.80	0.66
			counterfactual	0.83	0.85	0.82	0.68
PPI	Omeprazole	Losec	observed	1.40	1.25	1.08	0.85
			counterfactual	1.43	1.33	1.20	0.94
	Lansoprazole	Lanzor	observed	1.05	1.00	0.80	0.59
			counterfactual	1.07	1.02	0.86	0.71
	Lansoprazole	Takepron	observed	1.06	1.00	0.79	0.54
			counterfactual	1.09	1.04	0.82	0.56
	Pantoprazole	Pantozol	observed	1.04	0.93	0.86	0.63
			counterfactual	1.07	0.97	0.95	0.75
	Esomeprazole	Nexium	observed	1.40	1.16	0.83	0.66
			counterfactual	1.43	1.19	0.87	0.77
	Rabeprazole	Pariet	observed	1.06	0.97	0.95	0.83
			counterfactual	1.08	0.99	0.98	1.02
Prost.	Misoprostol	Cytotec	observed	0.31	0.31	0.33	0.33
			counterfactual	0.34	0.35	0.36	0.36

Notes: We have two rows per drug with observed price per year and counterfactual price below. Prices are in $US/std. unit.

Table B2: Observed and counterfactual (free pricing) prices for generics

Sub-Class	Molecule	Price	2003	2006	2009	2012
H2	Cimetidine	observed	0.41	0.25	0.25	0.26
		counterfactual	0.43	0.27	0.25	0.27
	Ranitidine	observed	0.55	0.67	0.44	0.43
		counterfactual	0.57	0.69	0.47	0.46
	Famotidine	observed		0.42	0.41	0.38
		counterfactual		0.44	0.42	0.39
PPI	Omeprazole	observed		0.67	0.53	0.41
		counterfactual		0.69	0.54	0.42
	Lansoprazole	observed			0.41	0.32
		counterfactual			0.43	0.45
	Pantoprazole	observed			0.42	0.32
		counterfactual			0.44	0.35
	Esomeprazole	observed				0.33
		counterfactual				0.36
	Rabeprazole	observed				0.29
		counterfactual				0.30

Notes: We have two rows per drug with observed price per year and counterfactual price below.

Empty cells when generics did not enter yet. Prices are in $US/std. unit.

Table B3: Average Quantity change for branded drugs from Free Pricing to Current Regulation

Subclass	H2				PPI					Prost.	Combi.	Total
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	20%	5%	2%	2%	1%	2%	3%	0%	1%	18%		5%
2004	17%	11%	6%	2%	-3%	3%	4%	10%	2%	18%		7%
2005	21%	16%	10%	3%	-11%	3%	5%	5%	3%	24%		8%
2006	29%	5%	2%	2%	-13%	3%	4%	4%	2%	23%		6%
2007	30%	5%	-5%	2%	-33%	6%	4%	4%	3%	19%		4%
2008	26%	3%	0%	1%	-22%	5%	3%	3%	3%	13%		4%
2009	-9%	3%	-9%	2%	-29%	4%	5%	4%	5%	12%		0%
2010	13%	-1%	0%	1%	-32%	3%	3%	4%	5%	14%		1%
2011	-56%	1%	-10%	-2%	-28%	1%	9%	8%	7%	11%		-5%
2012	42%	-10%	-3%	2%	17%	0%	20%	18%	-2%	8%		7%
2013		-12%		13%	10%	8%	2%	12%	15%	10%	8%	6%

Notes: Percent change are (counterfactual quantity - observed quantity)/counterfactual quantity.

Empty cells when branded molecules did not enter yet or exited. Column "Total": unweighted average of average changes by molecule.

Table B4: Average Quantity Change for Generics
From Free Pricing to Current Regulation

Subclass		H2				PPI				Total
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.		Total
2003	13%	5%								5%
2004	4%	10%	8%	0%						10%
2005	1%	9%	6%	0%						9%
2006	7%	13%	6%	2%						13%
2007	-2%	9%	-1%	-1%	2%					9%
2008	8%	11%	2%	2%	6%					11%
2009	-6%	10%	-1%	-1%	4%	4%				10%
2010	-3%	8%	1%	1%	8%	6%				8%
2011	-7%	6%	-1%	-1%	5%	4%	2%			6%
2012	0%	6%	-8%	-2%	6%	3%	2%	-4%		6%
2013	5%	4%	-109%	1%	4%	0%	-2%	3%		4%

Notes: Percent change are (counterfactual quantity - observed quantity)/counterfactual quantity.

Empty cells when the generics did not enter yet. Column "Total": unweighted average of average changes by molecule.

Table B5: Average Expenses change for branded drugs
from Free Pricing to Current Regulation

Subclass		H2					PPI			Prost.	Combi.	Total
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	12%	2%	0%	0%	-1%	0%	0%	-2%	-1%	9%		2%
2004	1%	5%	2%	-1%	-11%	0%	1%	8%	0%	9%		1%
2005	9%	9%	6%	0%	-19%	1%	1%	3%	0%	13%		3%
2006	17%	2%	-2%	0%	-20%	0%	1%	1%	0%	13%		1%
2007	17%	2%	-9%	-1%	-46%	1%	1%	1%	1%	10%		-2%
2008	9%	1%	-3%	-1%	-31%	0%	-1%	-1%	0%	6%		-2%
2009	-30%	1%	-13%	-1%	-44%	0%	-4%	0%	2%	4%		-7%
2010	3%	-3%	-3%	-1%	-45%	-1%	-5%	-1%	4%	5%		-4%
2011	-78%	-3%	-13%	-5%	-41%	-4%	-3%	-3%	5%	2%		-13%
2012	25%	-13%	-8%	-1%	8%	-6%	5%	4%	-27%	-2%		-3%
2013		-25%		5%	-11%	-4%	-24%	-11%	-9%	-5%	-2%	-10%

Notes: Empty cells when molecule did not enter yet or exited. Column "Total": unweighted average of average changes by molecule.

Large "erratic" changes of branded Cimetidine (Tagamet) are due to very small quantities after 2008 and progressive exit occurring in 2013.

Table B6 : Average Expenses Change for Generics
From Free Pricing to Current Regulation

Subclass		H2				PPI			Total
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Total
2003	5%	2%							3%
2004	-1%	4%	3%	-1%					1%
2005	-1%	4%	2%	-2%					1%
2006	1%	6%	2%	-1%					2%
2007	-3%	4%	-3%	-2%	0%				0%
2008	2%	4%	-1%	-1%	1%				1%
2009	-6%	3%	-3%	-3%	0%	0%			-1%
2010	-5%	2%	-3%	-2%	1%	0%			-1%
2011	-8%	0%	-5%	-5%	-2%	-2%	-3%		-3%
2012	-7%	-2%	-11%	-7%	-3%	-5%	-5%	-10%	-5%
2013	-9%	-4%	-60%	-9%	-9%	-11%	-12%	-9%	-10%

Notes: Empty cells when the generics did not enter yet.

Column "Total": unweighted average of the average changes by molecule.

B.2 Additional Tables on Counterfactual External Reference Pricing

Table B7: Observed and External Referencing average Prices for Branded Drugs

Sub-Class	Molecule	Drug	Price	2003	2006	2009	2012
H2	Cimetidine	Tagamet	observed	0.39	0.41	0.44	0.56
			counterfactual	0.36	0.38	0.41	0.54
	Ranitidine	Zantac	observed	0.65	0.46	0.49	0.53
			counterfactual	0.59	0.43	0.47	0.50
	Ranitidine	Raniplex	observed	0.74	0.44	0.46	0.46
			counterfactual	0.66	0.45	0.47	0.45
	Famotidine	Pepcidine	observed	0.79	0.77	0.73	0.97
			counterfactual	0.76	0.75	0.71	0.95
	Nizatidine	Panaxid	observed	0.81	0.83	0.80	0.66
			counterfactual	0.74	0.76	0.74	0.59
PPI	Omeprazole	Losec	observed	1.40	1.25	1.08	0.85
			counterfactual	1.44	1.28	1.08	0.86
	Lansoprazole	Lanzor	observed	1.05	1.00	0.77	0.59
			counterfactual	1.08	1.03	0.82	0.63
	Lansoprazole	Takepron	observed	1.06	1.00	0.79	0.54
			counterfactual	1.09	1.03	0.77	0.45
	Pantoprazole	Pantozol	observed	1.04	0.93	0.86	0.63
			counterfactual	1.08	0.97	0.82	0.69
	Esomeprazole	Nexium	observed	1.40	1.16	0.83	0.66
			counterfactual	1.44	1.20	0.91	0.82
	Rabeprazole	Pariet	observed	1.06	0.97	0.95	0.83
			counterfactual	1.08	1.01	0.91	0.90
Prost.	Misoprostol	Cytotec	observed	0.31	0.31	0.33	0.33
			counterfactual	0.26	0.25	0.24	0.24

Notes: We have two rows per drug with observed price per year and counterfactual price below ($US/std. unit).

Table B8: Observed and External Referencing average Generic Prices

Sub-Class	Molecule	Price	2003	2006	2009	2012
H2	Cimetidine	observed	0.41	0.25	0.25	0.26
		counterfactual	0.30	0.13	0.12	0.11
	Ranitidine	observed	0.55	0.46	0.44	0.43
		counterfactual	0.46	0.36	0.34	0.34
	Famotidine	observed		0.42	0.41	0.38
		counterfactual		0.32	0.31	0.27
PPI	Omeprazole	observed		0.67	0.53	0.41
		counterfactual		0.59	0.44	0.30
	Lansoprazole	observed			0.41	0.32
		counterfactual			0.31	0.19
	Pantoprazole	observed			0.42	0.32
		counterfactual			0.32	0.19
	Esomeprazole	observed				0.33
		counterfactual				0.21
	Rabeprazole	observed				0.29
		counterfactual				0.15

Notes: We have two rows per drug with observed price per year and counterfactual price below.

The price of the generic is capped at the observed percentage of the branded price.

Table B9: Average Quantity change for branded drugs
From Current Regulation to External Reference Caps

Subclass	H2				PPI					Prost.	Combi.	Total
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	21%	30%	14%	28%	-1%	-5%	-7%	-2%	-5%	33%		11%
2004	8%	11%	19%	29%	-1%	-5%	-12%	-1%	-7%	38%		7%
2005	7%	41%	23%	20%	0%	-5%	-4%	-3%	-11%	33%		11%
2006	12%	2%	0%	19%	-3%	-7%	-11%	-3%	-11%	38%		3%
2007	7%	-6%	-4%	17%	-1%	-7%	-8%	-6%	-7%	43%		1%
2008	-7%	-12%	-2%	6%	8%	-15%	-2%	-6%	-5%	42%		-2%
2009	-13%	-21%	-16%	2%	-7%	-7%	-3%	-11%	-10%	43%		-6%
2010	-19%	-8%	-19%	0%	-15%	-31%	-5%	-16%	-19%	30%		-12%
2011	-29%	0%	-28%	3%	-29%	-38%	-6%	-16%	-17%	21%		-15%
2012	-138%	-97%	-156%	-13%	-22%	-6%	-38%	-28%	-10%	3%		-51%
2013		-101%		5%	-7%	-13%	-5%	-10%	-11%	-27%	-11%	-27%

Notes: Empty cells when molecule did not enter yet or exited. Column "Total": unweighted average of average changes by molecule.

Large "erratic" changes of branded Cimetidine (Tagamet) are due to very small quantities after 2008 and progressive exit occurring in 2013.

Table B10 : Average Quantity Change for Generics
From Current Regulation to External Reference Caps

Subclass	H2			PPI					Total
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Total
2003	58%	36%							44%
2004	63%	39%	41%	13%					33%
2005	64%	38%	39%	17%					34%
2006	64%	42%	43%	24%					37%
2007	68%	45%	44%	24%	39%				38%
2008	63%	37%	38%	21%	36%				34%
2009	64%	34%	36%	22%	38%	35%			34%
2010	58%	26%	29%	27%	42%	36%			34%
2011	54%	16%	18%	22%	40%	37%	24%		30%
2012	45%	-1%	6%	7%	28%	31%	25%	36%	22%
2013	15%	-13%	-15%	1%	8%	13%	12%	11%	7%

Notes: Empty cells when the generics did not enter yet.

Column "Total": unweighted average of the average changes by molecule.

Table B11: Average Expenses change for all drugs
From Current Regulation to External Reference Caps

Subclass	H2				PPI					Prost.	Combi.	Total
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	14%	22%	10%	21%	1%	-2%	-4%	1%	-2%	19%		14%
2004	16%	16%	14%	22%	3%	-2%	-6%	1%	-3%	23%		10%
2005	17%	27%	15%	13%	6%	-5%	-4%	0%	-7%	17%		14%
2006	17%	13%	6%	12%	10%	-5%	-7%	1%	-6%	22%		10%
2007	19%	17%	17%	9%	11%	-5%	-6%	-1%	-5%	25%		9%
2008	12%	11%	13%	-1%	7%	3%	-8%	0%	-10%	21%		7%
2009	12%	8%	9%	-5%	5%	4%	-3%	-2%	-14%	21%		4%
2010	2%	1%	0%	-8%	3%	-5%	1%	2%	-25%	8%		0%
2011	-6%	-10%	-13%	-8%	-9%	-14%	-5%	2%	-12%	-5%		-8%
2012	-27%	-41%	-29%	-25%	-26%	-23%	-21%	-12%	-1%	-34%		-22%
2013	-76%	-46%	-47%	-3%	-55%	-46%	-52%	-47%	-46%	-67%	-27%	-49%

Notes: Empty cells when molecule did not enter yet or exited. Column "Total": unweighted average of average changes by molecule.

Large "erratic" changes of branded Cimetidine (Tagamet) are due to very small quantities after 2008 and progressive exit occurring in 2013.

Table B12: Average Expenses change for branded drugs
From Current Regulation to External Reference Caps

Subclass	H2				PPI					Prost.	Combi.	Total
Year	Cimet.	Ranit.	Famot.	Nizat.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Miso.	Combi.	Total
2003	13%	22%	10%	21%	1%	-2%	-4%	1%	-2%	19%		8%
2004	2%	11%	14%	22%	2%	-2%	-6%	1%	-3%	23%		6%
2005	1%	28%	15%	13%	2%	-5%	-4%	0%	-7%	17%		7%
2006	5%	-2%	-3%	12%	0%	-5%	-7%	1%	-6%	22%		1%
2007	2%	-7%	-6%	9%	1%	-5%	-6%	-1%	-5%	25%		0%
2008	-8%	-13%	-5%	-1%	10%	-10%	-8%	0%	-10%	21%		-4%
2009	-20%	-23%	-19%	-5%	-7%	-9%	-9%	-2%	-14%	21%		-10%
2010	-24%	-16%	-22%	-8%	-12%	-22%	-13%	2%	-25%	8%		-14%
2011	-32%	-16%	-31%	-8%	-25%	-29%	-15%	4%	-12%	-5%		-18%
2012	-150%	-108%	-162%	-25%	-20%	-23%	-27%	-3%	-1%	-34%		-57%
2013		-117%		-3%	-17%	-31%	-16%	-25%	-28%	-67%	-27%	-44%

Notes: Empty cells when molecule did not enter yet or exited. Column "Total": unweighted average of average changes by molecule.

Large "erratic" changes of branded Cimetidine (Tagamet) are due to very small quantities after 2008 and progressive exit occurring in 2013.

Table B13 : Average Expenses Change for Generics
From Current Regulation to External Reference Caps

Subclass	H2					PPI			Total
Year	Cimet.	Ranit.	Famot.	Omep.	Lanso.	Panto.	Esom.	Rabe.	Total
2003	22%	24%							23%
2004	27%	27%	28%	7%					19%
2005	28%	24%	25%	9%					19%
2006	25%	25%	26%	14%					20%
2007	27%	27%	27%	12%	23%				21%
2008	19%	17%	18%	7%	17%				14%
2009	19%	13%	15%	6%	16%	14%			12%
2010	6%	4%	6%	5%	10%	9%			7%
2011	-3%	-9%	-8%	-6%	0%	0%	-5%		-4%
2012	-27%	-30%	-29%	-27%	-23%	-19%	-22%	-23%	-24%
2013	-76%	-38%	-47%	-62%	-66%	-64%	-63%	-65%	-62%

Notes: Empty cells when the generics did not enter yet.

Column "Total": unweighted average of the average changes by molecule.

B.3 Additional Free Pricing Counterfactuals with Free Generic Prices

We present here the counterfactual simulations of free pricing equilibrium where the price of generics would also be let free by the regulator and not tied to the price of the branded version of the generics.

Table B14: Observed and counterfactual (free pricing) prices

Sub-Class	Molecule	Drug	Price	2003	2006	2009	2012
H2	Cimetidine	Tagamet	observed	0.39	0.41	0.44	0.56
			counterfactual	0.42	0.41	0.44	0.56
	Ranitidine	Zantac	observed	0.65	0.46	0.49	0.53
			counterfactual	0.67	0.46	0.49	0.55
	Ranitidine	Raniplex	observed	0.74	0.44	0.46	0.46
			counterfactual	0.76	0.48	0.48	0.48
	Famotidine	Pepcidine	observed	0.79	0.77	0.73	0.97
			counterfactual	0.81	0.77	0.73	0.97
	Nizatidine	Panaxid	observed	0.81	0.83	0.80	0.66
			counterfactual	0.83	0.85	0.82	0.67
PPI	Omeprazole	Losec	observed	1.40	1.25	1.08	0.85
			counterfactual	1.43	1.28	1.11	0.87
	Lansoprazole	Lanzor	observed	1.05	1.00	0.77	0.59
			counterfactual	1.07	1.02	0.82	0.61
	Lansoprazole	Takepron	observed	1.06	1.00	0.79	0.54
			counterfactual	1.09	1.03	0.82	0.56
	Pantoprazole	Pantozol	observed	1.04	0.93	0.86	0.63
			counterfactual	1.07	0.97	0.89	0.65
	Esomeprazole	Nexium	observed	1.40	1.16	0.83	0.66
			counterfactual	1.44	1.18	1.86	0.68
	Rabeprazole	Pariet	observed	1.06	0.97	0.95	0.83
			counterfactual	1.08	0.99	0.98	0.85
Prost.	Misoprostol	Cytotec	observed	0.31	0.31	0.33	0.33
			counterfactual	0.34	0.35	0.36	0.37

Notes: We have two rows per drug with observed price per year and counterfactual price below. Prices are in $US/std. unit.

Table B15: Observed and free pricing average generic prices

Sub-Class	Molecule	Price	2003	2006	2009	2012
H2	Cimetidine	observed	0.41	0.25	0.25	0.26
		counterfactual	0.43	0.29	0.29	0.31
	Ranitidine	observed	0.55	0.46	0.44	0.43
		counterfactual	0.57	0.49	0.47	0.46
	Famotidine	observed		0.42	0.41	0.38
		counterfactual		0.45	0.44	0.42
PPI	Omeprazole	observed		0.67	0.53	0.41
		counterfactual		0.69	0.55	0.43
	Lansoprazole	observed			0.41	0.32
		counterfactual			0.43	0.36
	Pantoprazole	observed			0.42	0.32
		counterfactual			0.45	0.36
	Esomeprazole	observed				0.33
		counterfactual				0.37
	Rabeprazole	observed				0.29
		counterfactual				0.33

Notes: We have two rows per drug with observed price per year and counterfactual price below.

The price of the generic is free (no link to branded price). Prices are in $US/std. unit.

Table B16: Counterfactual Savings and Surplus with Free Pricing

			2003	2006	2009	2012	2003-2013
Sub-Class	Molecule						
H2	Cimetidine		-588	-114	-77	-173	-1,627
	Ranitidine		-634	-432	-189	1,269	-944
	Famotidine		-8	-11	-16	25	-71
	Nizatidine		2	2	4	9	41
Sub-total H2			-1,228	-555	-278	1,130	-2,601
PPI	Omeprazole		5,425	467	1,277	11,181	50,676
	Lansoprazole		391	1,485	-215	2,809	14,861
	Pantoprazole		-510	182	1,099	3,035	13,712
	Esomeprazole		2,474	2,035	3,428	7,617	68,005
	Rabeprazole		592	869	1,457	6,384	22,042
Sub-total PPI			8,372	5,037	7,045	31,026	169,296
Prost.	Misoprostol		-211	-153	-50	-36	-1,038
Combi.	Bismuth/Antibiotic						210
Total			6,933	4,329	6,717	32,120	165,866
Sub-total		Branded	7,114	5,564	7,882	19,155	119,014
		Generics	-182	-1,234	-1,165	12,966	46,853
Consumer Surplus Change			+2%	+3%	+6%	+18%	+18%

Notes: Savings are in 1,000 $US. Negative numbers indicate increased expenditures as compared to observed.

Surplus change is in percentage of counterfactual estimated surplus.

B.4 Additional Counterfactual with External Referencing and Free Generic Prices

Table B17: Observed and counterfactual prices (external reference caps)

Sub-Class	Molecule	Drug	Price	2003	2006	2009	2012
H2	Cimetidine	Tagamet	observed	0.39	0.41	0.44	0.56
			counterfactual	0.36	0.38	0.41	0.54
	Ranitidine	Zantac	observed	0.65	0.46	0.49	0.53
			counterfactual	0.62	0.44	0.47	0.51
	Ranitidine	Raniplex	observed	0.74	0.44	0.46	0.46
			counterfactual	0.66	0.44	0.47	0.48
	Famotidine	Pepcidine	observed	0.79	0.77	0.73	0.97
			counterfactual	0.76	0.75	0.71	0.95
	Nizatidine	Panaxid	observed	0.81	0.83	0.80	0.66
			counterfactual	0.74	0.76	0.74	0.59
PPI	Omeprazole	Losec	observed	1.40	1.25	1.08	0.85
			counterfactual	1.43	1.28	1.08	0.86
	Lansoprazole	Lanzor	observed	1.05	1.00	0.77	0.59
			counterfactual	1.07	1.02	0.80	0.59
	Lansoprazole	Takepron	observed	1.06	1.00	0.79	0.54
			counterfactual	1.09	1.03	0.80	0.56
	Pantoprazole	Pantozol	observed	1.04	0.93	0.86	0.63
			counterfactual	1.07	0.97	0.82	0.65
	Esomeprazole	Nexium	observed	1.40	1.16	0.83	0.66
			counterfactual	1.44	1.19	0.86	0.69
	Rabeprazole	Pariet	observed	1.06	0.97	0.95	0.83
			counterfactual	1.08	1.00	0.91	0.86
Prost.	Misoprostol	Cytotec	observed	0.31	0.31	0.33	0.33
			counterfactual	0.26	0.25	0.24	0.24

Notes: We have two rows per drug with observed price per year and counterfactual price below. Prices are in $US/std. unit.

Table B18: Observed and external referencing average generic prices

Sub-Class	Molecule	Price	2003	2006	2009	2012
H2	Cimetidine	observed	0.41	0.25	0.25	0.26
		counterfactual	0.41	0.29	0.29	0.31
	Ranitidine	observed	0.55	0.46	0.44	0.43
		counterfactual	0.57	0.44	0.45	0.45
	Famotidine	observed		0.42	0.41	0.38
		counterfactual		0.45	0.44	0.42
PPI	Omeprazole	observed		0.67	0.53	0.41
		counterfactual		0.70	0.55	0.43
	Lansoprazole	observed			0.41	0.32
		counterfactual			0.43	0.35
	Pantoprazole	observed			0.42	0.32
		counterfactual			0.45	0.36
	Esomeprazole	observed				0.33
		counterfactual				0.37
	Rabeprazole	observed				0.29
		counterfactual				0.33

Notes: We have two rows per drug with observed price per year and counterfactual price below. Prices are in $US/std. unit. The price of the generic is free (no link to branded price).

Table B19: Counterfactual Savings and Surplus with External Reference Caps

			2003	2006	2009	2012	2003-2013
Sub-Class	Molecule						
H2	Cimetidine		-935	18	128	191	-232
	Ranitidine		-5,856	-839	217	-1,780	-23,343
	Famotidine		-608	26	40	-21	-2,145
	Nizatidine		-246	-80	-18	-30	-825
Sub-total H2			-7,644	-874	367	-1,639	-26,083
PPI	Omeprazole		-4,102	590	1,990	-8,878	-32,360
	Lansoprazole		3,134	-1,064	1,090	-2,264	5,506
	Pantoprazole		2,530	296	-218	-2,414	-4,706
	Esomeprazole		-1,801	-2,238	-5,607	-6,446	-68,591
	Rabeprazole		958	-426	3,857	-6,523	13,472
Sub-total PPI			718	-2,842	1,113	-26,526	-86,680
Prost.	Misoprostol		-561	-503	-609	-1922	-9,876
Combi.	Bismuth/Antibiotic						-428
Total			-7,487	-4,219	871	-30,087	-123,067
Sub-total		Branded	-7,778	-5,650	-4,851	-18,997	-110,533
		Generics	291	1,432	5,722	-11,090	-12,534
Consumer Surplus Change			+1%	-1%	-4%	-20%	-16%

Notes: Savings are in 1,000 $US. Negative numbers indicate increased expenditures as compared to observed. Surplus change is in percentage of counterfactual estimated surplus.