The impact of Portuguese generics drug legislation on the drug market: a structural break approach

by

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Biographical Note

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Abstract

The Economic and Financial Adjustment Program Portugal signed with international organizations included several recommendations whose objective was to reduce healthcare expenditures. These recommendations aimed primarily at stimulating generic drugs consumption, thus reducing the public expenditure on healthcare (by reimbursement and reference pricing). In this study, first we test for the presence of structural breaks on relative prices; then, we use a time series approach to determine the exact month on which a structural break in generic drugs consumption occurred, using monthly data on generic drugs market shares and relative prices from January 2007 to December 2013. We identify one structural break on generic drugs consumption that coincides in time with administrative reductions on relative prices. This result highlights the importance of relative prices on the demand for generic drugs.

JEL Codes: I18; K32; L16

Keywords: Generic drugs consumption; Portugal; Policy Measurement; Structural Change

Resumo

O Programa de Ajustamento Económico e Financeiro, que Portugal assinou com organizações internacionais, incluía diversas recomendações, cujo objetivo era reduzir os gastos nos cuidados de saúde. Estas recomendações visaram principalmente estimular consumo de medicamentos genéricos, reduzindo assim os gastos públicos em cuidados de saúde (por comparticipação e preço de referência). Neste estudo, primeiro testamos a presença de quebras estruturais de preços relativos; de seguida, usamos uma abordagem de séries de temporais para determinar o mês exato em que ocorreu uma quebra estrutural no consumo de medicamentos genéricos, usando dados mensais sobre as quotas de mercado de medicamentos genéricos e dos preços relativos entre Janeiro de 2007 e Dezembro de 2013. Identificamos uma quebra estrutural no consumo de medicamentos genéricos, que coincide no tempo com reduções administrativas dos preços relativos. Este resultado destaca a importância dos preços relativos da demanda por medicamentos genéricos.

Códigos JEL: I18; K32; L16

Palavras-Chave: Consumo de Genéricos; Portugal; Avaliação de Políticas; Quebra Estrutural

Table of Contents

List of Tables

List of Figures

Chapter 1

Introduction

Health, according to the World Health Organization, is a "*state of complete physical, mental and social well-being and not merely the absence of disease or infirmity",* and is a fundamental right both on The Universal Declaration of Human Rights (on its article 25) and on Constitution of Portugal (on its article 64 of the first chapter). However, the preservation of such rights underlies the creation of Health Systems, which implies costs and relocation of resources to the health sector of such economy. In Portugal, the burden of public and private expenditure on Health corresponds, in 2010, to 10.2% of Portuguese GDP[1], and had been rising since 2006. This subject deserves particular attention, since Portugal is, from 2011, under an external financial aid program.

[1] This data was collected from OECD 's website

Since Portugal signed with the Economic and Financial Adjustment Program, several recommendations were issued to the Portuguese Government in order to reduce the expenditures with health. These recommendations aim primarily on stimulating generic drugs consumption, thus reducing the public expenses on health (by reimbursement and reference pricing) and meeting the requirements established by that same document.

The market share of generic medicines, according to Mendonca (2011), was 21.4% in 2011, and *"(...) is consistently growing since 2000* (…)". However, the main objective is to reach 60% market share of generic medicines in 2014[2].

Several works study the impact of legislation on generic drugs consumption and the competition on drug markets, such as Aronsson *et al.* (2001), Dalen *et al.* (2006), among many others. There are also a few studies that study the impact of legislation and regulatory changes in Portugal, namely Barros and Nunes (2010), Barros and Nunes (2011) and Mendonca (2011). However, as far as we are aware, this study will be the first to study the impact of legislation imposed by the Economic and Financial Adjustment Program concerning a structural change in generic drugs consumption.

All this considered, and given the importance of the subject, we intend to study how the consumption of generic medicines has changed (using generic drugs market shares as a proxy for generic consumption) after the introduction of such legislation. Our main goal is to answer these two questions:

1. Were generic drugs consumption affected by legislation imposed by the MoU?
2. What legal acts were capable of structurally change generic drugs consumption in Portugal?

[2] http://expresso.sapo.pt/governo-quer-que-farmacias-aumentem-venda-de-genericos=f831018 (accessed in 11-01-2013.)

With these questions, we intend to find if the Portuguese drug market has structurally changed because of the legislation regarding generic drugs that came into effect after 2011 and identify which legal documents were responsible for that structural change.

The data we use for this study was collected in INFARMED's website and contained monthly information regarding generic and brand-name drugs market shares, as well their monthly average price that we use to calculate the relative prices. The methodology used was a structural break analysis, in which we follow a two-sided approach: First, we test the presence of structural breaks in relative prices of drugs, since several legal documents deal with pricing policies. Then, we estimate the demand for generic drugs using a method that indicates us the date when the structural breaks occurred as well as the different coefficients for each partition on the sample.

This study is organized as follows. After the introduction, presented in Chapter 1, Chapter 2 presents the literature review where some key-concepts are defined and some theoretical framework of the research question mentioned above are presented. In Chapter 3, we present a review of the main legislation published after 2011 that concerns generic drugs. In Chapter 4 we present a methodological overview of this work and in Chapter 5 we present our main results and discuss those same results. Finally, in Chapter 6, we present the main conclusions to our study, its limitations and suggestions for further research.

Chapter 2

Literature Review

2.1 Determinants of the demand for generic drugs

The literature has identified several determinants of generic drugs market share, namely the price of generic medicines, the Reference Pricing System, Brand Loyalty, pharmacy level incentives to promote generic substitution, the role of trademarks and brands, among many others.

2.1.1 Price

After a pharmaceutical patent expires, competition in that market may take place when firms offering generic drugs, as a perfect substitution for the originating drug, enter the market, as stated by Dalen *et al.* (2006). The dynamics of the pharmaceutical market are well described by Manova *et al.* (2010), where they state that "*Originating pharmaceutical companies seem to compete among themselves at a therapeutically level and with generics at a price level*.".

Several studies across the literature provide insights on the impact of price of brand-name drugs/generic drugs on its market share. Aronsson *et al.* (2001) studied how market shares for brand name drugs are affected by generic competition. They constructed a model where they estimate the relative change of market share for the original brand name drug as a linear function of the price of the original drug relative to the price of the generic drug. Using data from the Swedish Medical Product Agency, the authors have been provided with quarterly time-series data of prices and quantities for both original and generic drugs. The data refers to twelve different substances and its generic counterparts. Using a Cochrane-Orcutt technique to control serial correlation, they, ultimately, found that, on some substances, "(…) *relative prices have a significant effect on the change of market share of the original product. The higher the price of the original product, relative to the average price of the generic substitute, the larger the decrease of the market share of the original product*".

Dalen *et al.* (2006) studied the competition between generic drugs and original brand name drugs in the Norwegian market, specifically in what concerns the regulatory changes involving the yardstick-based price regulation. This regulation consisted on establishing a retail price cap or an "index price" on a drug, in order to trigger price competition. The authors used an empirical model with two steps: first, they estimated a demand model and, second, they derived a time-conditioned measure of market power for each product (Lerner Index), using the information on price elasticities acquired from step one. The results "(…) *suggest that the index price* [retail price cap] *helped to increase the market shares of generic drugs and succeeded in reducing overall market power*".

Manova *et al.* (2010) intended to study the impact of the entry of generic drugs in the pharmaceutical market, both on prices and market shares. They focused on the Bulgarian cardiovascular drug market between the years 2005-2007. The authors were trying to test two hypotheses: first, they tested the hypothesis whether the introduction of "*new medicinal products (originators or generics) affect the sales and/or market share within the group*"; and, second, they tested if "*the introduction of new products (originators or generics) decreases the prices of the competitors within the group*". The data was collected from the

Bulgarian Ministry of Health and the methodology was, for the first hypothesis, the Kolmogorov-Smirnov (K-S) test and a z-test analysis to find statistically significant differences among the proportions sold during the years under analysis. For the second hypothesis they carried out a two-way ANOVA analysis and, if the result sample was ambiguous, a one-way ANOVA analysis. The results showed that generic competition changes the market in the observed country.

Saha *et al.* (2006) developed a simultaneous equations estimation framework to perceive the interactions between generic drugs entry, market shares and prices. Using a panel data sample of 40 drugs that were exposed to competition over July 1992 to January 1998 period, they found out that there are differences in the levels of generic entry in the market, depending on its market size, i.e., the blockbuster drugs attract more entrants than the small market sized drugs. They also found out that the average generic-to-brand name price ratio declines over time: by the end of the second year after the entrance, the average price of the 40 drugs in the sample is only 41% of the brand name drug price; and, again, the price competition is much more intense on blockbuster drugs. Finally, their results suggest that "(…) *generic market share influences and is influenced by generic prices, supporting the simultaneous equations estimation framework*".

Frank and Salkever (1997) studied the price evolution in pharmaceutical market after the implementation of the Waxman-Hatch Act in 1984, in the United States of America. The authors collected a sample of 32 drugs that lost patents during that period and faced competition from generic drugs, and estimate models of price responses to that generic entry. Using a Two-Stage Least-Squares Fixed-Effects estimator and a Two-Step estimator on their models, they found that competition between generic drugs producers is related to price reductions for these drugs, besides price reductions on brand name drugs not being related to generic entry in that market. Finally, the authors found that "*the substantial shift in market share from brand name drugs to generic producers (40%-50%) along with the significantly reduced price of generic substitutes (25%-30% lower) means that the average price of prescription for a compound subject to generic competition has fallen*.", meaning that the market share shift was triggered by price competition.

2.1.2 Reference Pricing System

Pharmaceutical Reference Prices (RP) are, according to Dickson and Redwood (1998), "reimbursement ceilings set by payers in public and private sectors. Such payers will cover or reimburse the cost of listed drugs up to the reference price. Above that level, others (usually the patient or supplementary private insurers) have to pay the difference between the reference price and the actual price, or reimbursement of unlisted drugs may be refused". The authors, in this paper, provided a clear definition of what RP are and how they are structured; an extended review on its status at the time; and the main RP models, namely the European Model, the Canadian Model and the US Model.

According to Galizzi *et al.* (2011), the introduction of RP is due to the effort to control health expenditures both on public and private sector. RP policy resides in clustering drugs with some sort of criteria, for example, bio-equivalence and therapeutic equivalence, and establishing a reference price to that cluster. The authors aimed to comprehend the original scientific studies on the effects of the introduction of RP policies in OECD countries. The results showed that "*Following the introduction of RP, generics market share significantly increased whenever the firms producing brand-name drugs did not adopt one of the following strategies: lowering prices to the RP value; launching new dosages and formulations; or marketing substitute drugs still under patent protection*.", meaning that Reference Price Systems (RPS) have an important effect on generic drugs market shares.

Brekke *et al.* (2011) studied the impact on competition after the introduction of RPS on Norway in 2003. First, they built a theoretical differentiation model to analyse the impact of such regulation on prices and market shares of both brand name and generic drugs. After the model was defined, the authors postulated two hypotheses: the switch from the previous regulation (price cap regulation) to the RPS lead to reduction in brand name and generic drugs prices; and an increase in generic drugs market share. To test these two hypotheses, the authors used a database provided from Farmastat, a company owned by the Norwegian Association of Pharmaceutical Manufacturers, which contained information about volume and value of each package sold in the Norwegian pharmaceutical market. Using a detailed panel data covering the 24 most selling drugs in the Norwegian market in 2001-2004

period, the authors showed that *"(...) RP reduces brand-name and generic drug prices and increases generic market shares*", thus confirming the previous two hypotheses.

The same type of study is followed by Podnar *et al.* (2007). The authors studied the impact of the introduction of RPS (in 2003) on generic and brand name drugs market share, in the Slovenian market. Their results showed that "(…) *originator manufacturers tend to lose market share because of reference pricing.*".

Simoens *et al.* (2005) studied the effects of the introduction of RPS in Belgium on generic drugs market share, between the years 1998-2003. The authors used data from IMS Health Belgium to trace general trends and data from Ifstat to analyze price evolutions of certain drugs. They found that "*The market share held by generic drugs increased following implementation of the RP scheme*". They also found that "*the low market share of generic drugs in Belgium principally drives from lack of incentives for physicians to prescribe generic drugs*". This last result is particularly important because there are some studies in the literature that consider physician/patient role on prescription and brand loyalty as a relevant determinant of brand name and generic drugs market share.

2.1.3 Brand Loyalty, Physician/Patient/Pharmacy role on prescription

Hurwitz and Caves (1988) studied how promotion, marketing and information can influence consumers on buying certain type of drugs (brand name versus generic drugs). After they provided a general description of the brand name and generic drug market worked, they analysed health professional's decision-making process on drug prescription. They found that "*The physician has no substantial economic incentive to choose the lower-priced product, and doctors tend to be ignorant of specific drug prices. The brand name, simpler than the generic name, was learned when the drug was introduced and is easier to remember, and habit accordingly plays a strong role in the physician's prescription practice*". They also found that physicians have less faith in quality control on generic drugs manufacturers than of brand name drugs manufacturers. Using a sample consisting of 150 drugs that were available as generics and had, at some point, a patent held by originating manufacturers, the authors construct a model to study the impact of sales-

promotion on both generic and brand name drugs market shares. Their results showed that "*the trademark holders' sales-promotion outlays do preserve their shares against incursion by generic entrants*", showing that trademarks have an important role on the evolution of generic drugs market share.

Hellerstein (1998) studied the importance of physicians in the process of prescribing a brand name or a generic drug. The author argues that physicians, when playing as an agent for their patients, face some informational costs when prescribing medicines, such as collecting information on the availability and efficacy of generic drugs and price differentials between generic and brand name drugs, among others. It is costly, for the physician, to gather information about generic drugs, because its manufacturers do "(…) *very little advertising, while information about new trade-name drugs is widely disseminated formally through advertising and the published results of drug efficacy studies. It may therefore be much more costly to a physician to learn about the introduction of new generic drugs*". Using a sample of 38.384 patient's information, collected via a survey from 1.223 office-based physicians over the course of the year 1989 in USA, the author intended to establish a pattern in physicians' drug prescription. Their results showed that "*the central result is that the physician is an important agent in the prescription decision*".

The same type of study is followed by Coscelli (2000). The author studied the contribution of physician and patient habits to persistence of market shares in prescription drugs market. Unlike Hellerstein (1998), the effects of both patient and physician, on prescribing behavior, can be isolated. This allows a better understanding of dynamics of prescription than aggregated data. Using a probit specification and a panel dataset provided by Italian National Health Institute, the author tested the null hypothesis of whether physicians and/or patients are indifferent between "*different brands of the same molecule, as we would expect given their therapeutic equivalence [i.e. generic and brand name drugs]".* After rejecting this hypothesis, the author tried to isolate effects responsible for product differentiation. The results showed "*significant evidence of doctor and patient `habit', which imply that in molecular sub markets in which brands are not allowed to compete on the basis of price,*

habit persistence at the micro- level can translate into sticky and persistent market shares at the aggregate level". She also found that "*It is the state dependence at the micro level for the patients, and the habit persistence for the doctors, which lead to the persistence in market shares that we observe at the `macro' level".*

Brekke *et al.* (2013) studied the pharmacies role in promoting generic substitution and thus stimulating competition between generic and brand name drugs. The authors first constructed a theoretical model where pharmacies can persuade patients with a prescription for a brand name drug to buy its generic counterpart. With this model, they showed that pharmacies incentives to substitution are determined by relative margins and relative co-payments of drugs. This result meant that "*a larger difference in margins between generics and brand name drugs increases the generics market share*", because it is more profitable (for the pharmacy) to promote the first. The authors also found that, through this model, the effect was stronger where drugs are subjected to reference pricing. To test the theoretical model, mentioned above, the authors collected data from two different databases (the Prescription and Wholesale database) of Norwegian Institute of Public Health. The prescription database contains information about prescription bound sales at pharmacy level from 2004 onwards, average prices and volumes per month over the 2004-2007 period. The Wholesale database contains information about producer prices "*per product per wholesaler per month*". Using a fixed effect model regression and IV regression to control for endogenity issues, the authors found that "pharmacy margins on branded versus generic drugs have a strong association with generic market share". However, the authors stressed that "*that the empirical analysis has not established causality, and that* [their*] empirical findings can be interpreted as correlations only*.".

Liu *et al.* (2009) studied the hypothesis of whether financial incentives had an important role on physicians prescription habits (between brand-name and generic drugs) when they prescribe and dispense drugs. Using a data set containing detailed records of personal health care services "(…) *including outpatient visits, hospital admissions, and prescription drugs*" from 200.000 diabetes patients, the authors used a probit estimation to test the probability of a physician to prescribe a generic drug. Their results showed "(…) *that the*

profit margin between the reimbursement and the acquisition price has a significant effect on a physician's prescription making decision".

Iizuka (2007) studied the physician-patient relation in drug prescription in Japan. Using panel-data from 40 hypertension medicines, such as physician's mark-up, retail price, market share and product characteristics (representing a data sample of 258 observations), the author found that "(…) *physicians' decisions are influenced by the markup they obtain*.", which "(…) *suggests the existence of the agency problem in this market*". The author also found that physicians "(…) *prefer to dispense drugs that cost less to the patient, ceteris paribus. Estimated parameter values indicate that physicians are willing to give up one dollar of their profit in order to reduce the copayment of non-elderly patients by 28 cents. This implies that, although physicians do take advantage of markup, they care more about patient welfare than their own profits from markup*."

Rischatsch *et al.* (2013) analyzed the role of physicians and patients financial incentives, when choosing between generic and brand name drugs, in Switzerland. Considering physicians as an imperfect agent for patients (since in some Swiss cantons, physicians "(…) *are allowed to dispense drugs to their patients on their own account*") and using data provided by "(…) *a major Swiss health insurer*" representing 15% of Swiss population , the authors constructed a random-effects logit model where they tested some hypothesis, namely the likelihood of generic prescription compared to brand name drugs prescription due to higher income contribution; and generic drugs being more often prescribed to lower income individuals due to their marginal utility of income; amongst many others. Their results showed that "(…) *financial incentives, agency towards the patient, and agency towards insurers are all found to markedly influence generic substitution*" and "*generics are prescribed more often to patients with high copayments or low incomes.*".

2.2 Studies on Portugal regarding generic drugs

Mendonca (2011) reviewed the main policies intended to the generic drugs market in Portugal, since 2000. The author provides an overview of the key measures taken addressed to the generic drugs market since 2000 (such as the implementation of the RPS in 2002, price differentials between generic and brand drugs, among others) and provided, as well, an overview of new measures being prepared (at that time) to increase the prescription of generic drugs. The author argued that the measures taken in 2010 (changes in RPS) "(…) *were important steps in order to create substantial financial incentives for patients to buy generics and also contributed heavily to reduce the expenditure of the NHS* [National Health System] *with ambulatory medicines*.".

Barros and Nunes (2010) studied the impact of several policy measures on total pharmaceutical spending. The authors use data provided from public sources and checked with INFARMED between January 1998 and August 2008. The dataset contained information about payment made by NHS, information about total sales in value of pharmaceutical products and information about the number of boxes sold in the Portuguese market. Using a endogenous structural break approach, the authors found that "(…) *a transitory slowdown in NHS pharmaceutical expenditure growth in the first half of 2003, coinciding with the start of the reference pricing system. However, this slowdown was relatively short lived. Before the end of the year, growth of pharmaceutical expenditure had returned to the historical path*." They also found that *"Government determined price decreases have only a level effect. The underlying dynamics do not change.*",

Chapter 3

Legislation review

Governments and health authorities in particular, use legislation as their main instrument to implement policy and regulation to achieve the results proposed by themselves, or, in this case in particular, together with other authorities. Since those determinants of generic drugs consumption, discussed in the previous chapter, reveal what impacts the most on individuals and households process of choice, health authorities exploit those determinants as their object of legislation to achieve a better and faster impact on the drug market. As we will demonstrate next, by reviewing the main legal documents implemented by the Portuguese authorities, legislation and legislators use those determinants mentioned earlier as a mean to stimulate the generic drugs consumption and competition in the drug market, in Portugal.

Few studies present a review of legislation regarding medicines in Portugal. Mendonca (2011) and Barros and Nunes (2010), like we had seen in the last chapter, provided a good review on the results of the measures implemented by Portuguese legislators until 2010. A more detailed review on medicine policy was provided by Barros and Nunes (2011), in which the authors reviewed the previous ten years on medicine policy in Portugal, using different methodologies to determine the effects of all sorts of legislation created regarding medicines. Since there are several studies that review the legislation on medicines in Portugal until 2010, we will focus our legislation review on the main legislation implemented after 2010. We will review a few documents that came into effect in 2010 only because we consider that documents are important to explain some legislation that were published subsequently.

Law number 62/2011 from December 12 created a regime of disputes composition between generic and brand name drugs, when industrial and property rights are potentially being violated and altering reimbursement regime for drug prices. The main alterations to Law-Decree number 176/2006 from August 30, regarding industrial and property rights, were that the request for market introduction of certain drugs could not be based on intellectual property rights and that the market introduction authorization could not be revoked or suspend on terms of intellectual property rights. However, if the originating drug owners dispute the market introduction of a generic drug on arbitral tribunal, the latter cannot carry on its commercial activity (generic drugs commerce) due to intellectual and industrial property rights of the originating firm.

Inserted in set of measures, some of them imposed by the Memorandum of Understanding signed with International Monetary Fund and the European Central Bank, the Portuguese Government revised the drug policy with the Law-Decree number 112/2011 from November 29. This Law-Decree sets the maximum price for the first generic drug entering the market (a minimum 50% discount on the Stockist's price and a minimum 25% for the retailer's price, from the reference drug present in the market) and revised the reference

price system, altering the countries that serve as reference[3]. Regarding the revision of the reference price system, the countries that serve as comparison are Spain, Italy and Slovenia.

This Law-Decree was, however, changed many times along the years. The first time was by Law-Decree number 152/2012 from July 12. This document changed/revised some articles of the previous Law-Decree. The most relevant changes were: as assigning the regulatory powers regarding price revision exclusively to the Government member assigned with the Health affairs; changing the public entity responsible for the price authorization (INFARMED); and setting the originating drug's price as the average of the last two previous years.

The second change was made by Law-Decree number 34/2013 from February 27. This document intended to revise some articles in order reduce the burden on health expenses through National Health System (NHS). To do so, the Portuguese Government determined that the three countries used as comparison for price setting are determined annually [4], and the retail price for parallel imported drugs, to be introduced in the Portuguese drug market, should be 5% lower than the retail price for the same medicine and its equivalents.

Complementary to Law number 112/2011 are Portaria number 3/2012 and Portaria number 4/2012, both from January 2. Portaria number 3/2012 defines the criteria, deadlines and proceedings for exceptional price revision, predicted on Law number 112/2011. Portaria number 4/2012 set the rules and deadlines for price formation and revision.

Portaria number 4/2012, however, was altered two times since it came to effect. The first was by Portaria 335-A/2013 from November 15, altering the deadlines for price transition after the date the new price is approved. The second time that Portaria number 4/2012 was altered was by Portaria number 367/2013. This document suspended the application of the article that obliges for annual price revision, since the generic drugs average prices are lower than the maximum prices would be set after such price revision. Therefore, the

[3] According to this Law-Decree, the retailer's price is composed by the stockist's price plus the wholesaler's margin, the retailer's margin and taxes. These margins are regulated by the Portuguese Government, as we can see in Section IV of this document.

[4] The criteria used were GDP per capita similar to Portuguese's GDP per capita (comparable by purchase power parity) or a lower price for each drug in particular.

legislator considered that "(…) t*here is no justification at present to proceed with its review in 2014, if the same average level do not suffer significant changes*.".

The Law number 11/2012 from March 8 sets new rules on drug prescription and dispense. This document revises the rules on drug prescription, namely obligating physicians to declare the INN, among many other things, of the drug that they are prescribing; the receipt for such prescription must be filled electronically[5]. On the other hand, this document also regulates the pharmacy's way to proceed. Pharmacies must inform patients, in the act of dispense of drugs, of the existence of generic drugs (if they exist), and the patient has the right to choose between a generic or a brand-name drug, even if the drug prescribed was, in fact, a brand-name drug.

Complementary to the previous document, comes Portaria number 137-A/2012. This document establishes the legal regime to which the rules of prescription and dispense of medicines obey, created by the Law number 11/2012, and define new rules about to information provision to patients. These new rules obligate pharmacies to inform which are the cheapest drugs available, for that specific prescription and leave the patients the right to choose between the drugs available.

Related to the Law number 11/2012 and Portaria number 137-A/2012 is the Portaria number 340/2012 from October 25. This document creates Pharmaceutical and Therapeutic Comissions to evaluate and control the pattern of drug prescription and dispense. It also regulates the mechanisms of such evaluation in order to Health authorities have some degree of evidence about the effectiveness of prior legislation.

The Law-Decree number 48-A/2010 from May 13 showed the intents for a comprehensive review of the reimbursement system for medicines, with special focus on some regimes, in order to gain equity. The main objectives of this document is to improve access to medicines, to make the reimbursement system more efficient and sustainable and, finally, to promote the generic medicines substitution. To achieve those objectives, this Law-

[5] Due to Information Technologies (IT), the physicians have information regarding cheapest drugs (brand-name or generic) available on the market, which are set by the Government member responsible for the Health affairs.

Decree sets some measures, namely: 100% reimbursement rate, for the cheapest five medicines for each homogeneous group, to patients who are in the special regime; shortening the deadline for a decision on reimbursement in the price of a generic drug; new rules on generic drugs pricing, for each homogeneous group, when they have, at least 5% market share on generic drugs market. It also contains other amendments, "(…) *in particular fixing marketing margins to existing levels in 2005, without this entailing any modifications to approved retail prices or impact on costs for the National System of Health*.".

The previous document has been altered many times during the years. The Law-Decree number 106-A/2010 made the first alteration. This document's objective was to promote fairer rules to medicines access and to combat fraud and abuse on reimbursement from NHS. To achieve those goals, the legislator reviewed, among other things, the rules for reimbursement approval.

The second alteration came by Law number 62/2011, which had already been covered. The third amendment was by Law-Decree number 103/2013 from July 26. This document reviews the process reference prices approval for each medicine's homogeneous group and reviews the mechanisms of homogeneous group's formation, in order to promote savings from substitution to generic drugs.

As we can see by this chapter, all the documents directly intervened in the drug market through different determinants of generic drugs consumption suggested by the literature, such as price, Reference Pricing Schemes and Brand Loyalty and the Physicians and Pharmacies role on drug prescription, to ultimately promote generic substitution, whether by imposing to mention in the prescription that a generic drug is available for that particular originating drug or just by administratively reducing prices of drugs.

One final remark to this chapter is that it makes clear the bond between literature and Government regulation and policy, since the information and knowledge created by the scientific community is useful to Government authorities, and ultimately ends to being useful to patients too.

Chapter 4

Methodological Overview

4.1 Data

This study uses data from INFARMED- National Authority of Medicines and Health Products, IP [6] - that publishes reports, on a monthly basis, regarding the evolution of average prices and market shares (both on volume and value) of generic and non-generic drugs, in Portugal. This data was collected at INFARMED's website, specifically from the "*Market Monitorization*" section. This INFARMED's section follows the evolution of the

[6] http://www.infarmed.pt/portal/page/portal/INFARMED/MONITORIZACAO_DO_MERCADO/OBSERVATORIO/ANALISE_MENSAL_MERCADO

drug market accessibility and puts together the determinants of such evolution in order to provide support on political decision-making.

The reports contained in this section gather information related to generic and non generic drugs market shares, average prices and, in some years, the National Health Service's (NHS) expenses on drugs. These reports are published on a monthly basis and covered the period between January 2006 and January 2014, in Portugal. The months of both 2006 and 2014 years were not included in the sample since they were not included on the information provided by INFARMED about prices of both generic and non-generic drugs that we requested by e-mail.

The main indicators used in this study are Generic Drugs Market Share on Volume in Ambulatory and Relative Prices between generic and non-generic drugs (generic drug prices divided by non-generic drug prices). The information about these variables was all collected within the information provided by those reports. Additionally, I contacted INFARMED to provide information about non-generic drugs average prices (monthly discriminated), in order to accurately set the relative prices for each month of the analyzed period.

According to INFARMED, generic drugs market share in ambulatory is defined as the percentage of generic drugs on the total amount of drugs sold during the analyzed period. To set the relative prices, I divided the generic drugs average price to non-generic drug average price, for each month, using the information contained in those reports and the information supplied by INFARMED via e-mail. We choose this approach to better study the effects of price and price competition on generic drugs market share.

4.2 Methodology

We analyze the impact of the legislation regarding generic drugs in Portugal, introduced after 2010. The main objective of this study is to find out if there was a change in generic drugs consumption triggered by such legislation, in Portugal, in that period. Therefore, we

address this issue with a structural break perspective, i.e., we test if there was a structural break in the generic drug market share series, as a proxy for the generic drugs consumption pattern, after the introduction of the legislation. Hence, we follow an endogenous approach, as we use various methods and let the series itself determine the structural breaks and determine what legal acts were responsible for such break.

As it was said before, we use the relative prices, instead of the actual prices of generic drugs, to better capture the effects of competition based on price between generic and non-generic drugs.

The model we use to determine the impact of relative prices on generic drugs market share is: $mrkt\_share\_vol_t=\beta_1+\beta_2*relative\_prices_t+\beta_4*T+\varepsilon_t$, where $mrkt\_share\_vol_t$ stands for generic drugs market share over the period *t*, $relative\_prices_t$ stands for the relative price between generic and non-generic drugs over the period *t* and, finally T stands for the trend of the model. The growth trend in the *mrkt_share_vol* series can be seen clearly along the entire sample, as Figure 1 shows above, and, for that particular reason, we decided to include the trend in our model.

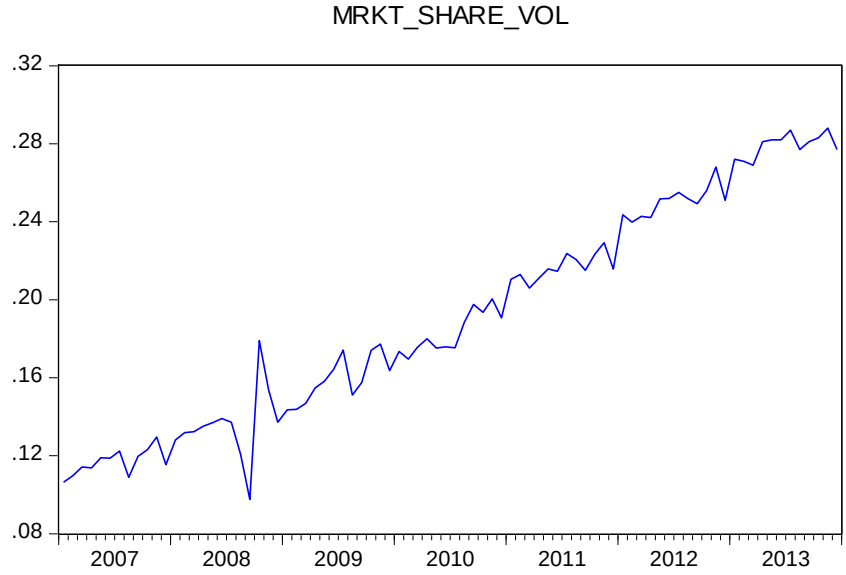

Figure 1- Generic Drugs Market Shares Evolution

However, this model is only valid if the relative prices are an exogenous variable, which is not clear. For that particular reason, we must analyze the presence of structural breaks in the relative prices series.

To test the presence of structural breaks in $relative\_prices_t$, we estimated it as $relative\_prices_t = \beta_1 + relative\_prices_{t-1} + \varepsilon_t$, as $relative\_prices_{t-1}$ stands for a one-period lagged variable of $relative\_prices_t$[7].

The method used, for both full model and relative prices analysis, was a built-in method in Eviews 8 named "Least squares with Breaks" (BreakLS), which follows an Ordinaray Least Squares (OLS) estimation with a similar approach of the Multiple Breakpoint Test, as described by Bai and Perron (1998).

The results of these estimations are presented in the next chapter, as well their main conclusions and implications.

[7] The presence of $relative\_prices_{t-1}$ on this regression controls and removes the presence of serial correlation and, thus, validates its results

Chapter 5

Results and Discussions

5.1 Relative prices

In this section, we present the main results of our estimations. Table 1 shows the summarized results of the estimation using the BreakLS method, regarding the presence of structural breaks in relative prices. The number of observations included in the sample was 83, which is the total number of months between February 2007 and December 2013, which was due to adjustments. Please note that the model used for this particular estimation was $relative\_prices_t = \beta_1 + relative\_prices_{t-1} + \varepsilon_t$, and that the lagged variable was included due to the inertia of relative prices. Additionally, the inclusion of this lagged variable helped to prevent serial correlation in the estimation[8]. An extended output of this estimation is presented in Appendix A.

[8] To test the presence of serial correlation, we used the Breusch-Godfrey Serial LM test. The results can be seen in Appendix B

Method	BreakLS		
Specifications	HAC standard errors & covariance (Quadratic-Spectral kernel, Newey-West fixed bandwidth); Allow heterogeneous error distributions across breaks		
Break Dates	2008M10; 2010M06; 2012M04		
Prob(F-statistic)	0		
R^2	0,9945		
	Variable	**Coefficient**	**P-value**
Partition 1(number of observations: 20)	**C**	0,5281	0,0425
	Lag_Relative_prices	0,6653	0,0001
Partition 2(number of observations: 20)	**C**	0,8146	0
	Lag_Relative_prices	0,2835	0
Partition 3(number of observations: 22)	**C**	0,0351	0,2535
	Lag_Relative_prices	0,9372	0
Partition 4(number of observations: 21)	**C**	0,4325	0
	Lag_Relative_prices	0,255	0,0667

Table 1 – Summarized results of the presence of structural breaks in relative prices, using the BreakLS method

As shown by Table 1, the BreakLS method revealed that there are three structural breaks in the series. These breaks occurred in October 2008, June 2010 and April 2012. To a more clear perception on the evolution of the relative prices and their structural breaks, please see Figure 2, showed below.

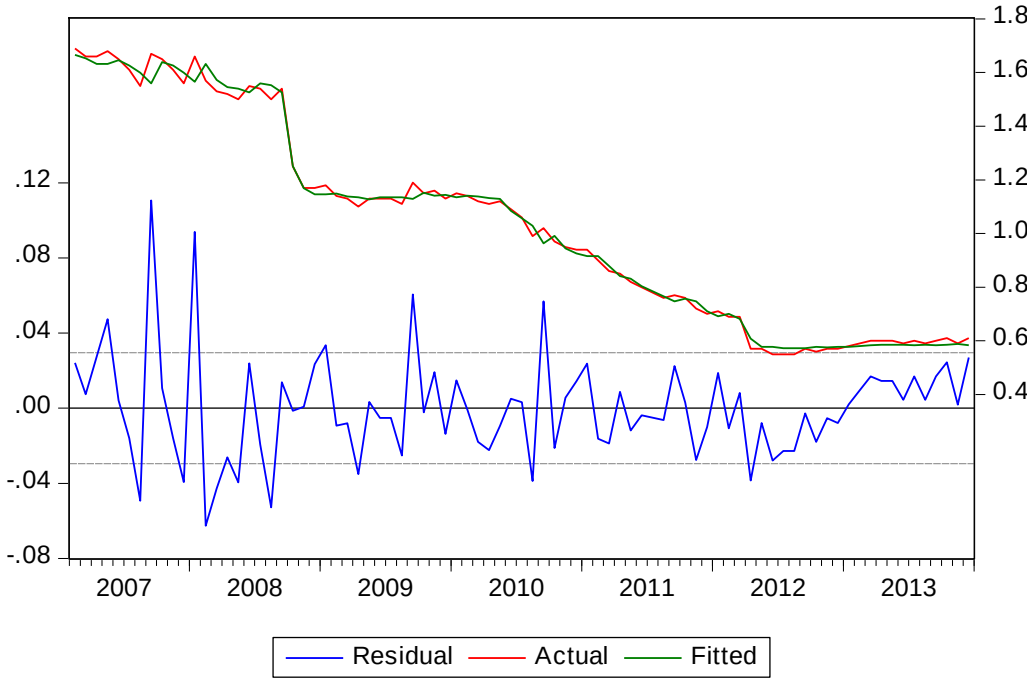

Figure 2- Graphical representation of structural breaks on relative prices

These results can be consequence of legislation published by the time the structural break occurred. The structural break in October 2008 can be consequence of the implementation of Portaria number 1016-A/2008 of September 8, which came into effect on October of the same year. This legal document reduced the maximum retail selling prices for generic drugs by 30%, for generics with retail prices above 5€.

The structural break in June 2010 can be the outcome of the implementation of two legal documents, namely Law-Decree number 48-A/2010 of May 13 (but the date it came into effect was in June 1st) and Portaria number 312-A/2010 of June 11 (but the date It came into effect was July 1st). The Law-Decree number 48-A/2010 reviews some regimes on reference pricing and reimbursement rates for generic medicines; and Portaria number312-A/2010 sets new rules on drug pricing, its annual review and its alteration. Additionally, this document set new rules on retail pricing for the new generic drugs to be subject to reimbursements.

The impact of these two documents cannot be identified separately, because they coincide in time. Although the last legal document has entered into effect after the month identified structural breaks, its effects may have been triggered in June, once it laid down the rules to be applied in the following month. The individual effect of these documents cannot be tested separately to know which of them has the dominant effect, because their effects coincide in time. So, we only can identify their aggregate impact, which lead to a structural break in June 2010.

Finally, the structural break in April 2012 can be consequence of two documents, namely Law number 11/2012, which dates March 2012 and Portaria number 137-A/2012, which dates in May 2012, and sets the legal regime described by the previous document. These two documents intended to encourage the use of generic drugs in Portugal, in detriment of brand-name drugs, by requiring the prescription of drugs by International Non-Proprietary Name (INN). The ultimate goal is improve the efficiency of National Health System, since legislators state that generic drugs "(…) *may play a pivotal role in promoting rationality and sustainability of the National Health Service (NHS), as well as generating significant savings for citizens*.".

Despite these two documents did not regulate prices of neither generic nor brand-name drugs, it is clear that they lead to a structural break in relative prices of drugs, hence producing an indirect effect on relative prices. This result can be explained with the fact that these two documents may have led to price competition between generic and brand-name drugs on the drug market, thus leading to a structural break.

However, these two documents have not been published or came into effect in April 2012. One reason to that is that retailers may have anticipated the publication of Portaria number 137-A/2012 after Law number 11/2012 (published in March), and may have triggered an increase in generic drugs prices, by generic drugs manufacturers, in April (one month before the legal regime for the latter document was created) of the same year, which led to an increase of relative prices. Please note that this increase can be seen in Figure 2, when analyzing the relative prices during 2013.

5.2 Generic drugs market Shares

In this section, we studied the impact of relative prices on the demand of generic medicines. Table 2 shows the summarized results of the estimation using the BreakLS method.

Method	BreakLS		
Specifications	HAC standard errors & covariance (Quadratic-Spectral kernel, Newey-West fixed bandwidth); Allow heterogeneous error distributions across breaks		
Break Date	2008M11		
Prob(F-statistic)	0		
R^2	0,9802		
	Variable	**Coefficient**	**P-value**
Before Breakpoint (number of observations: 22)	**C**	0,3346	0,0104
	Relative_prices	-0,1314	0,0775
	Trend	-0,0001	0,8794
After Breakpoint (number of observations: 62)	**C**	0,1238	0
	Relative_prices	-0,0267	0,0198
	Trend	0,0021	0

Table 2 – Summarized output of the estimation of the demand of generic drugs, using Least Squares with Breaks method

The number of observations included in the sample was 84, which is the total number of months between January 2007 and December 2013, and shows that the relative prices are responsible for explaining 98.02% of the variation of the generic drugs market shares. It should be noted that the variable *relative_prices* is statistically significant only after the identified break, since its p-value<0.05.

However, this model has some specifications for a more accurate estimation of the breakpoint dates, using a "*sequential test in all subsets*" method [9] and to prevent for serial correlation, namely the HAC (Newey-West) coefficient covariance matrix, as described by Newey and West (1986) and often used to correct the effects of correlation, and allowing errors distributions to differ across breaks. These specifications can be seen in the top part of the output presented in Table 2.

This method provided us a quicker and more efficient estimation of the dates where the structural break occurred, since it automatically conducted a Multiple Breakpoint Test described on Bai and Perron (1998), which presents a sequential application of breakpoint tests. A detailed description of how this test works is provided by Eviews 8 User's Guide (2013)[10]. Additionally, and since the object of this study is to test for a structural break, the output present the different coefficients for each partition of the sample on the date the break occurred, thus allowing us to interpret the different impacts of relative prices on the demand for generic drugs for each partition of the series.

On Appendix C is represented an extended visualization of the BreakLS estimation output and on Appendix D is presented an extended breakpoint specification analysis provided by Eviews at regarding this specific estimation and containing information about the test conducted to determine the breakpoint dates. Additionally, in Figure 3 is presented a graphical representation of this estimation.

Regarding the sign of the coefficients of relative prices, determined by the estimation present in Table 2, it is possible to verify that in all partitions of the sample, both are negative. Please note that the coefficient of the Trend is positive in the second partition.T his result shows not only that the impact of relative prices on the demand for generic drugs has changed after the structural break, but also that an increase in relative prices leads to a decrease on the demand for generic drugs in Portugal, as expected.

[9] This method uses a Bai test of breaks in all recursively determined partitions.
[10] Eviews user's guide is provided by EViews after the installation of the software.

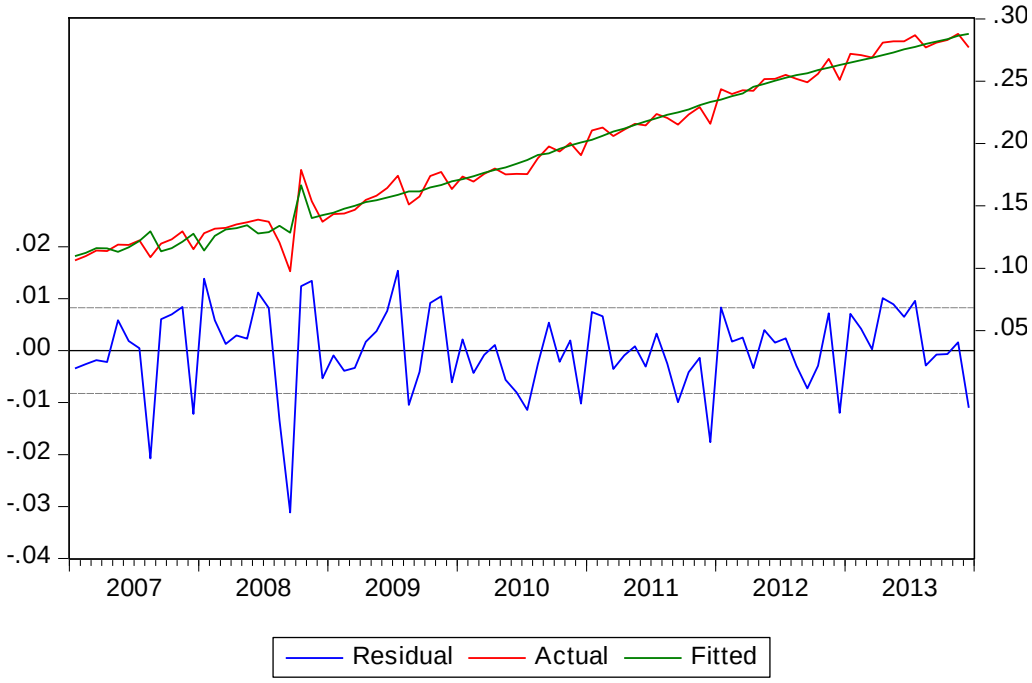

Figure 3 - Consumption of generic drugs, using the BreakLS method

The next step is to test the presence of autocorrelation in the model and thus validating the method used in this study. The presence of autocorrelation invalidates all of the statistical hypothesis tests done under the OLS method. Using the built-in test in EViews 8, we conduct a Breusch-Godfrey Serial correlation LM test, to test the presence of autocorrelation, as described in Godfrey (1978) and Breusch (1978) and the summary results are showed on Table 3.

Breusch-Godfrey Serial Correlation LM Test:			
F-statistic	2.180.572	**Prob. F(2,74)**	0.1200
Obs*R-squared	4.558.622	**Prob. Chi-Square(2)**	0.1024

Table 3 – Breusch-Godfrey Serial Correlation LM Test summary results

As Table 3 shows, there is no evidence of the presence of autocorrelation, since the Prob.Chi-Square is 0.1024, which leads us to not reject the null hypothesis of no serial correlation, thus validating the all statistical hypothesis of this estimation. An extended output, containing more information regarding this test can be found on Appendix E.

The estimation presented in Table 2 showed that there was only one structural break in the series, namely in November 2008.

The structural break that occurred in November 2008 can be consequence of the legislation pack composed by Law-Decree number 184/2008 and by Portaria number 1016-A/2008 both published in September of that same year. These two legal documents complement each other, since the first established that generic drugs prices can be subject to exceptional revision at any point in time and that revision must be published by Portaria, and the second legal documents sets the first generic drugs price revision authorized by the previous document. Please note that Portaria number 1016-A/2008 imposed reductions of 30% on generic drugs prices above 5€.

However, the reasons why the structural break occurred in different months may be due to the possibility of postponing the consumption of medicines, by the patients, thus leading to a structural change in the demand of generic drugs.

Just like a previous structural break identified on our relative prices analysis, the individual effect of these documents cannot be tested separately to know which of them has the dominant effect, because their effects coincide in time. So, we only can identify their aggregate impact, which leads to a structural break in November 2008.

Our results are consistent with the results of Aronsson *et al.* (2001), since relative prices have a significant impact on generic drugs market shares and, therefore, in the market shares of the brand name drugs, since the increase in relative prices resulted in the decrease in generic drugs market share, in all partitions. Additionally, our results are also consistent with the results found by Dalen *et al.* (2006), since that the introduction of a retail price cap in drugs prices helped to increase the generic drugs market shares.

In sum, these results present an interesting insight on the impact of legislation and its dynamics. First, on our relative prices analysis, we found that three structural breaks occurred during the entire period covered. The first two were motivated by legislation that regulates prices directly, thus reducing the relative prices. The last structural break was unexpected since it was a result of a legal document that targeted the demand for generic drugs and did not intend to regulate prices. Additionally, following the conclusions of Hellerstein (1998), the April 2012 structural break result reinforce the importance of physicians and pharmacies on the process of prescribing and dispense of medicines, since it is clear that the new rules on such matters led to a structural break after their implementation.

Finally, our main model studies the relationship between generic drugs market shares and relative prices in our generic drugs market share approach. Our results showed only one structural break and that structural break was motivated by a legal pack intend to reduce generic drugs prices. This structural break highlights the importance of relative prices on the demand for generic drugs. However, this model was not able to indicate any legal document, intended to stimulate directly the demand for generic drugs, capable to create a structural break in the consumption of generics. Despite this, it does not mean that this legislation has not produced effects the demand for generic drugs, since it may have contributed to the growth trend of generic drugs market shares during the entire period covered.

Chapter 6

Conclusion

This study was set out to stress the effectiveness of the legislation regarding generic medicines substitution, imposed the Economic and Financial Adjustment Program Portugal signed with international organizations. More precisely, our main objective was to determine which legal documents were more effective on creating a structural break in generic drugs consumption in Portugal.

The results in our relative prices structural break approach indicate three structural breaks on relative prices: in November 2008, in June 2010 and in April 2012. The breaks coincide in time with legislation regarding price reductions and new rules on prescription and dispense of medicines, by physicians and pharmacies, respectively. It was expected, since most part of the legislation published concerns relative prices, that there were structural breaks motivated by legislation concerning reductions in relative prices. However, the result in the April 2012 structural break, were unexpected, since it dealt with prescription

and dispense rules, thus not concerning relative prices directly. It seems that these two legal documents triggered a raise in generic drugs price (that ultimately resulted in relative prices increases), by generic drugs manufacturers.

Finally, our approach on generic drugs consumption showed that the structural break in generic drugs consumption occurred in November 2008 and coincides in time with a legal package that intended to reduce generic drugs prices. However, this model was not able to indicate any legislation intended to stimulate directly the demand for generic drugs capable to create a structural break in the consumption of generics. Despite this, it does not mean that this legislation has not produced effects the demand for generic drugs, since it may have contributed to the growth trend of generic drugs market shares during the entire period covered.

This result allows us to see that the legislation pack intended to stimulate the consumption of generic drugs, imposed by the Economic and Financial Adjustment Program, was not successful and Portuguese authorities lack policy tools to stimulate generic consumption.

On the other hand, the positive evolution of the generic drugs market shares has been important to competition on drug market, since it can drive prices down from both generic and brand-name drugs, lightening the household's expenses on medicines.

This study focused on aggregated data published on a monthly basis by INFARMED in its website. Taking that into consideration, future research may go through the same kind of study we conducted, but on a micro-level, selecting the most and/or least sold generic and its brand-name counterpart drugs, and see if that same legislation triggered some structural change in their consumption. Another subject that could be analyzed in further research is to study the impact on the top most imported drugs after the implementation of Law-Decree number 182/2009, and subsequent revisions, to see if there was an increase of importation of such drugs and its impact on prices and market shares. Finally, this study can also be replicated, for further research, but this time analyzing the hospital drug market.

This study has offered some insights on the effectiveness of legislation regarding generic drugs consumption, and was conducted using data provided by INFARMED. So, has a direct result of this methodology, it has encountered some limitations, namely the lack of variables .It is so because some data were not available in the entire period covered, namely the Public expenses on the National Health System (data only available since January 2012 onwards), average reimbursement rates (only available for the years 2010 and 2011) and the number of generic drugs available in the market (data only available for the years 2010, 2011 and 2012). It would be interesting to study the impact of these variables on the generic drugs market shares and, therefore, on generic drugs consumption. Although the relative prices can explain almost perfectly the variations of generic drugs market shares, we believe that adding more variables such average reference price and reimbursement rates and physicians prescription patterns, just as Coscelli (2000), can help to provide more insights on physicians and pharmacies role on the demand of generic drugs, in Portugal. Another issue that we faced was that the data of some variables mentioned was not available for the entire period covered, then, it could not be included in the model and we could not stress out the impact that those variable may have on generic drugs consumption.

In the face of such limitations, we presented a study that sought to analyze the impact of various types of legislation and found that prices are the only responsible for creating the structural breaks in generic drugs consumption in Portugal. This result enforces the idea, identified by Mendonca (2011), that generic drugs prices have important implications on generic substitution policy not only from potential savings of households and the Portuguese Government, but also on Health authorities on changing public perception on generic drugs.

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Relevant Legislation

Portaria number 1064-A/2008, of September 2008

Law-Decree number 182/2009 of August 2009

Portaria number 1047/2009 of September 2009

Law-Decree number 48-A/2010 of May 2010

Law-Decree number 106-A/2010 of October 2010

Law-Decree number 112/2011 of November 2011

Law number 62/2011 of December 2011

Portaria number 3/2012 of January 2012

Portaria number 4/2012 of January 2012

Law number 11/2012 of March 2012

Portaria number 137-A/2012 of May 2012

Law-Decree number 152/2012 of July 2012

Dispatch number 12648/2012

Portaria number 340/2012 of October 2012

Law-Decree number 34/2013 of February 2013

Law-Decree number 103/2013 of July 2013

Portaria 335-A/2013 of November 2013

Portaria number 367/2013 of December 2013

Appendices

Appendix A – Extended output for the estimation of relative prices using the BreakLS method

Dependent Variable: RELATIVE_PRICES
Method: Least Squares with Breaks
Sample (adjusted): 2007M02 2013M12
Included observations: 83 after adjustments
Break type: Bai tests of breaks in all recursively determined partitions
Break selection: Trimming 0.15, Max. breaks 5, Sig. level 0.05
Breaks: 2008M10, 2010M06, 2012M04
Allow heterogeneous error distributions across breaks

Variable	Coefficient	Std. Error	t-Statistic	Prob.
2007M02 - 2008M09 -- 20 obs				
C	0.528146	0.255960	2.063397	0.0425
LAG_REL_PRICES	0.665328	0.159487	4.171687	0.0001
2008M10 - 2010M05 -- 20 obs				
C	0.814696	0.063952	12.73920	0.0000
LAG_REL_PRICES	0.283587	0.054654	5.188715	0.0000
2010M06 - 2012M03 -- 22 obs				
C	0.035177	0.030568	1.150761	0.2535
LAG_REL_PRICES	0.937298	0.034645	27.05419	0.0000
2012M04 - 2013M12 -- 21 obs				
C	0.432507	0.080403	5.379226	0.0000
LAG_REL_PRICES	0.255070	0.137099	1.860476	0.0667

R-squared	0.994525	Mean dependent var	1.033735
Adjusted R-squared	0.994014	S.D. dependent var	0.382548
S.E. of regression	0.029597	Akaike info criterion	-4.110850
Sum squared resid	0.065700	Schwarz criterion	-3.877708
Log likelihood	178.6003	Hannan-Quinn criter.	-4.017187
F-statistic	1946.258	Durbin-Watson stat	2.241787
Prob(F-statistic)	0.000000		

Appendix B- Results of the Breusch-Godfrey Serial Correlation LM Test in the relative prices estimation

Breusch-Godfrey Serial Correlation LM Test:			
F-statistic	1.178808	Prob. F(2,73)	0.3134
Obs*R-squared	2.596712	Prob. Chi-Square(2)	0.2730

Test Equation:
Dependent Variable: RESID
Method: Least Squares
Sample: 2007M02 2013M12
Included observations: 83
Presample missing value lagged residuals set to zero.

Variable	Coefficient	Std. Error	t-Statistic	Prob.
@BEFORE("2008M10")	-0.201230	0.208522	-0.965027	0.3377
@BEFORE("2008M10")*LAG_REL_PRICES	0.125479	0.129996	0.965252	0.3376
@DURING("2008M10 2010M05")	-0.013489	0.085913	-0.157003	0.8757
@DURING("2008M10 2010M05")*LAG_REL_PRICES	0.011779	0.073454	0.160352	0.8730
@DURING("2010M06 2012M03")	-0.004141	0.042899	-0.096535	0.9234
@DURING("2010M06 2012M03")*LAG_REL_PRICES	0.004419	0.048614	0.090897	0.9278
@AFTER("2012M04")	-0.059712	0.134431	-0.444182	0.6582
@AFTER("2012M04")*LAG_REL_PRICES	0.101398	0.229118	0.442559	0.6594
RESID(-1)	-0.237025	0.154405	-1.535081	0.1291
RESID(-2)	-0.071924	0.129704	-0.554526	0.5809

R-squared	0.031286	Mean dependent var	-6.15E-15
Adjusted R-squared	-0.088145	S.D. dependent var	0.028306
S.E. of regression	0.029527	Akaike info criterion	-4.094442
Sum squared resid	0.063644	Schwarz criterion	-3.803016
Log likelihood	179.9194	Hannan-Quinn criter.	-3.977364
Durbin-Watson stat	2.014354		

Appendix C – Extended output for the BreakLS estimation of the demand for generic drugs, using HAC estimators to correct serial correlation

Dependent Variable: MRKT_SHARE_VOL
Method: Least Squares with Breaks
Sample: 2007M01 2013M12
Included observations: 84
Break type: Bai tests of breaks in all recursively determined partitions
Break selection: Trimming 0.15, Max. breaks 5, Sig. level 0.05
Breaks: 2008M11
HAC standard errors & covariance (Quadratic-Spectral kernel, Newey-West fixed bandwidth)
Allow heterogeneous error distributions across breaks

Variable	Coefficient	Std. Error	t-Statistic	Prob.
2007M01 - 2008M10 -- 22 obs				
C	0.334698	0.127438	2.626359	0.0104
Relative_prices	-0.131496	0.073513	-1.788734	0.0775
@TREND	-0.000178	0.001169	-0.152268	0.8794
2008M11 - 2013M12 -- 62 obs				
C	0.123816	0.017617	7.028057	0.0000
Relative_prices	-0.026767	0.011252	-2.378976	0.0198
@TREND	0.002175	0.000163	13.33926	0.0000

R-squared	0.980218	Mean dependent var	0.191498
Adjusted R-squared	0.978950	S.D. dependent var	0.056811
S.E. of regression	0.008243	Akaike info criterion	-6.690258
Sum squared resid	0.005299	Schwarz criterion	-6.516628
Log likelihood	286.9908	Hannan-Quinn criter.	-6.620460
F-statistic	772.9949	Durbin-Watson stat	1.970378
Prob(F-statistic)	0.000000		

Appendix D – Description of the breakpoint specification used in the BreakLS estimation

Breakpoint Specification
Description of the breakpoint specification used in estimation

Summary

Estimated number of breaks: 1
Method: Bai tests of breaks in all recursively determined partitions
Maximum number of breaks: 5
Breaks: 2008M11

Current breakpoint calculations:

Multiple breakpoint tests
Bai tests of breaks in all recursively determined partitions
Date: 08/28/14 Time: 02:28
Sample: 2007M01 2013M12
Included observations: 84
Breakpoint variables: C RELATIVE_PRICES @TREND
Break test options: Trimming 0.15, Max. breaks 5, Sig. level 0.05
Test statistics employ HAC covariances (Quadratic-Spectral kernel, Newey-West fixed bandwidth)
Allow heterogeneous error distributions across breaks

Sequential F-statistic determined breaks: 1

Break Test	Break	F-statistic	Scaled F-statistic
0 vs. 1 *	2008M11	19.53062	58.59187
1 vs. 2	---	---	---
1 vs. 2	2006M12	4.578280	13.73484

* Significant at the 0.05 level, Bai-Perron (Econometric Journal, 2003) critical value 13.98.

Break dates:

	Sequential	Repartition
1	2008M11	2008M11

Appendix E – Breusch-Godfrey Serial Correlation LM Test extended output results for the BreakLS estimation of the demand for generic drugs

Breusch-Godfrey Serial Correlation LM Test:			
F-statistic	2.180572	Prob. F(2,76)	0.1200
Obs*R-squared	4.558622	Prob. Chi-Square(2)	0.1024

Test Equation:
Dependent Variable: RESID
Method: Least Squares
Sample: 2007M01 2013M12
Included observations: 84
Presample missing value lagged residuals set to zero.

Variable	Coefficient	Std. Error	t-Statistic	Prob.
@BEFORE("2008M11")	-0.017025	0.052440	-0.324665	0.7463
@BEFORE("2008M11")*RELATIVE_PRICES	0.009714	0.030532	0.318154	0.7512
@BEFORE("2008M11")*@TREND	0.000175	0.000466	0.375679	0.7082
@AFTER("2008M11")	-0.006172	0.022144	-0.278706	0.7812
@AFTER("2008M11")*RELATIVE_PRICES	0.003686	0.014490	0.254359	0.7999
@AFTER("2008M11")*@TREND	5.73E-05	0.000192	0.298462	0.7662
RESID(-1)	-0.001941	0.116092	-0.016717	0.9867
RESID(-2)	-0.242819	0.116280	-2.088232	0.0401

R-squared	0.054269	Mean dependent var	-2.09E-18
Adjusted R-squared	-0.032837	S.D. dependent var	0.007990
S.E. of regression	0.008121	Akaike info criterion	-6.698436
Sum squared resid	0.005012	Schwarz criterion	-6.466930
Log likelihood	289.3343	Hannan-Quinn criter.	-6.605372
Durbin-Watson stat	1.991777		