

Replication package

Market size and strategic interaction in pharmaceutical price regulation

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R.1 Introduction

This document describes the simulations, data and empirical documentation required for the published article *Market size and strategic interaction in pharmaceutical price regulation*, by Simona Gamba, Paolo Pertile and Martin Forster. The simulation results (presented in Section A.1.6 and Figure A.1 of the Online Appendix) were obtained using Wolfram Mathematica and the Mathematica file is described in Section R.2 below. The empirical results (presented in Section 5 of the article and Section A.2 of the Online Appendix) were obtained using Stata and the steps in obtaining the data, cleaning it and obtaining the empirical results are described in Section R.3 below.

R.2 Simulation

Given a set of numerical parameters, the Mathematica file `simulation.nb` computes the best responses in price setting for both regulators and plots the figures that appear in Figure A.1 of the Online Appendix. The simulation uses a specific functional form for the function δ , i.e. $\delta(I) = \ln[I]$. The file includes two separate sets of input: ‘values1’ contains the main parameter values, whereas ‘values2’ assigns values to the parameters that characterise the regulators’ objective

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Theoretical model	Simulation file
κ^A	ka
κ^B	kb
$b^A = b^B$	b
m	m
C^A	Ca
C^B	Cb
α^A	αa
α^B	αb
λ	lambda

Table R.6: Correspondence between notation in Section 4 and the symbols used in the Mathematica file `simulation.nb`.

functions.

The code produces Figures A.1a to A.1d by changing the value of the parameter ‘na’ within ‘values1’ in `simulation.nb` from 0.22 to 0.28. The other parameters take the values reported in Online Appendix A.1.6. Unlike in the theoretical model, where the size of the global population is normalized to 1, in the simulation it is set equal to 100 ($N = 100$). The file can be also used to explore strategic interaction with different parameter sets.

The main steps of the simulation are explained in text boxes in the file `simulation.nb`. Table R.6 provides the correspondence between parameters of the theoretical model of Section 4 of the article and the variables in the file `simulation.nb`.

R.3 Empirical analysis

The main data set for the analysis was provided by IQVIA (<https://www.iqvia.com/>, previously IMS Health). We describe the three main steps taken to prepare and analyse the data:

1. *Obtaining the data.* All medicines must be authorised before they can be marketed and made available to patients. In the European Union (EU), there are two main routes for authorising medicines: a centralised route and a national route. We downloaded the list of the 108 non-generic medicines classified as ‘L01 Antineoplastic agents’ and approved by the European Medicines Agency (EMA) between its founding date in 1995 and 30/03/2017, some of which contain the same active substance. In April 2017, IQVIA provided us with the data set containing quarterly prices.
2. *Cleaning the data.* The process of cleaning the data set that was provided to us by IMS

Health/IQVIA was complex. Here we describe the principal steps in that process.

- (a) Each medicine from the EMA list ‘L01 Antineoplastic agents’ was assigned to one (or more) disease(s), as identified in the Global Burden of Diseases database. To do this, the indication assigned by EMA to each drug was considered. When doubts arose, two medical doctors, one for haematology and one for oncology, were consulted.

The EMA list was taken as the reference point, and IQVIA’s assigned product names were harmonized to match those on the EMA list. IQVIA data include both the local product name and the international product name and, in the process of matching, the international product name was preferred. However, in a limited number of cases, the international product name was different from the name(s) included in the EMA product list. In such cases, we used the local product name to make the match. When the local product name was not helpful – for example, because it was the same as the international product name – an internet search was carried out, using the name of the product’s molecule, to determine whether, in some countries, the product had been commercialized with a different name.⁴

- (b) A number of products were dropped for reasons that are explained in the Online Appendix (Section A.2.1). We also dropped observations which referred to parallel imports. IQVIA data also include the patent status. For three products, the patent status was ‘protection not covered’ for all observations. In this case, we searched the internet (e.g. www.drugpatentwatch.com) to identify the patent status of the product.⁵ Given our focus on innovation, we kept only products that were on patent in at least one country in at least one period.
- (c) We are interested in the date of launch of each product in each country, independently of the formulation or the pack size. We determined it from the date on launch, referring to the single observation, provided by IQVIA. In a few cases, the date of launch that we computed was subsequent to the date of the first price, with more than a month lag. To understand whether the error was in the launch date, or whether the first price was indeed not the first, we verified the date of approval by EMA: if the date of EMA

⁴To give an example, for some observations referring to the molecule ‘Cabozantinib’ (for which there are two medicines in EMA’s list: Cometriq and Cabometyx), on some occasions the local product name was Cabometyx and the international product name Cometriq, while on other occasions the opposite was true. In order to determine the correct product name, the medicine’s formulation (which is different for the two medicines) was considered.

⁵For a single product (Xagrid) in Luxembourg, the patent status is ‘protection under investigation’. Since the same product was no longer on patent in the other countries, and no information on patents for that product in that country were found on the internet, we assumed the product was not on patent in Luxembourg either.

approval was before the first price date, we assumed the date of the first price was the date of launch, and that the error was in the declared launch date. We replaced the launch date with the first date on which the InternationalProduct was available in the country (according to the existence of a price) when this was antecedent to the launch date. Similarly, when the launch date was missing, we replaced it with the date of the first observed price, provided that this date occurred after the first date for which data are available in the corresponding country. If the date of the first observed price coincided with the first date for which data are available in that country, no value was imputed for the launch date.

- (d) To ensure comparability of prices across countries, we computed the quantity of active substance contained in each local pack using IQVIA information on pack strength, volume, and size. When this information was missing for a given product-country pair, or when an international comparison suggests misreporting in the IMS data, the quantity of active substance was determined using information obtained from web searches, the LocalPackDescription variable, the InternationalPackDescription variable (when the former was unavailable), or, as a last resort, quantities reported for the same product in other countries.⁶
- (e) We computed the ‘price per mg’, so as to allow for the comparison of observations characterized by a different pack size and/or a different strength, for all price variables - manufacturer selling price (with and without mandatory rebates), pharmacy price, price to hospital, and retail price. When the same product was marketed in a country at different concentrations during the same period, we retained the lowest price per mg.
- (f) Price-per-milligram values deemed unreasonable were recoded as missing. Unreasonable values were identified by comparing the price per milligram of a given product with that observed for the same product in other periods within the same country and with corresponding values reported in other countries.
- (g) We considered the manufacturer less mandatory rebate price. When this was not available, we replaced it with the price to the hospital and, if needed, with the price to pharmacies. Finally, if required, we replaced it with the retail price (this happened for a limited number of products in Switzerland).

⁶One product, Cometriq, required special treatment because individual packs contain tablets with different strengths. In this case, the total quantity of active substance was calculated using information on both the number of tablets and the strength of each tablet contained in the pack.

- (h) We retained a single observation for each country, InternationalProduct and time period (quarter). In the presence of multiple observations for the same product in the same country and period, the reimbursement status (as reported in the IQVIA data) was coded as ‘reimbursed’ whenever at least one of the underlying observations was reimbursed, while the patent status was coded as ‘protected’ whenever at least one of the underlying observations was classified as protected.⁷
- (i) Observations referring to periods when the product was not reimbursed, or classified as ‘never protected’ or ‘no longer protected’, were excluded from the sample.
- (j) We created the variable ‘number of years since launch date’, which is the time (in years) from the first launch in our sample of countries.
- (k) Data on disease prevalence, GDP per capita, and pharmaceutical exports were merged with the IQVIA data set. As prevalence estimates are available only at five-year intervals, each estimate is carried forward and assumed to remain constant until the next observation becomes available. Because a single product may have multiple indications, prevalence was calculated as the sum of the prevalences of the corresponding diseases. We then constructed the variable ‘relative market size’, as described in Section 5.3 of the article. For consistency with price data, GDP and export data were converted into current Euro using the quarterly exchange rate as reported in IQVIA data.

3. *Analysis of the final data set using Stata.* The Stata do file `mktsize.do` provides the commands used to obtain the results of the empirical analysis reported in the article and in the Online Appendix.

⁷In a small number of cases, multiple observations referring to the same product, country, and period are assigned different patent statuses, with some coded as ‘protected’ and others as ‘protection not covered’.