Measuring performance in off-patent drug markets: A methodological framework and empirical evidence from twelve EU Member States[☆]

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A R T I C L E   I N F O

A B S T R A C T

This paper develops a methodological framework to help evaluate the performance of generic pharmaceutical policies post-patent expiry or after loss of exclusivity in non-tendering settings, comprising five indicators (generic availability, time delay to and speed of generic entry, number of generic competitors, price developments, and generic volume share evolution) and proposes a series of metrics to evaluate performance. The paper subsequently tests this framework across twelve EU Member States (MS) by using IMS data on 101 patent expired molecules over the 1998–2010 period. Results indicate that significant variation exists in generic market entry, price competition and generic penetration across the study countries. Size of a geographical market is not a predictor of generic market entry intensity or price decline. Regardless of geographic or product market size, many off patent molecules lack generic competitors two years after loss of exclusivity. The ranges in each of the five proposed indicators suggest, first, that there are numerous factors – including institutional ones – contributing to the success of generic entry, price decline and market penetration and, second, MS should seek a combination of supply and demand-side policies in order to maximise cost-savings from generics. Overall, there seems to be considerable potential for faster generic entry, uptake and greater generic competition, particularly for molecules at the lower end of the market.

1. Introduction

Over the past few decades spending on prescription pharmaceuticals has increased faster than total health spending and gross domestic product in most OECD countries [1,2]. As a result of the observed and projected growth in pharmaceutical expenditures there is a need for increased scrutiny and reform of pharmaceutical markets and regulatory practices [3]. Generic medicines can play an important role in curbing rising pharmaceutical costs and their cost-saving potential is significant as they provide both a lower-priced option for prescribers and patients and a tool to drive-down prices of originator drugs [4]. The extent to which generic drugs contribute to pharmaceutical cost containment depends, in part, on the price competition incited through generic entry and diffusion. While the potential of generic medicines as an expenditure-optimisation tool is widely recognised, studies examining how competition from generic entry affects originator prices and market share have often drawn opposing conclusions [5–8,16], whereby in some instances originator prices decline, whereas in others they increase.

A key policy imperative among OECD countries has been the maximisation of potential savings through the wider use of generics, after patent expiry or the loss of market exclusivity of the originator. Yet, irrespective of price levels for originator brands at patent expiry and their spread across countries, significant variation in the prices of generics has been observed in a number of studies [4,9]; in these, the price spread is significantly more apparent in generic medicines than it is in branded originators both at and after patent expiry [9]. Considering this variation in prices post-patent expiry and the market shares that generics command a debate exists as to what policy mix is most appropriate in fulfilling this dual objective of achieving low prices and high market shares for generic medicines and how this can be measured objectively. Pertinent questions in this context are, among others, the kind of supply-side regulation, also on generic medicines, that delivers higher price reductions post-patent expiry; the demand-side policy mix that delivers greater market share for low-cost generics; and whether low prices for originators pre-patent expiry influence entry prices for generics post-patent expiry and determine their path over time.

Significant developments have taken place in most OECD settings in terms of policies favouring the uptake and use of generic medicines, including regulatory interventions on prescribing and dispensing. Yet, an assessment of how effective these measures and interventions are in promoting wider generic use at a faster pace and at reduced cost to health insurers is an issue that merits evaluation and systematic appraisal. In this paper we address this gap in three ways. First, we develop a methodological framework comprising five indicators that can be used as a benchmark for generic policy evaluation in non-tendering settings and once originators lose exclusivity. Second, we propose a number of metrics that help assess the performance of each of the proposed indicators over time, for example, one and two years post-patent expiry. Third, we use market data from a large number of patent-expired molecules to test and measure the performance of the above indicators and metrics in 12 EU Member States. Trends across each indicator and metric are benchmarked against generic policies in the study countries in order to highlight the effect of supply and demand-side policies on generic drug entry, competition, price evolution and volume share.

2. A methodological framework for generic drug policy assessment

2.1. Empirical observations

Evidence suggests that across OECD countries over 65% of the pharmaceutical market comprises off-patent medicines [8]. Health insurers implement combinations of supply-, proxy demand- and demand-side policies aiming to increase the diffusion and use of generics as well as maximise their price effect. Through competition after the expiry of intellectual property for the originator (patent expiry, expiry of data exclusivity period), generic drug entry and diffusion are expected to influence both the price and volume share of branded products [10,11].

However, the literature on the influence of generic competition on originator brand name prices and market share is somewhat divided. While some studies [5,12] have found that the price response to generic entry is as expected, in that originator prices decline following generic entry, others have found that prices of originator brands may rise upon generic entry [6,7,13]. In addition, while increased competition between generic producers has been found to decrease prices of generic drugs, the price of branded drugs is not necessarily reduced by increased generic competition [14]. It has also been shown that originator brand manufacturers do not respond to generic market entry by decreasing prices, but rather generic entry may correspond to a decrease in the speed of originator price increase [15,16]. Evidence also suggests that manufacturers will often not compete on price once generic competitors enter the market [6,17].

Similar concerns exist about the price levels achieved and the rate of price decline following generic entry. The literature points to significant price declines after generic entry [15–17]; yet it has been argued that different forms of regulation may have an effect on the amplitude of such a price decline and the generic market share [4,16,18]. The interface between competition and regulation seems to lead to different pricing outcomes across countries; for example, whereas price variation for originator brands in ambulatory markets was found to be two- to three-fold between highest- and lowest-priced country, price variation for generics was found to be five- to twenty-fold between highest- and lowest-priced country [9].

The effect of generic competition on volume or market share of branded drugs following originator patent expiry is less controversial than that of price response. Indeed, the generic volume share grew from 30% after one year to 45% two years after patent expiry [4]. Overall, the originator volume share decreases post-patent expiry, while generic volume share increases.

The ambiguity identified in the results obtained above, particularly with regards to pricing developments post-patent expiry, remains because of the numerous external factors that influence the effect of generic entry and competition on a country's pharmaceutical market. Both supply of and demand for pharmaceuticals in general, and generics more specifically, are determined by factors such as consumer needs, insurance structures, prescribing policies and incentives, and pricing and reimbursement schemes [18].

2.2. Indicators and metrics to assess generic drug policy

The indicators proposed in this section underscore generic entry, intensity of entry, price developments and diffusion of generics over time. They are related to the penetration of a product market by generics, following patent expiry, the speed of that penetration, the price diminution over time, the size of generic volume market share and the speed of its evolution. In sum, the proposed indicators are: (a) generic drug availability post-patent expiry; (b) time delay to generic entry; (c) number of generic competitors; (d) price development of originators and generics after loss of exclusivity; and (e) evolution of generic volume market share.

Generic drug availability outlines the extent to which generic alternatives are available in a patent-expired molecule. It is measured by the entry of generics and the time at which this occurs. This indicator helps determine the proportion of patent-expired molecules that have available generics and at what point after loss of exclusivity this occurs.

In terms of metrics to assess performance, generic drug availability can be assessed through (a) the share of total molecules studied in each country with generic entry within the first 12 and 24 months following patent expiry, (b) the proportion of total sales facing generic entry within the same timeframe and (c) the proportion of sales facing generic entry in the top and bottom decile of each market by sales, 12 and 24 months post-patent expiry. The 12 and 24 month benchmarks have been used widely in the literature to measure entry, penetration, competition and availability [4,16] and are considered to be appropriate in the sense that if generic entry does not occur up to 24 months after loss of exclusivity, the benefits from genericisation are likely to be modest.

Delayed availability, occurring significantly after patent expiry would suggest that the potential pecuniary savings to health insurers from genericisation and price competition would occur with significant delay. Non-availability of generic medicines would imply that patent-expired originator drugs retain their level of monopoly and that the benefits of price competition post-patent expiry do not exist. By selecting the top and bottom decile by sales, we are also able to study the extent of availability at the top and bottom segment of each product and country market. The top decile of sales accounts for a small number of molecules, whereas the bottom decile of sales has a significantly greater variance in terms of molecules included.

Time delay to generic entry is defined as the number of molecules, as a proportion of total molecules that have generic entry following patent expiry, the proportion of sales that are switched to generics, and the speed at which generic entry is occurring. The proportion of molecules and of total sales with generic entry can be studied quarterly at appropriate benchmarks (e.g. 3, 6, 12 and 24 months post-patent expiry). A further differentiation can be made based on delays studied for the top and bottom decile of sales in order to gauge differences across molecules with high and low sales, respectively. The rationale for including this indicator and the associated metrics in the analysis relates to the importance of generic entry occurring immediately after patent expiry, if health insurers are to capitalise on genericisation. Delays in generic entry are likely to prove costly to insurers and beneficial to patent-expired originator brands.

The number of generic competitors measures the intensity of entry in a molecule market post-patent expiry and its evolution over time. Economic theory confirms that the number of competitors per molecule may be associated with downwards impact on prices and, potentially, greater market penetration by generics [8,12]. The number of generic competitors can be recorded for each molecule at 12 and 24 months after loss of exclusivity and a further differentiation can be made for the top and the bottom decile

by sales over the same timeframe. Trends are observed by calculating the average number of generic entries per molecule according to the market size of molecules by sales. By calculating the average number of generic entries for molecules in the top and bottom decile of each market by total sales, it is possible to identify further trends in the number of generic entries.

The price development indicator measures the response of prices to the impact of generic entry post-patent expiry. The extent of price decline post-patent expiry is dependent on a number of parameters including the number of entrants on the market, the size of the market and the type of regulatory interventions in place [8]. Patent expiry information can be combined with pricing data to identify the price of the originator brand 12 months prior to patent expiry and the price of the same brand and all available generics 12 and 24 months post-patent expiry. Additional metrics can include pricing dynamics for the top and bottom decile by sales 12 and 24 months post-patent expiry.

The inclusion of generic volume market share is based on the ratio of generic volume sold over total (brand and generic) molecule volume sold in the ambulatory prescription pharmaceutical market and its evolution over time, calculated quarterly at molecule level. Average generic volume share for all molecules studied allows for comparison between study countries. This indicator helps determine the amplitude and speed of generic penetration as measured by market share of generics at molecule level. Combined with reduction in prices, a high degree of generic penetration would maximise benefits to health insurers. The metrics developed for this purpose are generic volume market share 12 and 24 months post-patent expiry in the total number of off-patent molecules as well as the top and bottom decile by sales. The framework comprising both indicators and the metrics proposed for this purpose are shown on Fig. 1.

3. Methods

3.1. Data sources

In order to test empirically the indicators and metrics developed in the previous section, we used proprietary data from Intercontinental Medical Statistics (IMS) [19]. The data covered the period from the last quarter of 1998 (Q4, 1998) to the last quarter of 2010 (Q4, 2010). The available variables included the date of patent expiry (available monthly), prices, volume and sales data (all three available quarterly) for a total of 101 molecules (originator brands and generics) and their combinations, which lost patent protection between January 2000 to December 2008 individually across 12 EU MS (Austria, Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Portugal, Spain, Sweden and the United Kingdom), and the number of generic competitors for each molecule. The analysis aimed to understand what drives entry and generic competition in the study countries, and to identify and examine any associated changes in prices, sales and market shares over time, following the expiry of the originator patent.
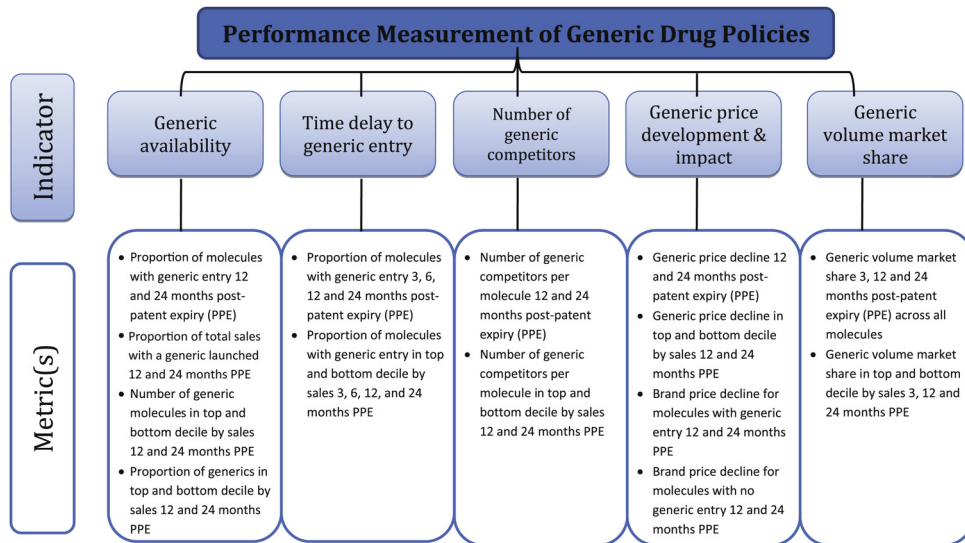
Fig. 1. Methodological framework comprising indicators and metrics for performance measurement in off-patent markets.   *Source*: The Author.

3.2. Data organisation

Although the maximum number of molecules considered in this analysis that lost patent protection during the study period was 101, not all molecules were available or had patent expiries across the 12 study countries and the number of patent-expired molecules available for study ranged from 53 (the Netherlands) to 101 (France). In order to enable pricing dynamics to be studied pre- and post-patent expiry, the molecules included in the analysis had their patent expired between Q1 2000 and Q4 2008, allowing a minimum of 4 and 8 quarters, respectively, of price and volume evolution data to be studied on either side of patent expiry (before and after).

The 12 study countries were divided into three tiers based on the perceived strength of their generic policies (Table 1) [8,20,21]. Tier I (UK, Denmark, the Netherlands, and Germany), had high levels of generic prescribing and substitution in addition to allowing competitive pricing of (generic) pharmaceutical products. Tier II (Austria, Finland, France, Spain, Sweden), had moderate levels of generic prescribing and employed intense generic price reduction strategies, including stepwise price reduction in some cases. Tier III (Greece, Portugal, Italy), implemented price capping on generics and had fewer incentives for generic prescribing and substitution during the study period. While these categorisations are in some way arbitrary and subject to exceptions, they were thought to be useful in highlighting key similarities and differences in generic policies among the study countries.

Pricing data were available at ex-factory level. Original prices were available at retail level and prices were based on Intercontinental Medical Statistics (IMS) Midas standard historical prices for each originator brand. Standard historical prices are calculated by converting different formulations and dosages of a drug to a standard solid dosage of one tablet (standard unit), providing a comparable price measure independent of dose and pack size across countries [19]. We used local currency sales converted to US dollars at constant exchange rates to convert price and sales data to US dollars and thus also avoid the effect of exchange rate fluctuations. In order to arrive at ex-factory level prices, average wholesale and retail mark-ups and VAT rates applicable during the study period were taken into account and were sourced from EU-wide surveys and national sources [9].

Volume data were available in standard units (SU), which were calculated by dividing the number of tablets sold by the smallest common dose of a particular product [22]. To compare drug prices across the study countries, we used volume data for each study country to construct weighted price indices, whereby the price of each drug in the sample was weighted according to its relative frequency of use (volume). Unweighted averages would probably result in an inaccurate measure of the relative costs of drugs across countries because they do not take into account the market shares and consumption of each product [2,18,23]. As a result, we opted for country-specific volume market shares (Paasche index) in order to produce price indices. The Paasche index is calculated as follows:

$$P_S = \frac{\sum_{j=1}^{n} P_{jt} q_{jt}}{\sum_{j=1}^{n} P_{j0} q_{jt}} 100$$

where P_S is the price index weighted by country-specific volume market shares (own-country weights); p_{jt} is the price of product j at time t; p_{j0} is the price of product j at the base period; q_{jt} is the quantity of product j at time t; n is the number of products.

When comparing prices and indices across countries, one important conceptual advantage of the Paasche index is that the use of each country's volume weights enables

Table 1
Summary of key supply- and demand-side policies related to generic drugs in 12 EU Member States, 2010[a].

Tier	Country	Supply-side policies			Demand-side policies		
		Generic price capping[b]	Internal price reference (IPR)	Reimbursement linked to originator	Mandatory generic substitution[c]	Generic (INN) prescribing[d]	Generic promotion[e]
Tier I	United Kingdom	√[f]		√		√	√
	Denmark		√		√[g]	√	√
	Netherlands		√		√	√	√
	Germany		√		√[g]	√	
	Finland	√	√	√	√[g,h]	√	√
Tier II	Austria	√		√			√[i]
	France	√	√	√	√[g]	√	√
	Spain	√	√		√	√	
	Sweden	√	√		√[g]	√	
Tier III	Italy	√	√	√	√	√	√
	Greece	√	√	√		√	
	Portugal	√	√	√	√	√	

Source: Based on [8,20,34].

[a] As the study period ranges from 2000 to 2010, this table reflects policy measures implemented in the study countries during that period and summarises policy interventions as of 2010.

[b] Generics are subject to an official maximum price which cannot be more than a certain proportion of the branded originator price.

[c] For the majority of Member States, patients may refuse substitution but will have to pay the price difference.

[d] It is mandatory in Portugal and strongly encouraged and practiced in the UK, but indicative (and widely monitored) in all other cases.

[e] Generic promotion refers to a number of interventions seeking to elicit response by prescribers, pharmacists and patients and increase the rate of generic drug uptake. For physicians, both financial incentives (e.g. budgets) and non-financial incentives are indicated; for example, beyond mandatory INN prescribing, policies such as "generic prescribing unless brand is medically necessary", prior authorisation for originator brands, reference pricing, prescribing guidance are key in promoting use of generics. For pharmacists, the use of the payment method (either fixed fee per prescription or regressive markup) to incentivize generic dispensing beyond generic substitution, is key. And for patients, cost-sharing policies, including differential co-payments (higher cost-sharing for originators and lower for generic equivalents, are essential in incentivizing generic use. Additionally, information campaigns undertaken by government or health insurance promoting the value of generics in the general population, are considered to be helpful.

[f] In the UK, this is applied to only a very limited number of generics, as outlined in the Maximum Price Scheme (MPS) of 1999.

[g] Generic substitution is "mandatory" in Germany, Denmark, Finland and Sweden.

[h] Finland: Until 2006, pharmacists were provided with discounts in order to choose specific generic products in substitution.

[i] Austria: as of 2007, generic promotion was in beginning to be developed.

differences in consumption patterns across countries to be taken into account. This is relevant and important in the present study, also because of the different product sample sizes in each country. This is in contrast to the Laspeyres index, which can also be used for cross-country comparisons but requires one reference country's volume weights to be used across all countries or the Fisher index, which would require that both Paasche and Laspeyres indices be constructed.

Patent expiry data were available for the month during which expiry occurred in each country. Finally, it was possible to identify and record all producers of generic products by the extent to which sales by them were registered in individual countries and, in this way, were able to report time to generic entry after loss of exclusivity.

The data were organised to study the performance of the five distinct indicators and their associated metrics as outlined in the previous section and shown on Fig. 1. By cross-referencing patent-expiry dates, pricing data, sales data and market of generic entrants, averages for each molecule were produced for each study country and over time across these indicators. Across all study countries, the top decile of sales is attributed to no more than 5 molecules in the majority of cases, demonstrating the dominance of certain high selling (by volume) or expensive products (high price). There is far greater variation in the bottom decile, in which there is typically a range of 40–60 molecules depending on the country studied.

3.3. Study limitations

The analysis is not without limitations. A first limitation relates to the data sources, in particular patent expiries and pricing data; the former may be subject to some bias due to the collection method, whereas the latter are calculated based on average margins, rather than actual margins, implying that there may be an upward or downward bias in some of the prices reported. Researchers and competent authorities undertaking this type of analysis ought to check the accuracy of their patent or data exclusivity expiry data and price data collection. The second limitation is that we cannot study price dynamics in the case of tenders for outpatient generic medicines in some countries, whereas we can in others. In particular, although tenders for outpatient pharmaceuticals have been used routinely in the Netherlands and Germany since mid-2008 (the Netherlands) and 2007 (Germany), we cannot capture their effect and although their implementation coincides with the end of the study period, their effect is unknown. However, we can capture Danish and Swedish tender prices, as these are publicly available. The third limitation relates to the method used to provide volume weights. In this study, we have used the Paasche index (own country weights) to weigh prices, but there are also two other indices (Laspeyres and Fisher) that can be used in this context. While we believe that the Paasche index is most appropriate for the type of analysis pursued in this study, we would encourage competent authorities to also use the

Laspeyres and Fisher indices in order to obtain a more complete picture of the impact of volume weights on prices. The fourth limitation is that we are not in a position to study prescribing switches [24,25], a practice whereby when the patent of a molecule expires, prescribers are likely to move to a different molecule within the same therapeutic class, or to a different therapeutic class. While this phenomenon cannot be studied directly, the proximity of generic entry to patent expiry and the amplitude of generic penetration share potentially limit the likely effect this phenomenon might have. Finally, we are not able to quantify the likely effect of market strategies that may be employed by originator manufacturers aiming to inhibit early generic entry, such as the creation of "patent clusters", the phenomenon of ever greening or prolonging patent litigation.

4. Results

4.1. Generic availability

In terms of overall generic availability, there are substantial differences across countries. Tier I countries have a significantly higher rate of generic availability (46.7% of all patent-expired molecules in the UK and 47.1% in Germany) than Tier III countries (32% in Italy and 24.6% in Greece) (Table 2). These differences are also directly correlated with the share of total sales that have launched a generic alternative. Depending on the country, 11–59% of total molecules sales are not facing generic competition 24 months post-patent expiry, but the proportion of molecules without generic sales was higher in tier III countries (Greece 59%, Portugal 30%) than it was in tier I (10% in Denmark, 11% in the UK, 15% in Germany).

The top-10 molecules by sales had generic entry 24 months post-patent expiry in Germany, Denmark, the Netherlands or Finland (Tier I countries), compared with only 5, 7 and 8 top-10 selling molecules in Greece, Portugal and Italy (Tier III countries), respectively. In the bottom 10% of the market the proportion of molecules facing generic entry was significantly higher in tier I and II countries (73% in the UK, 68% in Sweden and the Netherlands, 64% in Denmark) than it was in any tier II country (63% in Italy, 50% in Portugal and 45.6% in Greece). The size of the market in population terms does not seem to be, *ceteris paribus*, a predictor for low generic penetration at either the top or the bottom end of the market, as Denmark, Sweden, Austria and Finland, all having small to medium-sized markets, had among the highest generic penetration rates.

4.2. Time delay to generic entry

The time to generic entry following loss of exclusivity was found to vary considerably both between study countries and between molecules. Over 75% of generic sales were attributed to molecules that had generic entry in the UK 3 months after loss of exclusivity, followed by Finland (71.6%), Germany (71%), France (65.1%) and Denmark (60.4%). This is testament to the speed of genericisation in the UK, Germany, Finland and Denmark. At the other end of the spectrum, Greece only had 12.4% of sales

Table 2
Availability of generic alternatives 24 months post-patent expiry for all study molecules and for the top 10 and bottom 10% of the market (as % of the total number of patent-expired molecules and as % of sales).

Member State (number of molecules studied)	Molecules with generic launched up to 24 months after patent expiry	Total sales at patent expiry (in constant US$ 000)[a]	Proportion of sales with generic launched 24 months post-patent expiry	Top 10 molecules and % of total molecules studied	% of top 10 molecules facing generic entry within 24 months post-patent expiry	Number of molecules in bottom 10% (% of total number of molecules)	% of molecules facing generic entry within 24 months post-patent expiry
	Total number of patent expired molecules			Top 10 molecules by sales		Bottom 10% of the market by sales	
Tier I							
UK (90)	42 (46.7%)	2,990,465	88.6%	10 (11.1%)	90%	39 (43.1%)	73%
Denmark (66)	30 (45.5%)	178,193	90.4%	10 (15.1%)	100%	34 (35.7%)	63.60%
Germany (87)	41 (47.1%)	2,300,528	85.3%	10 (11.5%)	100%	26 (30.0%)	57.50%
The Netherlands (53)	23 (43.4%)	261,210	64.3%	10 18.9%)	100%	24 (44.4%)	67.90%
Finland (67)	26 (38.8%)	209,774	81.2%	10 (14.9%)	100%	11 (16.2%)	55.20%
Tier II							
Austria (94)	36 (38.3%)	175,471	71.7%	10 (10.6%)	90%	15 (16.3%)	52.10%
France (101)	33 (32.3%)	2,992,032	67.8%	10 (10%)	80%	29 (29.1%)	54.50%
Spain (84)	27 (32.1%)	1,298,675	76.3%	10 (11.9%)	100%	15 (18.0%)	59.50%
Sweden (88)	30 (34.1%)	408,664	72.4%	10 (11.3%)	80%	21 (23.3%)	68.20%
Tier III							
Italy (97)	31 (32%)	1,293,162	74.3%	10 (10.3%)	80%	24 (24.6%)	62.90%
Greece (57)	14 (24.6%)	318,468	41.2%	10 (17.5%)	50%	7 (11.5%)	45.60%
Portugal (56)	26 (46.4%)	256,050	70.1%	10 (17.8%)	70%	12 (21.4%)	50%

Source: The author based on IMS data.

[a] Sales included in this analysis refer to retail sales, except for Denmark and Sweden, where only combined hospital and retail data available.

Table 3
Time delay to generic entry (proportion of total sales).

	Member State	0–3 Months	Between 3 and 6 months	Between 6 and 12 months	Between 12 and 24 months	At 24 months	No generic sales after 24 months (%)
		Proportion of patent-expired sales with generic entry (%)					
Tier I	UK	75.6	0.9	6.0	2.7	2.0	11.4
	Denmark	60.4	15.1	4.7	6.1	2.8	9.6
	Germany	71.0	8.8	1.9	1.7	3.2	14.7
	The Netherlands	36.9	0.5	18.0	23.8	2.0	35.7
	Finland	71.6	4.2	1.2	4.5	6.4	18.8
Tier II	Austria	34.4	15.4	6.0	6.0	4.4	28.3
	France	65.1	0.9	1.6	4.4	7.4	32.2
	Spain	51.8	6.9	4.4	12.1	10.9	23.7
	Sweden	31.8	13.4	15.2	10.3	9.3	27.8
Tier III	Italy	54.2	14.0	10.0	3.9	2.0	25.7
	Greece	12.4	11.1	9.3	7.5	24.7	58.8
	Portugal	38.8	6.9	9.7	13.6	20.4	29.9

Source: The author based on IMS data.

generically available within 3 months after loss of exclusivity (Table 3).

Across the study countries, except Greece, over 55% of total sales faced generic competition within the first 12 months following loss of exclusivity. The rate of generic penetration 12 months after loss of exclusivity was highest in the UK (83%), Germany (82%), Denmark (80%), Italy (78%) and lowest in Greece (33%), Portugal (55%), and Austria and the Netherlands (56%, respectively). The share of sales that did not have generic entry 24 months after loss of exclusivity was lowest in Denmark (9.6%), the UK (11.4%), and Germany (14.7%) and highest in Greece (58.8%), France (32.2%) and Portugal (29.9%).

4.3. Number of generic competitors

Both country and individual molecule market size seem to influence the amplitude and depth of generic entry across the study countries. Overall, the number of generic competitors increases post-patent expiry and in some cases it does so very significantly (Table 4). Country market size in terms of overall sales value does matter and there is a striking difference in the number of generic competitors entering the market for molecules facing a large country market compared to molecules facing a smaller country market. For example, in Germany the number of generic competitors 12 months post-patent expiry ranges from an average of 19 for the top selling molecules to 4 for the lowest end of the market, compared with 4.5 and 0.9 on average, respectively, in Austria. The variation between top and bottom decile of the market is also significant between Tier I and Tier III countries. For example, in Denmark, there are 5.6 competitors on average for the top selling molecules and 0.8 competitors on average for the bottom selling, compared with 0.9 and 0.4 generic competitors, respectively, in Austria (12 months post-patent expiry).

4.4. Price developments

Price developments are summarised on Table 5. Three types of trends are reviewed for the period after loss of exclusivity: first, the price decline for all molecules that

had generic entry and the speed of price decline; second, the price decline in the top and bottom decile by sales and the speed of that decline; and third, pricing developments in originator brands.

Across all molecules that had generic entry, prices seem to decline, but significant variability exists with regards to the amplitude of decline and its speed across settings. The price decline ranges from 16% (Italy) to 59% (Sweden) 12 months post-patent expiry, increasing to 21% (Italy) and 70% (Sweden) 24 months. Tier I countries have a higher and faster decline than tier II (except Sweden) and tier III countries. Significant differences exist across all study countries with regards to price developments after loss of exclusivity in the highest and lowest decile of the market by sales. Irrespective of country market size, prices are substantially lower in the highest decile; the speed of decline is also considerably higher in tier I than in tier III countries. In Denmark, for example, the price index declines to 19% 12 months after patent expiry (=100), compared with Italy (price index 85.5%) or Greece (82.2%) for the same period. Prices of molecules in the lowest decile by sales decline less fast across the board and similar differences between tier I and tier III countries can be observed as before.

In order to study the effect of loss of exclusivity on originator brands, we separated the brands that had generic entry from those that had no generic entry after 24 months. The price index of originator drugs that had generic entry remains much closer to the price pre-patent expiry than that of the generics in all study countries (Table 5). However, in the majority of cases and at 12 months post-patent expiry the originator price is lower than the price pre-patent expiry and declines further 24 months post-patent expiry. In Denmark and Germany, prices of originators seem to increase 12 and 24 months post-patent expiry as generic entry increases, confirming the generics paradox, while in Greece, the prices of originators do not react to generic entry and are slightly higher post-patent expiry, probably indicating some exit across dosage forms. By contract, the price index of originators that did not have generic entry after loss of exclusivity, was significantly higher than in the previous case; additionally, originator prices seemed to increase in many cases between 12 and 24 months after loss of exclusivity, rather than decrease.

Table 4
Generic entry measured by the average and total number of observed entrants for the total number of study molecules and the top and bottom 10% of the market.

	Average number of generic competitors across all molecules that had generic entry (maximum observed number of generic competitors)		Average number of generic competitors at top-10 selling molecules that had generic entry (maximum observed number of generic competitors)		Average number of generic competitors at bottom 10% of market of molecules that had generic entry (maximum observed number of generic competitors)	
	12 months post-patent expiry	24 months post-patent expiry	12 months post-patent expiry	24 months post-patent expiry	12 months post-patent expiry	24 months post-patent expiry
	All patent expired molecules		Top 10 selling molecules		Bottom 10% of molecules	
UK	2.0 (6)	2.4 (7)	3.9 (6)	4.4 (7)	1.4 (5)	1.6 (5)
Denmark	3.5 (11)	3.8 (12)	5.6 (10)	5.7 (9)	0.8 (3)	1.5 (3)
Germany	10.8 (32)	13.6 (40)	18.9 (32)	22.3 (40)	3.9 (17)	5.3 (16)
The Netherlands	1.9 (14)	4.7 (20)	6.0 (13)	7.6 (10)	3.4 (9)	4.1 (10)
Finland	3.4 (12)	4.8 (10)	4.3 (12)	6.4 (10)	2.2 (4)	2.8 (5)
Austria	2.8 (9)	3.9 (12)	4.5 (9)	6.4 (12)	0.9 (3)	1.2 (3)
France	4.8 (14)	6.5 (19)	7.7 (14)	10.2 (18)	1.4 (10)	2.3 (14)
Spain	4.9 (19)	6.7 (23)	7.7 (19)	10.2 (23)	2.7 (9)	3.3 (11)
Sweden	2.5 (8)	3.2 (11)	3.1 (7)	4.7 (10)	0.9 (4)	1.4 (4)
Italy	3.1 (24)	5.8 (38)	9.5 (24)	16.5 (38)	1.1 (4)	1.7 (8)
Greece	1.0 (9)	2.6 (21)	0.9 (3)	4.4 (21)	0.8 (3)	1.6 (5)
Portugal	2.0 (14)	4.7 (20)	0.9 (2)	0.6 (1)	0.4 (1)	0.9 (3)

Source: The author based on IMS data.

4.5. Generic volume share

The degree of generic penetration measured by the share of generic volume in total volume sold differs between study countries in terms of both absolute sizes at a particular point in time and over time (Table 6). Across all study countries, generic penetration increases post-patent expiry. This increase is highest in the Netherlands (62.1% overall generic penetration 24 months after loss of exclusivity), Denmark (55.7%), Germany (54.9%) and the UK (46.5%). These countries also display the highest speed at which generics become available immediately after patent expiry, measured by the market share of generics one quarter after patent expiry (9% in the Netherlands, 15.5% in the UK, 18% in Denmark and 21.5% in Germany). By contrast the degree of generic penetration is lowest in Greece (9.1%), Spain (15.3%) and Italy (21.5%) and the same occurs for the speed at which these markets attract generics immediately after patent expiry (0.2%, 2.2% and 2.8%, respectively). Importantly, the degree of generic penetration declines

Table 5
Volume-adjusted price indices[a] measuring price developments 12 and 24 months post-patent expiry for generics and patent-expired originator brands.

	Price index at patent expiry	Price index for generic drugs						Price index for patent-expired originator brands			
		All molecules with generic entry except originator brand		All molecules with generic entry (except originator) in the top decile by sales		All molecules with generic entry (except originator) in the bottom decile by sales		Nominal price developments for ori-ginator brands affected by generic entry		Nominal price developments for ori-ginator brands not affected by generic entry[b]	
		12 Months	24 Months	12 Months	24 Months	12 Months	24 Months	12 Months	24 Months	12 Months	24 Months
UK	100	60.6	34.9	54.3	26.5	76.7	56.5	99.1	96.8	107.8	103.4
Denmark	100	42.9	31.2	18.6	19.4	43.3	34.8	105.9	102.6	117.5	118.5
Germany	100	61.8	56.1	48.4	43.4	93.8	85.6	105.1	106.2	103.8	103.4
The Netherlands	100	61.7	58.5	42.9	45.6	77.1	69.4	91.5	85.6	98.2	98.4
Finland	100	50.5	36.9	30.3	22.7	59.8	45.1	88.5	75.8	94.0	100.3
Austria	100	61.5	59.9	53.6	53.3	66.4	64.8	83.9	76.1	111.3	109.8
France	100	69.5	66.3	56.8	53.8	85.2	80.4	98.1	94.5	111.7	114.4
Spain	100	68.1	61.3	66.5	58	68.8	62.1	101.7	98.6	100.9	101.6
Sweden	100	40.6	29.4	32.5	15.6	55.2	52.2	93.4	93.9	112.1	101.5
Italy	100	84.2	79.0	85.5	78.0	93.0	89.0	86.8	84.8	99.6	100.4
Greece	100	81.2	79.8	82.2	73.3	94.1	87.2	103.2	103.4	103.5	104.8
Portugal	100	67.9	66.8	57.7	55.5	82.7	72.4	97.3	95.7	102.9	105.3

Source: The author based on IMS data.

[a] Own country weights were used to construct price indices (Paasche index).

[b] The molecules that did not have generic entries 24 months post-patent expiry were as follows: UK (48), Denmark (36), Germany (46), the Netherlands (30), Austria (58), Finland (41), France (67), Spain (57), Sweden (58), Italy (66), Greece (43), Portugal (30).

Table 6
Market penetration by generics post-patent expiry (average volume market share measured in standard units [SU], %).

	All molecules with generic entry					All molecules with generic entry in the top decile by sales			All molecules with generic entry in the bottom decile by sales		
	At Q1 post-patent expiry (%)[a]	At 12 months (%)	At 24 months (%)	Change in MS 0–12 months (%)	Change in MS 0–12 months (%)	At Q1 post-patent expiry (%)[a]	At 12 months (%)	At 24 months (%)	At Q1 post-patent expiry (%)[a]	At 12 months (%)	At 24 months (%)
UK	15.5	35.8	46.5	23.5	7.4	25.4	35.0	46.6	13.9	36.5	43.4
Denmark	18.0	35.9	55.7	21.9	15.9	9.4	54.7	65.1	16.7	34.7	50.5
Germany	21.5	39.0	54.9	21.1	12.4	51.1	69.1	82.8	16.3	37.8	50.9
The Netherlands	9.0	38.9	62.1	34.7	18.4	7.6	39.6	60.4	0.5	23.4	50.7
Finland	8.1	23.1	38.4	19.1	11.2	10.2	30.2	39.6	1.5	18.2	30.9
Austria	1.9	12.75	26.9	14.2	10.7	11.0	25.1	33.7	0.75	14.5	24.5
France	5.2	17.7	31.0	14.8	11.0	19.0	55.7	67.9	3.3	11.9	23.3
Spain	2.2	8.2	15.3	7.8	5.3	1.2	9.4	15.7	1.7	9.4	14.9
Sweden	5.1	21.9	41.7	21.5	15.1	0.5	57.95	93.5	5.3	24.8	39.5
Italy	2.8	8.5	21.5	9.0	9.7	0.03	14.9	21.4	3.5	10.6	20.8
Greece	0.2	3.3	9.1	4.7	4.2	0.2	7.4	12.9	0.1	1.8	2.1
Portugal	0.7	11.6	28.3	14.2	13.4	3.3	17.9	27.4	0.03	14.8	26.0

Source: The author based on IMS data.

[a] Measured by 1 quarter (3 months) post-patent expiry.

significantly 12 months following the loss of exclusivity, implying that the first 12 months are critical for generic market entry and penetration (Table 6).

Significant variability can also be observed in the top and bottom deciles by sales. Across all study countries, the molecules included in the highest decile by sales genericise much faster and display a significantly higher degree of generic penetration 12 and 24 months after loss of exclusivity, than molecules in the bottom decile by sales.

5. Discussion and policy implications

In developing the methodological framework shown on Fig. 1, our aim was to address key concerns of decision-makers about the performance of their generic policies, focusing on a number of pertinent questions. Key among them were: whether a generic is available after loss of patent exclusivity; how soon does a generic enter the market; is there a sufficient number of competitors to stimulate price competition; do prices decline significantly post-patent expiry; does generic volume increase its share relative to the originator brand; is the amplitude of price reduction following generic entry related to the price level at patent expiry; and is there a link between the magnitude of price reduction post-patent expiry and generic market share?

In addressing these questions we have proposed a methodological framework comprising five indicators and several metrics per indicator, as a means of evaluating whether generic policies are delivering the benefits they are purported to do or not. Our perspective in proposing these reflect the priorities of decision-makers in different settings: availability of generic medicines is a key concern, particularly in small markets, where patent expiry is not accompanied by generic entry due to small overall market size [20]; the time to generic entry is of considerable interest because if pecuniary benefits are to accrue from genericisation, the best time to do so is immediately after loss of exclusivity. Generic entry occurring several months or even a year after loss of exclusivity is more likely than not to be less beneficial as utilisation may have been switched to other therapeutic options that are patent protected. Maximising generic market share and achieving low prices are two fundamental policy aims and ones that decision-makers judge the success of generic policies by. Finally, the extent to which there are sufficient numbers of competitors on the market is an indication of the robustness of generic markets. Each of the proposed indicators is relevant to decision-makers and all of them put together provide an understanding and the framework of how different components of generic market dynamics come together. While the indicators have been selected based on objective criteria reflecting key variables of interest, the selection of metrics corresponds to potentially suitable endpoints for decision-makers. Additionally, while the choice of top and bottom deciles by sales and the selection of one, two or four quarters post-patent expiry as appropriate endpoints to judge performance may appear arbitrary, they still represent valid endpoints, used already in earlier research [4,6,16]. Despite the significant advantages to considering these indicators and their respective metrics together, an

obvious limitation could be the intensity of information required to monitor these.

The focus of empirical and policy-related research is a testament of the relevance of the proposed methodological framework: a great deal of the debate has focused on price and market share developments post-patent expiry [26,27]; in addition, availability, competition and time delay to generic entry have featured strongly on the research and policy agenda [4,8,16]. Independent analysis has also highlighted the importance of demand-side interventions in achieving greater savings for health care [28,29], whereas economic theory and empirical evidence predict that generic penetration will be greater in countries with less strict regulatory policies because, ultimately, regulation reduces competition [10,11].

By relying on the proposed methodological framework, the empirical findings in this study confirm some of these general predictions [4,16,30,31,37]. However, they also question the expected effects of individual policies. In summarising the findings by indicator, Fig. 2 highlights which countries consistently demonstrate the highest and lowest levels of price developments, generic penetration, time delay to generic entry and competition relative to others. Countries in Tier I (UK, Germany, Finland, Denmark, the Netherlands) consistently show less time delay to generic entry, higher numbers of generic competitors, faster price decline and higher generic volume share, compared with Tier III countries (particularly Greece and, to a lesser extent, Italy and Portugal), which display almost the opposite trends. Tier II countries are clustered in between the other two tiers.

A pertinent question at this stage is the likely impact that supply-side interventions (on prices) and proxy demand-side interventions (on prescribing and dispensing) have on each of the five indicators of performance.

With regards to supply-side measures, some countries with administrative controls on prices, such as price capping or linking the generic price to the originator (e.g. Greece, Italy, France) show a significantly slower price reduction over time than countries that do not have these controls (UK, Germany, Denmark, the Netherlands). The latter also show the shortest delay in time to generic entry and the highest rates of generic penetration. This seems to be compatible with other evidence suggesting that price reduction is greater in countries with competition than regulation related to generics [37].

The evidence on price development and volume share provide important insights into how generic entry is related to achieving two specific policy goals, namely: providing cost-effective drug options and decreasing drug prices. With the exception of Austria, Sweden and the UK, all other countries employed internal reference pricing (IRP) systems during the study period.

Reference pricing systems are expected to increase overall competition by making demand more "elastic" [32]. While reference pricing may not directly affect faster and more expansive generic entry, it follows that increased competition will, eventually, corresponds to decreased delays to generic entry and increased number of generic competitors entering the market post-patent expiry. The findings on delays to generic entry and number of generic competitors question the extent to which reference pricing allows for faster and more pervasive generic competition post-patent expiry. For example, two study countries with no IRP (UK, Sweden) seem to have experienced considerably fewer delays to generic entry than countries with IRP.

Reference pricing systems should result in significant cost-savings by influencing both the price and volume share of the molecules they encompass. First, reference prices should reduce the average price per molecule through incentives for originator companies to reduce prices in order to maintain market share post-patent expiry [33]. Second, the generic volume share should correspond to the response of the originator company's price reduction (i.e. the generic volume share would not be expected to rise if the originator company lowers their price accordingly). Finally, whether reference pricing systems will affect total expenditures depends on whether they influence the price or volume sales of either generic or originator drugs, and whether they influence the mix of expenditures on off-patent drugs. Reference-pricing schemes will not, however, increase overall generic use if the originator price decreases to the level of the reference price [34].

The UK, an example of a liberal and open-market pricing system in the off-patent segment, exhibits a well-developed generic market according to the indicators measured, particularly in terms of evoking post-patent price competition quickly. In addition, the decrease in price of both generic and originator products is relatively high 12 and 24 months following patent expiry. While the UK does not use reference pricing, several policies have been employed to target generic prescribing including teaching medical students the cost-saving benefits of generic products and implementing INN prescribing on a mandatory basis. In contrast to the UK, Germany was one of the first countries to implement an internal reference pricing scheme but has developed a similarly competitive generic market. Although the specifications of the IRP scheme have evolved over time, price developments observed in Germany for molecules with patent expiries during the study period suggest a relationship between reference pricing and a pattern of high prices for originator drugs and continually decreasing generic prices following patent-expiry. Furthermore, the generic volume share 24 months following originator patent expiry is largest in Germany, which corresponds to recent policy analysis showing that changes in generic substitution and increased budgetary pressure are changing prescription behaviour and increasing the use of generics in Germany [35]. The results show similar trends in other MS with internal reference pricing systems but not as distinctly successful as in Germany. Greece is once again an outlier; whereas a version of internal reference pricing was implemented with the specific intent of increasing competition and encouraging generic sales [35], the findings suggest this has not been accomplished judging by the insignificant generic volume share increases. Greece provides an example of why reference pricing schemes must be reinforced with more pressure on the demand-side, particularly INN prescribing or mandatory generic
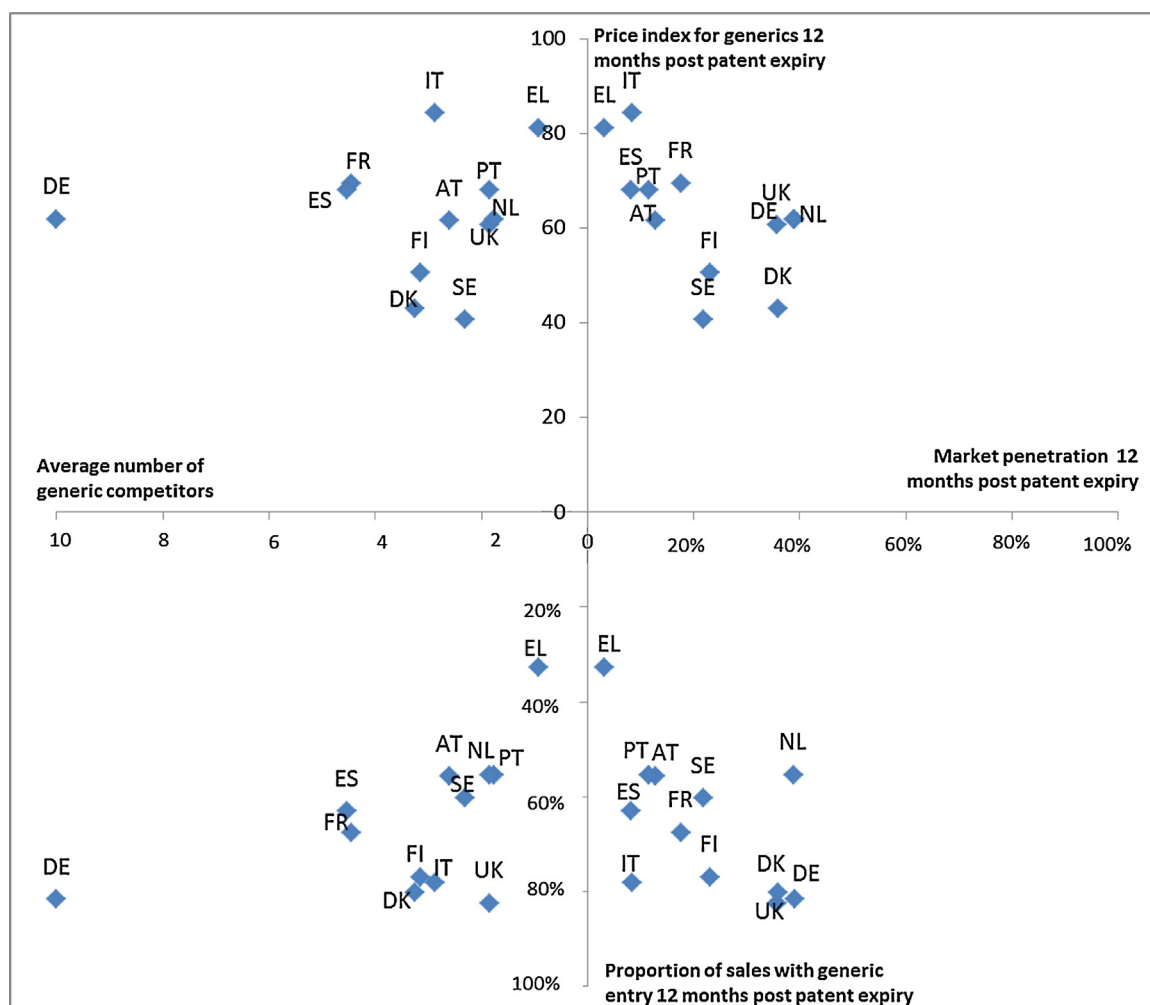
Fig. 2. Summary of generic policy performance indicators across 12 EU Member States.   *Source:* The author from IMS.

substitution, in order to increase generic entry, uptake and competition.

A further question that we are able to address is the impact genericisation has on the prices of patent-expired originators. In the vast majority of cases, prices of those originators that face generic entry decline in response to generic entry, with the exception of Germany and Denmark, where they increase. This shows signs that the generics paradox is confirmed for those two countries, compatible with other evidence [6,7]. In the case of Greece, prices of off-patent originators show no reaction to patent expiry. Prices of patent-expired originators that do not face generic entry, by contrast, are in most cases sticky downwards and in several cases, they increase post-patent expiry. This seems to suggest that generic competition and the availability of generics are important determinants of price reduction of off-patent originator brands and their absence can lead to price escalation in these products.

Countries with strong demand-side policies, for instance mandatory or strongly encouraged INN prescribing (UK) and/or mandatory generic substitution (Germany, Denmark, Finland, Sweden) show the highest degree of generic penetration post-patent expiry and also seem to have the lowest time delay to generic entry. Countries that do not strongly encourage INN prescribing or do not have mandatory generic substitution (e.g. Greece and to a lesser degree, Italy and Austria) have very low levels of generic penetration and significant delays in generic entry.

The effect of aggressive INN prescribing or substitution policies on generic entry and penetration may not be as predicted. In principle, mandatory generic substitution may decrease competition despite increased demand for generics, as the lowest priced option will capture the majority of sales, eventually reducing the number of generic competitors able to compete on price [36]. Using the findings to compare two contrasting approaches to regulating the demand-side of the market, suggests that little difference is observed. In Sweden, where generic substitution is mandatory, and in Austria where it is not allowed, the average number of generic entries is very similar (in terms of molecule numbers and when taking an average of generic competitors facing all molecules, molecules in the top 20% of sales and molecules in bottom 50% of sales). In addition, in both study countries the majority of molecules

experience the greatest number of generic competitors within the first 12 months post-patent expiry.

The effectiveness of generic prescribing and substitution policies may be related to specific components of the policies such as whether physicians or patients may overrule generic substitution, the incentives or disincentives for pharmacists to dispense generic over branded products and the price difference between originator brand and generic. For example, the number of generic entries is greatest in Germany, where generic substitution is considered mandatory, except that physicians may overrule substitution. This is in contrast to Greece, where generic substitution was disallowed during the study period, whereas pharmacists were paid on a percentage basis across all medicines and there are fewer generic entries per molecule compared to the majority of other study countries. Similar trends arise in the examination of different forms of policies on generic prescribing. In the UK, Denmark, France, Germany and the Netherlands there are long-standing policies and in some cases explicit incentives for generic prescribing, resulting in high generic volumes and larger numbers of generic competitors per molecule 12 and 24 months following originator patent expiry. In the majority of cases a large generics market share is also associated with greater price declines than a smaller generics market share, as also shown elsewhere [38].

6. Conclusions

In this paper we have proposed a methodological framework comprising five indicators and several metrics that enable the assessment of performance of generic drug policies across different settings. This framework is independent of the policy mix for generic drugs pursued in different settings, but helps evaluate the impact of such mix on generic policy effectiveness. The subsequent empirical analysis of generic entry and diffusion, price development and generic market share confirmed the diversity of outcomes across regulatory settings, the differences that exist at the high and low end of each market by sales, and the likely impact of regulatory frameworks on generic entry, competition and availability. Both the broad conclusions and the specific findings of this study may have important public policy implications: first, regardless of the size of the pharmaceutical market or the policy mix pursued, there is considerable potential for faster generic entry and more generic competition, particularly at the lower ends of the market. Second, the differences in generic entry and competition and the experiences from different regulatory measures suggest that there is considerable space for cross-national policy learning. Finally, the need is highlighted for further research into generic markets and the more effective policy mix that will maximise generic entry and penetration and lead to greater expenditure optimisation by health insurers.

Acknowledgements

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