ABSTRACTED SCIENTIFIC CONTENT

A comparison of European and US generic drug markets

Introduction

Comparative research on the European and US generic drug markets based on 2013 IMS data across 13 European countries with different generic drug policies has recently been accepted for publication in the *Milbank Quarterly* [1], and abstracted here from a pre-print of the accepted article published on *LSE Research Online* [2].

In a price-index analysis, generic drug prices and market shares of 200 active ingredients were compared across 13 European countries to establish the extent of variation between them. The selected countries were Belgium, Denmark, France, Germany, Greece, Italy, The Netherlands, Poland, Portugal, Spain, Sweden, Switzerland and the UK.

Recently published peer-reviewed studies, academic books and grey literature published since 2000 were reviewed for additional information on prices and use of generic drugs in Europe and the US. Published data on existing generic drug policies, and measures to increase generic drug use and to stimulate price competition, were also reviewed.

Methods

The investigators used Laspeyres indexes to compare drug prices for the 200 active ingredients selected. These are price ratios used to monitor change in price levels over time.

The first step was to calculate the average price per dose (total sales across form-strength combinations divided by number of doses sold). Both ex-manufacturer and retail prices of each active ingredient were calculated.

A subset of 80 active ingredients prescribed in all 13 countries were then identified and comparative statistics generated, e.g. proportion of generic drug spend accounted for by the sample and generic drug market share.

The Laspeyres indexes were calculated using weights from a base country. In this case, Germany was selected, as it is the largest drug market in Europe by revenue. The base country was assigned a base value of 100. The authors give an example of a country with a price value of 140 and explain that it would have 40% higher prices than Germany, and a country with a price value of 60 would have prices 40% lower than Germany.

Findings

Price index

The price-index analyses showed that prices and market shares varied widely across Europe. Swiss ex-manufacturer prices, for example, were more than 2.5 times those in Germany, and more than six times those in the UK.

The gap, however, was smaller for retail prices, which include distribution costs and markups charged by wholesalers and pharmacies. Belgium, Portugal and Spain had lower retail prices but higher ex-manufacturer prices than Germany.

The proportion of prescriptions filled with generics (generic drug market share) was low (< 40%) in Switzerland (17%), Italy (19%), Greece (20%), France (30%), Belgium (32%) and Portugal (39%); moderate (between 40% and 60%) in Sweden (44%), Spain (47%), Denmark (54%) and Poland (57%); and high (> 60%) in The Netherlands (70%), Germany (80%) and the UK (83%).

The authors acknowledge a number of limitations to their price comparisons. Generic drugs sold in hospital pharmacies, biosimilar products, off-patent originator drugs, and parallel-traded generics were excluded. Retail data were unavailable for The Netherlands and the UK.

The Laspeyres index also assumes that demand for prescription generic drugs is price inelastic, i.e. change in the price of a generic drug does not affect demand. The authors also acknowledge that IMS Health data do not reflect confidential rebates and discounts; therefore, the list prices, i.e. official prices before discounts, may overestimate the actual prices paid for some products.

Generic drug use in Europe and the US

The additional review of published data undertaken by Wouters et al. shows that cost savings can be made in off-patent drug markets in Europe and the US.

For example, a report by the European Commission (EC) [3] found that the average time taken for a generic drug to reach market from the time a brand-name drug loses its exclusivity was seven months, estimating the cost to EU payers to be US$3 billion a year based on retail prices. After two years, generic drug penetration accounted for less than half of EU sales. The report also found that price reductions took longer in Europe, and that EU countries had different pricing and reimbursement regulations, prescribing policies and generic substitution laws.

Wouters et al. also cite a report published by the Organisation for Economic Co-operation and Development (OECD) [4] showing that in 2013, 84% of drug prescriptions in the US were for generic drugs, following the US trend of low generic drug prices and high volume use [5].

They also found research demonstrating decreased competition in the US generics sector. In a study by Schondelmeyer et al. for the AARP Public Policy Institute [6], a slower rate of decline (4%) of the total cost of 280 widely used generic drugs was reported between 2012 and 2013 compared with the previous seven years. This was attributed mainly to supply-chain disruptions, market conditions forcing firms out of business, mergers and acquisitions, and delays in processing generic drug applications by the US Food and Drug Administration (FDA) [6].

According to Greene et al. [7] reduced competition has enabled some pharmaceutical companies to drive up the prices of generic drugs. The US Government Accountability Office reported 'extraordinary' price increases of 100% or more for 315 out of 1,441 generics studied [8].

Wouters et al. found a range of reports on other factors affecting utilization rates and the adoption and effectiveness of

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policies, including the perception by US and European physicians, pharmacists and patients that generic drugs are not bioequivalent; different regulatory structures; lobbying powers of special-interest groups; patent litigation systems; and political economies of healthcare systems.

Published data on drug policies in Europe and the US were also reviewed to identify best practice. Although many European countries share common policies, they found that the method of implementation varied widely, and pricing, prescribing, and substitution policies can affect prices and usage of generics.

The authors establish that generics substitution in Europe is mandatory in 13 countries, voluntary in 14 and forbidden in five. In the US, where generics prescribing is universally voluntary, substitution laws differ between states.

In researching internal reference pricing and tendering, the authors found that most European countries used internal reference pricing and, in some, health insurers use a tendering process to obtain generic drugs in bulk from manufacturers offering the best prices. In the US, internal reference pricing and tendering is not used for generic drugs sold in non-hospital pharmacies.

The authors have produced useful maps to show the distribution of internal reference pricing, generics prescribing, generics substitution and tendering in the EU and four European Free Trade Association countries, and laws governing drug substitution in the US, respectively.

Another report by the EC [9] showed that, with the exception of Denmark, Germany and the UK, price controls are imposed on generics, i.e. maximum allowable prices, and are often linked to the prices of brand-name drugs. The authors also identify a World Health Organization report [10] that highlights the extent to which EU governments block price increases in the interests of public health and spending. The US Government, however, does not impose price controls on generics.

Measures taken to increase generic drug use and stimulate price competition

On the basis of available evidence from Europe and the US, Wouters et al. identify measures that are effective in promoting price competition among pharmaceutical companies and increasing the use of generic drugs.

The authors believe that one important measure is to streamline the generic drug approval process to facilitate market entry. They highlight work by Kesselheim et al. [5, 11], who found that regulators tend to prioritize applications from manufacturers attempting to bring to market a generic medicine sold by three or fewer firms, thereby exerting downward pressure on prices and ensuring that individual companies have less influence over prices. For off-patent drugs facing limited or no competition, Kesselheim et al. [5] suggest that FDA import new generic drugs temporarily from countries such as Canada and EU Member States, with high regulatory standards to avoid paying high premiums.

For those countries experiencing a backlog of applications for generic drug approval, the authors again refer to Kesselheim et al. [5] who suggest that resources could be allocated to national regulators to speed up the review process or a fee could be charged to generic drug firms, as in the US, to increase resources available for the drug approval process.

Wouters et al. highlight new US legislation proposed in 2015 to make it easier for drug companies to challenge patents without enduring lengthy and costly litigation [12]. The bill is still under consideration, and the EC has called for similar measures.

According to research published by the US Federal Trade Commission [13], a ban on pay-for-delay deals by regulators could save US$3.5 billion a year. Wouters et al. discuss how these deals involve brand-name pharmaceutical companies offering generics manufacturers cash to delay bringing their generic drug to market, thereby ensuring that brand company monopoly is retained and higher prices can be charged to consumers.

They also discuss how regulators could facilitate access to samples of brand-name products; since 2007, a legal loophole in the US has prevented generics companies accessing samples for the purpose of conducting bioequivalence testing before patent expiry [14, 15].

In countries such as Denmark, Sweden, the UK and the US, price competition is encouraged, and Wouters et al. identify studies showing that, where generic drug companies are permitted to set their own prices, and physicians and pharmacists are incentivized to prescribe and dispense the least expensive generics, over time prices are effectively reduced. Tendering has also been shown to lower administrative costs, reduce the price of generics and improve price transparency.

The authors believe that countries should require pharmacists to substitute generic drugs for brand-name drugs based on a report by the EC [16] showing that such policies result in generic drugs entering the market more quickly and having more immediate take up.

One study by Shrank et al. [17] showed that blocking the use of generic drugs costs the US US$7.5 billion a year, including US$1.2 billion in out-of-pocket fees for patients. Wouters et al. argue that generic drugs should be encouraged or even required, unless there are legitimate reasons to prescribe a brand-name drug over a generic equivalent.

They also review research on academic detailing, showing that the practice of using trained, impartial experts to provide unbiased information to clinicians about the effectiveness, safety and costs of drugs, improves compliance with desired prescribing practices [18].

The authors found published research on the positive effect of financial incentives in improving rates of generics prescribing, but evidence for this effect was limited.

In some countries, regulators permit pharmacists to substitute a generic drug for a brand-name drug with a different active ingredient if both drugs belong to the same therapeutic class and have the same indication. Wouters et al. cite a report by Johansen et al. [19] who estimate that an extra US$73 billion per year is spent in the US (about 10% of total drug spending) on brand-name drugs with available therapeutic substitutes.

Therapeutic substitution, however, is not as straight forward to implement, and Wouters et al. suggest that the relevant authorities

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and clinical organizations should develop appropriate protocols and strengthen coordination between physicians, pharmacists and insurers to encourage its wider practice [19-20].

The authors conclude their policy evaluation with a discussion of the obstacles preventing generic drug policies, using a historical case study example from the US to help explain why similar initiatives previously failed. This part of the discussion will be abstracted in a future edition of *GaBI Journal*.

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