Pricing of medicinal products: considerations in a small market state

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Thomas Szasz, the leading Hungarian psychiatrist, once stated: "Formerly, when religion was strong and science weak, men mistook magic for medicine; now, when science is strong and religion weak, men mistake medicine for magic."

Indeed, advances in science have had a great impact, not only on the ability to discover new drug molecules, but also on research undertaken to assure their quality, safety and efficacy. The pharmaceutical industry has an excellent track record in this regard but is a victim of its own success, since society sometimes expects the industry to produce medicinal products with the same ease as a conjuror. Such a perspective has, inevitably, led to certain unrealistic expectations when considering the effect that the market prices of these medicines have on their accessibility.

Introduction

The discovery and development of medicinal products is expensive and time-consuming. The Pharmaceutical Research and Manufacturers of America (PhRMA) quote the time required to develop a medicinal product, from drug discovery to market launch, as lasting from 10 to 15 years.[1] The process is, moreover, characterized by a high attrition rate: only one in ten thousand molecules entering drug discovery becomes a marketable product[1], with the lowest chances of success being registered in the phases of preclinical development (40%) and phase II clinical trials (50%).[2] The costs of producing a successful marketable product - approximately €980 million in 2006[1] – have been described as "impressively large numbers, usually associated with a purchase of jet fighters".[3] This figure takes into account both the cost of the successful candidate and those of the failures, the latter representing over 70% of the total cost in 1995.[2]

For the pharmaceutical industry to survive and flourish, its sales revenue must exceed its research, development, manufacturing and marketing costs. At any stage in the development process, the decision whether or not to proceed is, in part, determined by the product's net present value (NPV) – the estimate of future sales revenue less future development and marketing costs. However, sales estimates only become reliable when the product is close to launch, at which point a company will invariably proceed with the marketing of the product even if the NPV is insufficiently positive to recover costs incurred to date – to do otherwise would mean that none of the already incurred costs would be recovered.[2] It comes as no surprise to learn that only 34% of new drugs introduced between 1990 and 1994 registered revenues that exceeded the average research and development cost, with 70% of the industry's profits coming from 20% of the products marketed; nevertheless the profits generated by the profitable candidates more than compensated for the losses incurred by the remaining products.[4] In this climate therefore, the need to discover 'blockbuster' drugs has become more significant. In 2003, it was estimated that in order to maintain a healthy revenue growth rate of 10%, the ten largest pharmaceutical companies would need to launch about three new compounds per year; however, less than two launches per company were actually achieved in 2000.[5]

The situation is further complicated by the fact that patent protection of any new discovery is typically 20 years.[6] Thus, in order to guarantee market protection, it is inevitable that companies need to take a strategic decision as to the timing of the registration of a patent covering a new discovery. The earlier the patent is registered, the less are the risks that a competitor might be the first to market a similar discovery, rendering useless all research efforts undertaken to date. However, given the timeframes involved from product discovery to market launch, this means that any pharmaceutical company has a limited timeframe in which to maximize the returns on its investment since upon expiry of patent protection, generic versions of the medicinal product enter the market. The registration requirements for generic medicinal products do not require the results

of either toxicological and pharmacological tests, or clinical trials to be presented[7] – understandably so since these are largely determined by the identity of the medicinal product at the molecular level, this being the same in both the originator and the generic product. Since the product discovery and clinical trial costs represent over 80% of the expenses incurred in bringing a product to market[2], it follows that generic manufacturing companies can afford to place products on the market at significantly lower – and thus much more competitive - prices than their originator counterparts.

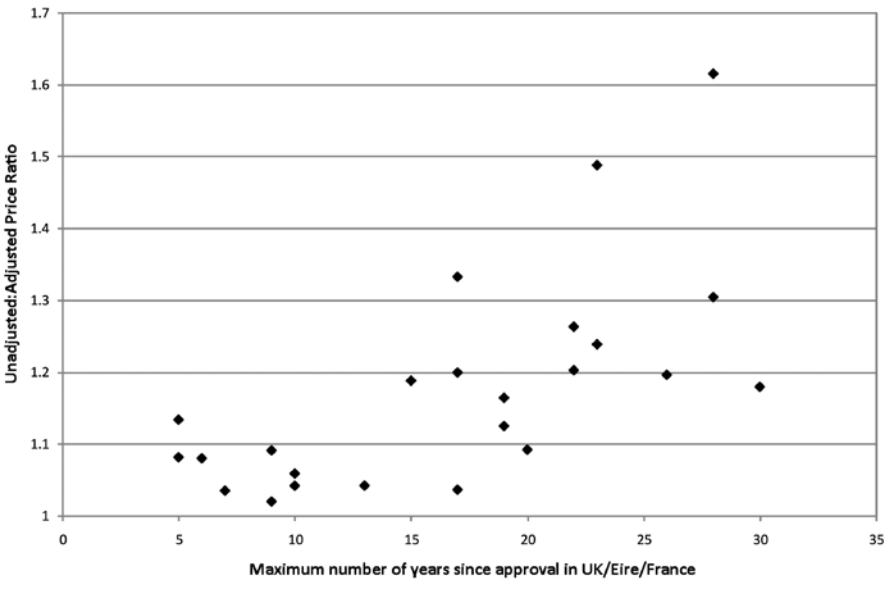
It thus appears that in order to maintain a healthy growth rate in the face of rising research costs, with the current rate of product launch in what is ultimately a fixed worldwide market, pharmaceutical companies can only generate the necessary revenue in a limited time by increasing the market prices of their products. Such a solution is obviously at odds with the health care need and ethical responsibility to provide accessibility to medicinal products at a reasonable cost, both at the individual patient level in the private market and at the national level through state-funded national health schemes. Many EU member states have consequently adopted a series of direct and indirect price-setting schemes in an attempt to control the extent of such price increases and guarantee accessibility, whilst not compromising the viability of both the originator and generic pharmaceutical industry.[8] The European Union, whilst recognizing that national policies regarding the adoption of such measures remained the prerogative of the individual member states, was also concerned that an excessive diversity of measure could unbalance intra-Community trade and have a negative influence on the functioning of a common market in medicinal products. Consequently in 1989 the community implemented Directive 89/105/EEC with the objective of minimizing any disparities in price-control measures and ensuring their transparency.[9]

Discussion

Malta has recently begun the process of transposition of this directive into national legislation through Legal Notice 58 of 2009.[10] However, efforts to verify the market prices of medicinal products date back to 2007, when a Medicines Committee was established by Government for this purpose. As a result of an agreement reached by the members of the Medicines Committee, it was established that prices of medicines in the local market were not to be above the average price established after comparing the prices prevailing in a basket of countries made up of three different categories, namely high, medium and low-priced categories. In a series of three press releases between 2007 and 2008, the prices of a small number of products were reduced to conform to the calculated European average[11-13], indicating that, in the vast majority of cases, prices on the local market were indeed close to the calculated European average. An analysis of the ratio of the unadjusted to adjusted market prices for the minority of products requiring price adjustment, as quoted in the press releases, showed the mean ratio between the unadjusted and adjusted prices to be 1.173 ± 0.143 (mean ± SD). A comparison of the price ratio with respect to the highest number of years the medicinal product had been authorized in the United Kingdom, France or Ireland at the time of the comparison exercise was also carried out, these countries being chosen due to the availability of information in the public domain. A statistically significant difference (Student's two-tailed t-parameter = 3.72, $p < 0.01$) was seen to be present between the average price ratios of products that had been present in at least one of the three markets mentioned for less than 15 years (1.063 ± 0.034) and for which no generic was present in the Maltese market at the time of the exercise, and those that had been present for 15 years or more (1.242 ± 0.149), and for which 40% of the products had a generic present in the Maltese market.

The commencement of the price monitoring exercise in Malta was a result of the significant awareness of the relativity between local market prices and those in other countries triggered by the publication of the Eurostat review on comparative price levels for medicinal products in European countries.[14] Much attention was focused on Malta's price level index of 1.06, with respect to an EU25 average of 1.00, as being indicative of the higher prices of medicinal products in Malta. Unfortunately, the report gave little, if no, indication of how such prices impacted public and private expenditure on medicinal products at a national level. The data given in the Eurostat report was simply a comparison of the average of the prices of a basket composed of the top 181 selling products, divided as 75% originator products and 25% generic products. However, two facts fail to be taken into account if one attempts to transpose, without further analysis, the numbers of the Eurostat report into expenditure on medicinal products. The first fact is that patients in countries across Europe do not purchase their medicinal products in a ratio of 3 originator per 1 generic; if this were the case, then the market share by volume of generics in all EU countries would be 25%. In actual fact, figures quoted by the European Generic Association[15] for generic market shares by

Figure 1: Scatter plot showing relationship between unadjusted:adjusted price ratio and maximum years of registration of product in United Kingdom, Ireland or France, for medicinal products whose prices were adjusted in Malta in 2007 and 2008



volume in EU countries in 2004 varied from as low as 4% in Italy (a purchasing ratio of 24 originator per 1 generic), to as high as 86.5% in Poland (a purchasing ratio of approximately 2 originator per 13 generics). The second factor is that the ratio of prices between originator and generic medicinal products varies across Europe too. The fact that in 2004, Sweden had a generic market share by volume of 39.4% but a market share by value of only 12.3% indicates a generic/originator price ratio of 0.216. At the other end of the scale one finds Belgium, where an 8.7% market share by volume translated into a 6.1% market share by value, indicating a generic/originator price ratio of 0.682. These factors are inapparent if one considers only the overall average price: a basket of four medicinal products with identical prices of €1.00 (price ratio 1.000) would have the same average price as a basket of three originator products costing €1.30 and one generic product costing €0.10 (price ratio 0.077).

The figures published by the European Generics Association for market shares by volume allow the division of the 181 product base quoted in the Eurostat report into a country-specific ratio. Moreover, knowledge of both the market shares by volume and by value allow the average generic/originator price ratios for each country to be calculated. The combination of these figures with the price indices generated in the Eurostat report allow the computation of country-specific price indices for both generic and medicinal products, compared to an overall European average of 1.00 (Figure 2): the results indicate an average European originator product price index of 1.072 ± 0.236, and an average European generic product price index of 0.476 ± 0.171, with an average generic/originator price ratio of 0.448 ± 0.139. It is also possible to compute the relative expenditure on medicinal products in select European countries.

The results of this computation, in comparison with the Eurostat data, are shown in Figure 3.

The results of this analysis show that the economic impact of the cost of medicines does not depend uniquely on the average cost of medicines. It also depends on three additional factors: the degree of generic penetration, the generic/originator ratio of

Figure 2: Originator and generic medicinal product price indices in select EU countries, compared to a Eurostat overall average of 1.00

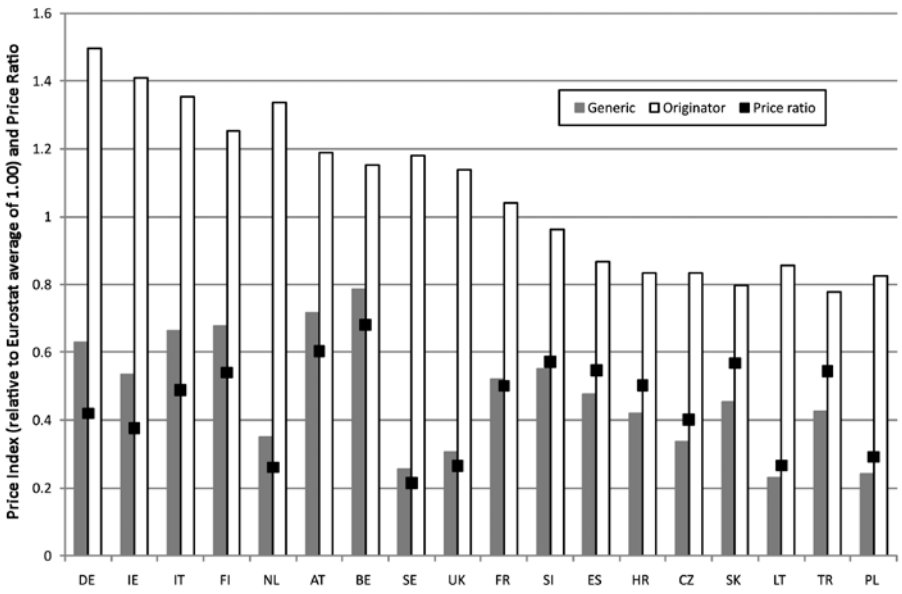
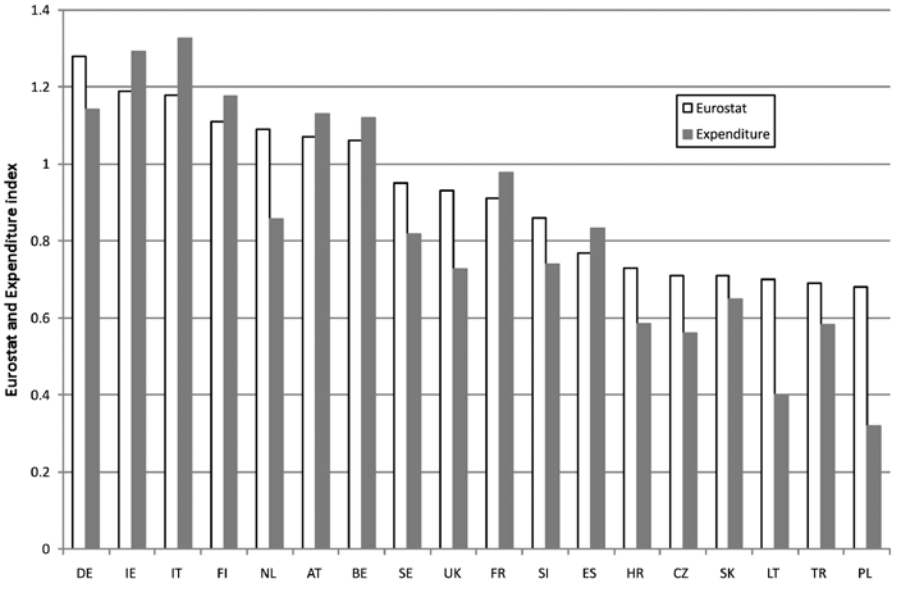


Figure 3: Eurostat average price indices and computed expenditure indices in select EU countries, compared to a Eurostat overall average of 1.00



Abbreviations: country abbreviations as used in figures

DE Germany	NL Netherlands	UK United Kingdom	CZ Czech Republic
IE Ireland	AT Austria	FR France	SK Slovakia
IT Italy	BE Belgium	SI Slovenia	LT Lithuania
FI Finland	SE Sweden	ES Spain	TR Turkey
		HR Croatia	PL Poland

Practice points

- Pharmaceutical research and development, and clinical trials are expensive ventures.
- Originator medicinal products require higher market prices to promote the elevated level of return on investment needed to sustain economic growth.
- Negative impacts on public and private spending can be avoided through penetration of lower-priced generics and a positive public/prescriber opinion of generics.
- Lower prices are not indicative of a compromise on quality, safety and efficacy.
- Pharmacists have a professional and ethical responsibility to provide truthful, accurate and objective information when dispensing medicinal products.

the market prices, and the outlook towards generic medicinal products. Austria (1.07) and Belgium (1.06) have a similar Eurostat average to Malta (1.06). The analysis of their market shows them to have moderate generic/originator price ratios (0.603 and 0.682, respectively) and poor generic sales (12.3% and 8.7%, respectively). This combination leads to the financial impact of sales of medicinal products being actually higher than the average price would infer (1.13 and 1.11, respectively). This situation is, in turn, linked to the policies on generic drugs present in the two countries: neither Austria nor Belgium engage in generic promotion and prescriber/public views on generics are not favourable.[8]

In contrast to the above, one finds countries like Netherlands (1.09) and Sweden (0.95), with remarkably low generic/originator price ratios (0.262 and 0.216, respectively) and appreciable generic sales (48.5% and 39.4%, respectively); the financial impact of sales of medicinal products is thus lower than the average price would indicate (0.86 and 0.82, respectively). In contrast to Austria and Belgium, the Netherlands and Sweden both engage in generic promotion, and have a favourable public/prescriber view on generics. However, the Netherlands – unlike most other European countries – also operates a system of reference pricing on originator medicinal products, a policy that is not favourable towards the establishment of market prices by the originator industry at a level that will promote its economic sustainability. Indeed, an oppressive pricing climate for originator medicinal products which are under patent protection is clearly undesirable, in consideration of the need of originator pharmaceutical companies to generate revenue in excess of the total costs of product discovery and development. Thus, the policy of the United Kingdom in allowing some degree of freedom, subject to profit controls, to originator pharmaceutical companies in establishing the market prices of new products is recommendable, albeit resulting in an originator price index of 1.14. The higher originator prices in the United Kingdom are counterbalanced by a generic/originator price ratio of 0.267, and whilst such low ratios are unfavourable for the sustainability of the generic industry, the United Kingdom enjoys a healthy generic penetration of 49.3%, achieved by strong generic promotion and a positive public/prescriber view on generics.[8] Thus, the United Kingdom has a Eurostat average price index of 0.93 and an even healthier spending index of 0.73.

Conclusion

The recommendable situation for Malta therefore appears to be one which advocates some degree of freedom in market pricing for new medicinal products during their on-patent life, during which period the budget available to the national health insurance schemes should aim at supporting the public and private expenditure that this policy will engender. A valid situation, based on the United Kingdom scenario, would appear to involve a significantly reduced generic/originator price ratio coupled with a high degree of generic penetration in the off-patent period to ensure that the overall spending index is not elevated. However, such low ratios for generic products are unlikely to be sustainable in a small island state such as Malta, unless the market penetration is appreciable. The latter can only be achieved through strong generic promotion and a campaign to engender positive public/prescriber opinions of generics. It is a professional and ethical responsibility of pharmacists to provide truthful, accurate and objective information in the process of dispensing medicinal products. In particular, great care should be sought to ensure that one does not, through one's actions or words, allow the impression to be transmitted that lower prices are indicative of a compromise on quality, safety and efficacy, as this only serves to undermine collegiality and mislead patients, to the detriment of the public interest.

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