

Comparative Approaches to Pharmaceutical Price Regulation in the European Union

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Aim. To review pharmaceutical price regulation methods in countries of the European Union (EU), in terms of the anticipated impact of regulation on pharmaceutical expenditures and evidence of actual outcomes.

Methods. An extensive search was performed of medical and economic studies on regulatory interventions specifically targeting pharmaceutical prices in EU countries, published between January 1990 and April 2002. Both peer-reviewed and "gray" literature were systematically reviewed.

Results. Four principle approaches to pharmaceutical price regulation with some methodological differences were identified in EU countries, as follows: fixed pricing, cost-effectiveness pricing, profit controls, and reference pricing. Actual evidence of the impact of price regulation was limited in many of these countries. Cross-country comparisons suggested that limiting the rise of pharmaceutical prices did not equate to controlling the rise of pharmaceutical expenditures because of the volume effect of utilization.

Conclusions. Supply-side regulation without the simultaneous use of demand-side incentives and volume controls does little to control the rise in pharmaceutical expenditures. The types of needed demand-side controls depend on the context of the individual country, on political priorities, and on the type of supply-side regulation in place.

Key words: *cost control; drug costs; drug industry; European Union; health policy*

Despite the integration of member states of the European Union (EU) at many levels, health care and in particular pharmaceutical pricing remains an area of national autonomy. Whether and how pharmaceutical prices are regulated in EU member states varies from country to country, ranging from free pricing to fixed prices. Differences also exist between Member States as to whether the same price regulation method that applies to in-patent medicines also applies to off-patent and over-the-counter pharmaceuticals, if these latter two are regulated at all. The different approaches reflect distinct national policy priorities within the historical and cultural context of the health care system, including the need to contain pharmaceutical expenditures, the regulation of the demand for pharmaceuticals, and the extent to which health policy objectives must be balanced against industrial policy objectives, ie, promotion of pharmaceutical research and development, employment, and a positive balance of trade.

In an attempt to control rising health care and pharmaceutical costs, particularly during the 1990s, pharmaceutical expenditures have become a common target of cost-containment efforts. Pharmaceuticals are targeted because decision-makers see them as a visible expenditure that can yield cost savings through direct intervention, and as less politically sensitive than a reduction in services or salaries. Ris-

ing pharmaceutical expenditures can partly be accounted for by the introduction of new technologies and changing demographic patterns. Equally important are the imperfections that lead to market failure: supply-side entry barriers, ie, patents, the process and length of regulatory approval, product differentiation, and brand loyalty (1); agency relationships; and moral hazard associated with the four-tiered structure of demand, where the physician prescribes, the pharmacist dispenses, the patient consumes, and, in most cases, an unrelated third-party pays.

Efforts to correct these market imperfections has generated a substantial portion of the regulatory interventions to contain costs in the market for pharmaceuticals, as it is believed that competition alone would not be sufficient to secure efficient prices, although such assertions are disputed even in in-patent markets because of therapeutic competition (2). Evidence from the off-patent segment of the market also points to competitive potential such that this segment of the market may not need to be subject to the same regulatory controls (3,4). The European Commission has also indicated its concerns over national drug pricing policies, which target short-term policy needs and limit competition by fixing prices (5).

Comparison of data on health and pharmaceutical expenditures in EU countries between the early

Table 1. Health and pharmaceutical expenditures in European Union (EU) countries^a

Country	Total expenditure on health as % of GDP ^b		Public pharmaceutical expenditure as % of public health expenditure ^b		Public pharmaceutical expenditure as % of total pharmaceutical expenditure ^b		Public pharmaceutical expenditure per capita, US\$ PPP ^b		Self-medication market as % of the total pharmaceutical market ^c		Average ex-manufacturer's price per package in PPP ^d	
	1990	most recent year	1990	most recent year	1990	most recent year	1990	most recent year	1996	2000	1989	1998
Austria	7.1	8.2 (1999)	10.3 ^e	13.6 (1997) ^e	57.2 ^e	74.5 (1997) ^e	NA	NA	8.5	7.4	53	90
Belgium	7.4	8.8 (1999)	NA	11.4 (1999)	46.8	44.7 (1997)	91	177 (1999)	17.2	15.8	64	110
Denmark	8.5	8.4 (1999)	3.1	5.2 (1999)	34.2	47.5 (1999)	37	97 (1999)	16.3	13.5	NA	NA
Finland	7.9	6.8 (1999)	5.5	9.8 (1999)	47.4	48.9 (1999)	58	114 (1999)	16.5	13.3	65	113
France	8.6	9.4 (1999)	14.5	17.1 (1999)	56.7	58.6 (1999)	172	283 (1999)	11.1	8.4	42	49
Germany	8.7	10.3 (1998)	13.7	11.6 (1998)	73.1	69.2 (1998)	167	209 (1998)	17.4	14.9	83	113
Greece	7.5	8.4 (1998)	16.3	19.4 (1998)	70.3	61.6 (2000)	72	152 (2000)	NA	NA	49	71
Ireland	6.7	6.8 (1998)	10.1	10.5 (1998)	65	81.9 (1998)	58	124 (1998)	21.0	18.2	83	103
Italy	8.1	8.2 (1999)	17.0	12 (1998)	72.3	44.0 (1997)	175	165 (1999)	7.9	7.8	70	88
Luxembourg	6.1	6.1 (1999)	13.6	10.2 (1999)	84.6	80.8 (1999)	188	241 (1999)	NA	NA	NA	NA
Netherlands	8.5	8.7 (1999)	8.9	10.3 (1999)	66.6	64.2 (1999)	85	160 (1999)	10.0	12.2	NA	NA
Portugal	6.2	7.7 (1998)	23.7	26.5 (1997)	62.3	66.1 (1997)	95	205 (1997)	11.6	7.7	96	134
Spain	6.6	7.0 (1998)	16.2	20.9 (1998)	71.7	77.3 (1997)	104	191 (1998)	12.4	8.7	54	84
Sweden	8.5	7.9 (1998)	6.4	10.9 (1997)	71.7	71.2 (1997)	86	157 (1997)	6.7	9.7	105	170
United Kingdom	6.0	6.9 (1999)	10.7	12.5 (1997)	66.6	64.2 (1997)	88	147 (1997)	20.7	20.4	88	120

^aAbbreviations: GDP – gross domestic product; PPP – purchasing power parity; NA – not available.

^bSource: ref. 7.

^cAdapted from ref. 9.

^dAdapted from ref. 10.

^eSource: ref. 8.

and late 1990s suggests that pharmaceutical cost-cutting efforts in the public sector did achieve savings in some EU countries, in particular Germany, Italy, and Luxembourg (Table 1). Total health care expenditures as a percentage of gross domestic product (GDP) remained unchanged or increased in most EU countries between the early and late 1990s. The largest increases were in Germany, Portugal, and Belgium, whereas decreases were found in Denmark, Finland, and Sweden. In the case of Sweden, the difference can in part be accounted for by a change in the way the accounts were calculated (6).

Public funding (funding by state, regional and local government bodies, and social security schemes) on pharmaceuticals and other medical non-durables (ie, medicinal preparations, branded and generic medicines, patented medicines, serums and vaccines, vitamins and minerals, and oral contraceptives) as a percentage of public health expenditure was highest in Portugal (26.5%) by the late 1990s, followed by Spain (20.9%), and Greece (19.4%). In all countries except Germany, Italy, and Luxembourg public pharmaceutical expenditures as a percentage of total public health care expenditures increased by the late 1990s, with the largest increases in Spain and Sweden. Over the same time period, public pharmaceutical expenditures per capita increased in all countries except Italy. Both France and Luxembourg had the highest levels of public pharmaceutical expenditures per capita at the beginning as well as the end of the 1990s.

Interestingly, public pharmaceutical expenditures as a percentage of total pharmaceutical expenditures decreased in over half the EU countries during this same time period. In 1990, public pharmaceutical expenditures as a percentage of total pharmaceutical expenditures was highest in Luxembourg (84.6%), Germany (73.1%), and Italy (72.3%). By the late 1990s, despite decreases, Luxembourg still remained among the highest public spenders on pharmaceuticals (80.8%), along with Ireland (81.9%) and Spain (77.3%). Decreases in public pharmaceutical spending in the Netherlands and Sweden can be accounted

for in part by increases in the self-medication market. The shift away from public pharmaceutical spending can also be accounted for by increases in co-payments, reference pricing schemes, as well as the wider use and expansion of negative and positive lists.

Comparing the average ex-manufacturer pharmaceutical price per package in purchasing power parity in both 1989 and 1998 in EU countries, France, Greece, and Spain consistently had the least expensive average ex-manufacturer prices (Table 1). Sweden and Portugal were ranked among those with higher ex-manufacturer's prices in both 1989 and 1998, as well as the United Kingdom (UK) by 1998. It would be expected that a country with cheaper pharmaceutical prices would have higher levels of pharmaceutical consumption, which is true for France. However, this relationship does not hold perfectly for other countries (Table 1). Also, downward price pressure in EU countries is increasingly coming from parallel imports (11).

To control pharmaceutical expenditures, health care payers can focus on both demand (volume) and supply (price) (Fig.1). The combination of demand and supply interventions used, or the regulatory frameworks, varies from country to country. Among EU countries the tendency has been to focus on supply and regulate pharmaceutical prices, often with little attention to the volume-side of the equation. The analysis in this paper excludes an examination of demand-side interventions, some of which can have an effect on pharmaceutical prices, such as positive or negative lists. Also, the regulation of pharmaceutical prices can occur at various points along the distribution chain, from manufacturer to wholesaler to pharmacist and individual consumer or hospital. However, the focus here is only on the methods to regulate ex-manufacturer's price.

The regulation of the ex-manufacturer's price may be direct or indirect. Measures for the direct fixing of prices include negotiations, price setting, international price comparisons, price cuts or freezes, and

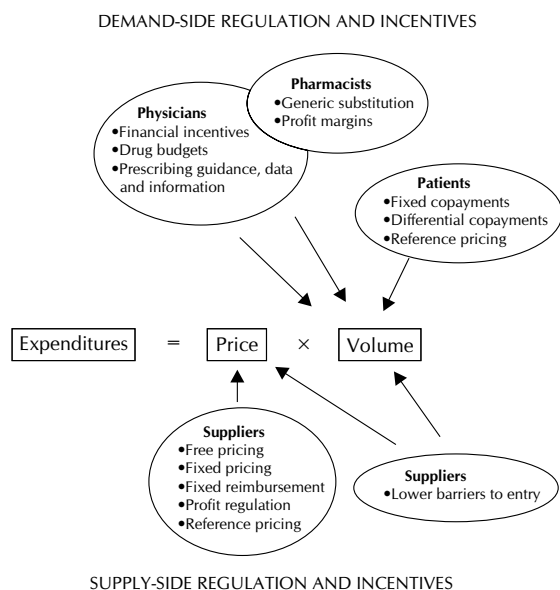


Figure 1. Regulatory frameworks for pharmaceutical markets. Source: ref. 4.

price/volume trade-offs. Other measures have taken a more indirect approach to regulating pharmaceutical prices by regulating profits, calculating “cost-effective” prices or setting maximum reimbursement prices.

Specifically this study asks the following questions: what methods of pharmaceutical price regulation are used in EU countries, and what evidence is there of their impact on containing pharmaceutical expenditures?

Methods

To examine the strengths and weaknesses of these alternative approaches to price regulation, an extensive search of both peer-reviewed and “gray” literature was undertaken. The evidence was collected following the methods of a systematic review of the literature (12,13). Studies were included if they discussed a regulatory intervention that specifically targeted pharmaceutical prices in a EU country and was published between January 1992 and April 2002. Gray literature included published reports, booklets, conference proceedings, discussion papers, as well as Internet sources. Electronic databases, such as MEDLINE, EconLit, and BIDS, and Internet sites EconPapers and JSTOR were searched. Internet search engines Altavista and Google were also used. Furthermore, bibliographies of studies identified through the database searches were used to identify additional studies.

The searches of MEDLINE (the health literature) and EconLit (the economics literature), two databases that each includes different sets of literature, provided the largest number of studies given the search criteria (Table 2). More studies were identified through Medline than through EconLit. It is impossible to provide a full list of the various search terms used, but the strategy was to use general terms, such as pharmaceuticals, price, and regulation, as well as specific ones, such as reference pricing. These terms were then cross-matched to specific countries. The largest number of studies related to the terms “pharmaceuticals”, “price”, and “regulation” were comparative studies for some European countries, including studies of the UK and German systems. For a number of EU countries, no relevant peer-reviewed studies were identified.

All published work identified in the searches was reviewed and those meeting the criteria set out above were included. Although there was no restriction on the study design, preference

Table 2. Key words used for comparative search of published work on MEDLINE and EconLit^a

Search term ^b	Hits	
	Medline	EconLit
Pharmaceutical	61,858	840
Pharmaceutical regulation	5,248	189
Pharmaceutical regulation price	150	30
...and Europe	40	2
...and Austria	0	0
...and Belgium	0	0
...and Denmark	1	0
...and Finland	0	0
...and France	9	3
...and Germany	12	4
...and Greece	0	0
...and Ireland	0	0
...and Italy	5	2
...and Luxembourg	0	0
...and Netherlands	5	0
...and Portugal	2	0
...and Spain	5	1
...and Sweden	4	0
...and United Kingdom	16	3

^aSearch conducted in April 2002.

^bLimited to the last 10 years.

was given to prospective studies with and without control groups, retrospective studies with and without controls, and case studies that were reinforced by similar supporting case studies or anecdotal evidence. A number of studies identified were found not to be relevant. Most of the relevant studies were descriptive.

Results

Four main methods of regulating pharmaceutical prices were identified through the survey of the literature: fixed pricing, profit controls, cost-effectiveness pricing, and reference pricing. EU countries take different approaches and often use more than one method to regulate pharmaceutical prices (Table 3). However, limited evidence was identified of actual policy impact on cost-containment for many countries.

Germany and Denmark, which both allow for new products to be freely priced, have applied subsequent mechanisms to lower prices of products already on the market, including reference pricing for off-patent medicines, price reductions, and price freezes. Some countries use a different method when regulating in-patent vs multi-sourced medicines. Even when applying the same pricing scheme to both in-patent and off-patent medicines, there is an expectation that generics will be priced lower than the original brand, as is the case in Belgium, Greece, Italy, and Portugal. The hospital market may also be regulated separately, as in France where hospital pharmacies are responsible for determining pricing contracts (14).

Other countries, including Finland, France, and Sweden, have free pricing of pharmaceuticals if the product is not reimbursed by the public health care system. However, in general, if regulation is linked to reimbursement, the fixed price becomes the market price. For example, the price negotiated in France and Ireland for reimbursement is the price at which the drug must be sold even for private prescriptions. This is because regulations in many EU countries stipulate that a medicine may be sold only at a single

Table 3. Summary of approaches to the regulation of pharmaceutical prices in European Union (EU) countries

EU country	Free pricing	Fixed pricing	Cost-effectiveness pricing	Profit controls	Reference pricing	Applies to in-patent drugs	Applies to multi-sourced drugs ^a	Applies to OTC ^b
Austria		√				yes	yes	yes
Belgium		√				yes	no	no
Denmark	√		√			yes	no	yes
Finland		√	√		√	no	yes	no
France		√	√			yes	yes	no
Germany	√					yes	no	no
Greece		√			√	no	yes	yes
Ireland		√	√			yes	yes	no
Italy		√	√			yes	no	no
Luxembourg		√				yes	yes	yes
Netherlands		√			√	yes	yes	no
Portugal		√	√			yes	yes	no
Spain		√	√			yes	no	no
Sweden		√	√		√	yes	yes	yes
United Kingdom			√	√	√	no	yes	no
		√				yes	no	no
						no	yes	no

^aMulti-sourced drugs – brand name drugs that have generic equivalents.

^bOver-the-counter pharmaceuticals.

price and, generally, market access is severely restricted without reimbursement (15).

Also, since 1989, the pricing of medicinal products in EU countries has been loosely governed at the supranational level by the transparency directive (89/105/EEC). This directive establishes that authorities must make a price decision within 90 days of receipt of adequate information and the manner in which any negative decisions are to be communicated. It also specifies that in the event of price freeze, an annual review must be conducted to determine whether the macroeconomic conditions justify continuing of the freeze. The directive also indicates that any direct or indirect mechanisms for controlling profits of those placing a medicine on the market need to be explicit, as must the decisions of including products on a positive list or excluding them from reimbursement through a negative list.

Fixed Pricing

All EU countries except Germany and the UK apply or have applied price fixing on in-patent drugs, including Denmark, which introduced price ceilings between 1998 and 2000 (16). As previously mentioned, there are multiple combinations and approaches used to setting fixed prices. What these approaches have in common is that their objective is to fix pharmaceutical prices that are "reasonable" and affordable to the given (generally public) health care system. Acceptable price levels vary from one country to another and are dependent on a number of factors, including budget limits, prescribing behavior, patterns of utilization, as well as the political importance of the pharmaceutical industry or other relevant interests.

Either prices are fixed through negotiations, as in France and Spain, or product prices are fixed by na-

tional authorities according to a defined list of factors. Even through negotiation, regulators generally take into consideration the manufacturers' costs, but may also consider therapeutic benefit and innovativeness, investment in research and development, price of similar products, international prices, volume sales, advertising costs, as well as the contribution of the industry to the economy. Increasingly economic evaluations influence the outcomes of this price fixing process. Fixing prices, in theory, offers a better alternative to cost-based regulation alone, giving companies both an incentive to produce efficiently and the flexibility to price according to its changing market environment if there is potential for competition below the maximum price (17).

However, the factors taken into consideration when fixing pharmaceutical prices may be open to bias, subjective or not transparent. There is potential for bias in Austria's dependency on companies submitting approved cost data while trying to bear in mind the consumers' interests (18). Other price determinants can be subjective, such as the unfavorable view taken by regulators of companies in Belgium with large overheads and high salaries to executives (19). Similarly, rewarding companies that contribute to the national economy is not transparent; determining what contributions should be rewarded and how much they should be worth is not directly evident.

Price comparisons between similar products within a country, or comparisons to identical or comparable products in other countries, particularly other EU countries, are also a common factor in price fixing. Countries may consider an average EU price, as do Austria, Belgium, France, and Italy, or a basket price from selected countries, as in Finland, Ireland, the Netherlands, and Portugal. Sweden compares the prices not only with other EU countries but also re-

quests data from Norway, Switzerland, and the United States. Until 1998, Italy had limited its comparator countries to Spain, France, Germany, and the UK, but changed to include all EU countries over concerns that the previous scheme may have been violating the rule of free movement of goods by keeping prices so low that it discouraged imports (20). Although Ireland compares prices of a selected number of EU countries, it specifically identifies the UK wholesale price as a point of comparison. In some countries these comparisons are used only as one factor in price determination, whereas in other countries price comparisons are the main factor and cannot exceed those of the comparator countries, as in Greece. Finland includes the prices of comparable parallel imports (21). Whereas this comparative element limits the discretionary power of individual companies in price setting, there are a number of difficulties associated with making such product price comparisons. Although the external comparison of the prices of medicines in other countries is meant to provide some basis on which to assess reasonableness, these comparisons may have methodological problems: difficulties in selecting appropriate products for comparison as product availability varies from country to country; obstacles in comparing prices across different formulations and pack sizes; or problems in converting comparator country prices into national currency (6,22).

Some countries apply a form of fixed pricing, which varies with volume. More commonly referred to as price/volume agreements, these have been implemented in Austria (since 1998), France (up to 1999), Spain, and Sweden. This mechanism works by setting prices according to volume, such that if volumes pass a threshold, the price level will decrease or alternatively companies can pay a cash rebate, as in Austria. Belgium has been due to implement price-volume contracts for innovative products since March 1994. However, implementation has been delayed due to a debate between insurance funds and the pharmaceutical industry on how to classify products as innovative (19). Although Italy does not have formal price-volume agreements, it does consider the number of patients using the medicine and the sales level in price determination.

Evidence that specifically examines the impact of fixed pricing as a mechanism of controlling pharmaceutical expenditures is almost non-existent, with the exception of some general international price comparisons. Experience from the UK Drug Tariff scheme that set maximum reimbursement prices for unbranded generic medicines (reformed in 2000 and now known as the Maximum Price Scheme) shows that between 1994 and 1998 generic prices decreased by approximately 25% in real terms because of competition below the maximum price (23). A similar increase in competition was expected in the Netherlands, following the introduction of the Maximum Price Law in 1996 because of the lowering of the discounts offered to pharmacists, leading to a subsequent weakening of the chain between wholesalers, the industry, and pharmacists (24). However, in many of the countries with fixed prices, there is no potential

for competition below the maximum price, either because this is not allowed or because there is no incentive to do so.

What can perhaps be said is that price fixing does not seem to have achieved the pharmaceutical cost-containment goals, as is reflected in changes in the pricing methodology, or the addition of subsequent price control methods or demand-side policies in many countries. France, for example, tried numerous supply-side policies to control drug prices as a primary target for cost-containment since 1975, and did achieve the lowest prices in Europe (Table 1). However, with volumes unconstrained and increasing to compensate for decreasing margins so too did pharmaceutical expenditures leading the government to seek alternative approaches, which included limiting advertising expenditures, informing physicians of rational use, and more recently, adding pricing based on product value (25). Price decreases and freezes have also been common in many of these countries. Price fixing seems to achieve only short-term cost-containment, while increases in volume also led to expenditure increases.

Cost-effectiveness Pricing

As previously mentioned, more EU countries are using economic evaluation along-side other methods for regulating pharmaceutical prices, as a factor in price fixing or as guidance for resource allocation decisions. Finland, France, Portugal, Sweden, and the UK have introduced guidelines for conducting economic evaluations of pharmaceuticals. In Finland, the reimbursement price is dependent on the costs and benefits of a given therapy being justified through an economic evaluation as compared to therapeutic alternatives. Economic guidelines were introduced in France as part of reforms that attempted to improve the transparency of the price fixing process, although they remain optional (14). Economic evaluation can be requested in Portugal and Sweden if a price premium is requested. In the UK, economic evaluation is used as guidance in informing resource allocation decisions.

Although there are no formal guidelines, economic evaluations may be required or requested in other EU countries. Italy considers a cost-benefit ratio in determining the price for reimbursement, and also requires pharmacoeconomic data for companies wishing to renegotiate a product's price. Since 1997, the Irish Department of Health has reserved the right to seek a cost-benefit analysis for the purpose of price determination (26). Pharmacoeconomic data is being voluntarily encouraged in Denmark when applying for reimbursement status, as reimbursement is dependent on price being balanced with the therapeutic effect of the product (16). In the future, this is also expected to be applied in the Netherlands.

Although economic evaluations may not be specifically called for, in some countries there seems to be increasing attention to cost-effectiveness considerations. In Belgium, for example, to justify a new product, a manufacturer must demonstrate that total health care costs are lower with the given product

compared with competing products. Austria is to conduct "economic reviews" of all reimbursed drugs.

In theory, evaluations attempt to provide value for money justifications for a product's price by relating costs associated with the intervention strategy to resulting health outcomes (defined in terms of a monetary valuation of benefit, gains in effectiveness or utility) as a means of choosing between different therapies and courses of treatment. A price premium on an intervention compared with competing alternative strategies may be justified if the analysis shows that the former could provide substantial cost savings to the health care system or society.

Most of the published work on economic evaluation focuses on the obstacles and problems associated with its use. Despite the implementation of guidelines, methodological disputes remain (appropriate discount rate or generic measures of quality of life) and significant problems can be identified (27). These are important because the results of a model are generally sensitive to small changes in parameters and consequently an option that was previously considered cost-effective may be dominated under alternative scenarios and a given product may not achieve the cost savings estimated. The external validity of the results needs to be considered if the ranking of therapies according to their cost-effectiveness ratios is to be used to inform choices in real world settings (28). Ranking in this way also ignores issues of equity, which are important particularly when the rationing of resources is an explicit consideration. For the pharmaceutical industry, funding studies and/or modifying clinical trials to collect the robust data required for the evaluations impose practical problems regarding appropriate end-points and sample size (29). It is not an alternative to apply study results from one setting to another or from one country to another, as the results may be biased both in terms of the costs used and the population examined. As the stakes are high, such an analysis may lead some firms to forego the development of some drugs if the expected price premium to be gained is too small to justify further product development (17).

The evidence of the effectiveness of using economic evaluation to secure value prices is limited. Some evidence from Sweden suggests that higher margins are gained by drugs considered to be both vertically differentiated and innovative, which may be a reflection of the use of economic evaluations (30). The use of economic evaluation has raised new controversies, particularly because its use may in some cases lead to overlaps with other price control mechanisms. The example of the risk-sharing agreement for multiple sclerosis drugs in the UK (31), which evolved subsequently to a negative ruling by National Institute for Clinical Excellence as an alternative way to reimburse the products, raises a number of issues including whether such an approach is appropriate and necessary given the existence of a profit control scheme.

Profit Controls

Since 1957, the UK has been operating a unique profit control scheme, called the Pharmaceutical

Price Regulation Scheme, which indirectly regulates the prices of branded pharmaceuticals sold to the National Health Service by setting profit limits (32). The voluntary scheme is the result of periodical negotiations between the Association of the British Pharmaceutical Industry and the Department of Health. The current scheme came into effect in October 1999 and will stay in force for at least five years, although either the industry or the National Health Service can request an interim review after no less than two and a half years of the scheme.

The Pharmaceutical Price Regulation Scheme aims to achieve a balance between securing medicines for the National Health Service at reasonable prices while encouraging a strong and profitable pharmaceutical industry capable of competitive and sustained development of new, innovative medicines. Since a "reasonably priced" medicine is not defined in the Pharmaceutical Price Regulation Scheme, it may be asked whose definition should be used, as industry, different arms of government, and tax payers may have differing views about reasonableness. The definition that is chosen in the context of the Pharmaceutical Price Regulation Scheme will depend on the ranking of the scheme's goals.

Member companies of the scheme with National Health Service sales of £25 million are required to submit an Annual Financial Return identifying those products with National Health Service sales of £500,000 or more and also any details on the capital employed by each company supplying medicines. The data are used to assess the overall profitability of the company on sales to the National Health Service and to assess an application for a price increase. New active substances may be priced at the discretion of the company on entering the market.

Companies within the scheme have an allowable profit (or cap) of 21%, measured as a return on capital employed or return on sales for those companies that do not have major capital investments in the UK. If a company exceeds its target return, it can retain up to 40% over the originally permitted return, but only if it has not received a price increase for any product in the same year. If profits exceed the margin of tolerance, the company must reduce profits by either cutting the prices, thus repaying the excess profit to the Department of Health, or delaying or restricting previously agreed future price increases. The amount allowed for research and development can comprise up to 20% of total National Health Service turnover and, in addition, companies are permitted an additional 3%, depending on the number of patented products they sell in the UK. Companies are also allocated 6% of National Health Service sales for promotional spending.

The success of the Pharmaceutical Price Regulation Scheme in securing low prices of medicines for the National Health Service is inconclusive. Some have argued that the Pharmaceutical Price Regulation Scheme has done little to control the prices of medicines for the National Health Service (33), as the National Health Service pharmaceutical budget had been increasing approximately 10% a year from 1967

to 1997 (34). Savings of £89.8 million resulted from price reductions introduced in 1993 but this effect is a one-off (35). The increase in the profit cap was not found to be associated with changes in the medicine prices, although there may be some differences in specific therapeutic categories (36). Compared with other countries of the EU in 1989, the UK was middle to high in terms of pharmaceutical prices (Table 1). However, by 1998 the UK prices were amongst the highest in the EU. The UK is often included as a reference country for international comparisons by other EU countries, and consequently relatively free pricing in the UK, means that companies are likely to establish UK prices first (37). One reason that there are no conclusive findings of the affect of the Pharmaceutical Price Regulation Scheme on National Health Service drug prices is because the scheme is not that transparent and therefore has been difficult to assess.

The scheme is thought to have encouraged investment by both maintaining a stable and predictable regulatory environment and by allowing levels of expenditures on research and development above the worldwide average (38). However, as the Pharmaceutical Price Regulation Scheme is a rate-of-return scheme, like other regulatory schemes of this type, it lacks incentives for operational efficiency, since increased costs can be recovered through increased prices being allowed. To increase its allowance of capital invested, a company may over-invest in capital equipment or shift production costs from an unregulated to a regulated division.

Reference Pricing

Reference pricing schemes set fixed reimbursement limits for products assigned to the same group. The purpose of reference pricing or fixed reimbursement levels is to limit the rise in pharmaceutical expenditures by setting a limit on the price that health care payers will fully reimburse. In the EU, it has been applied in Germany, Sweden, Denmark, Spain, and the Netherlands. It has gained popularity as a policy tool because it can be effective in eliminating price differences between therapeutic substitutes and improving the transparency of the market (39).

Schemes differ between countries in terms of coverage, pricing method, and whether they are inclusive or exclusive of in-patent medicines. In Denmark, Germany, Spain, and Sweden the reference pricing scheme includes only multi-sourced drugs. In general, reference pricing applies only to products that have been defined to be in the same category and are considered interchangeable because they have similar mechanisms of therapeutic action or produce similar clinical outcomes. However, these classifications are often considered controversial (40). Also, different mechanisms are used to calculate the reference price. It may be based on the average price of drugs in the category, the price of the cheapest drug or two drugs in the category (as in Denmark), or on the price of the cheapest generic drug plus an additional sum (as in Sweden).

The patient must pay the difference between the price of the prescribed drug and the reference price if the former is higher. A common reimbursement price

for products that are close equivalents creates an incentive for physicians and patients to consider cost when making choices. In this way, reference pricing was expected to bring the prices of all products in the same reference price category down to the same level. Although new products for which there are no clear substitutes are most often excluded from reference pricing schemes, there may nevertheless be a convergence to the reference price of competitor products.

Although there are differences in the methodology of reference pricing, a similar effect has been observed in the different countries where it has been applied. A comprehensive review of the published work on reference pricing by Lopez-Casasnovas and Puig-Junoy (41) found that although the prices of products covered by reference pricing tended to decrease, leading to reductions in third-party pharmaceutical expenditures, these were not long-term savings. This is partly because medicines that were not part of the reference price scheme often had their prices increased at levels greater than the price decreases, so that the overall effect was for higher expenditures. One reason for the decrease in the price of these medicines was that patients were not willing to pay the additional cost of medicines priced above the reference price out of pocket (42). However, the effect of reference pricing on expenditures is often difficult to disentangle from other measures. In Germany, for example, one study attributed longer-lasting cost-containment impact to global budgeting rather than reference pricing (43).

International Price Comparisons

Despite the lack of evidence on specific country price control mechanisms, many international comparative pricing studies attempted to investigate the impact of regulation on securing reasonable pharmaceutical prices. Beyond the methodological difficulties that plague many international comparative pricing studies, it is difficult to separate out causal effects in the cross-country comparisons because of the many factors influencing drug prices in a given market, ie, differences in health system structure and financing, pharmaceutical subsidies, cost-containment policies, product mix, and production costs (22,44,45). Nevertheless, a study by the United States General Accounting Office, covering the late 1980s and early 1990s, found that prescription drug spending controls in France, Germany, Sweden, and the UK were effective in restraining drug prices (price increases were less than the overall inflation rate) but were unable to prevent escalation of overall drug expenditures because of the volume effect (46). Also, the countries with strict price regulation (France, Italy, and Spain) have systematically lower prices than countries with less stringent price regulation (Germany, Sweden, and the UK) (47-49). Yet other studies suggest that in markets with less regulation and more market freedom, such as the UK and Germany, prices tend to be kept lower through competition (50,51). Differences in results between countries are dependent on the comparator countries included in the study, the therapeutic categories included for com-

parison, and whether any differentiation was made for in-patent vs off-patent markets.

Conclusion

In an attempt to control rising pharmaceutical expenditures, most EU countries have targeted the supply-side of the market and introduced some form of either direct or indirect price regulation. The evidence of the impact of these schemes is limited and varies. In terms of controlling the rise in pharmaceutical prices, evidence from cross-country comparisons suggests that those with strict direct price regulation schemes have been more successful than those with less stringent or no price regulation. However, the quality of these comparisons of prices between countries is dependent on the methodology applied, but even then there are issues of comparability.

Evidence of specific supply-side interventions is growing. The evidence of reference pricing schemes suggests that these have been effective in controlling the price increases of products that are included in schemes, but that any savings may only be short-term. Only the UK Pharmaceutical Price Regulation Scheme attempts to take balanced account of a firm's investment in innovation and production while trying to achieve reasonable prices for the National Health Service, and the evidence suggests that the scheme has operated quite successfully for the UK over the years. The increasing use of economic evaluation attempts to consider product value when determining a price for reimbursement. As this approach is still relatively new, evidence is limited but a caution can be given to the need to ensure that appropriate methodological guidelines are followed if the results are to inform decision-makers in a real world setting.

What is clear is that supply-side regulation on its own does little to control the rise in pharmaceutical expenditures. Without the simultaneous use of demand-side incentives and volume controls, pharmaceutical expenditures will continue to rise. The types of demand-side controls that are needed will depend on the context of the individual country, on political priorities (health policy vs industrial policy objectives) and on the type of supply-side regulation in place, if any. It is important that these factors be taken into consideration, as transferring a policy from one country to another may not result in similar outcomes.

References

- Comanor WS. The political economy of the pharmaceutical industry. *J Econ Lit* 1986;24:1178-217.
- Green DG. Is price regulation necessary? A Summary of the arguments. *Pharmacoeconomics* 1998;14 Suppl 1: 137-42.
- Danzon PM, Chao LW. Does regulation drive out competition in pharmaceutical markets? *Journal of Law and Economics* 2000;43:311-357.
- Mrazek M. The impact of different regulatory frameworks on the post-patent pharmaceutical market of the United Kingdom, United States and Germany, 1990 to 1997 [dissertation]. London: London School of Economics and Political Science; 2001.
- Hodges CJ. Pricing and reimbursement issues in the European economic area. *Drug Information Journal* 1997; 31:251-8.
- Kanavos P, Mossialos E. International comparisons of health care expenditures: what we know and what we do not know. *J Health Serv Res Policy* 1999;4:122-6.
- Research and Information Center For Health Economics, Organization for Economic Co-operation and Development. *OECD health data 2001*. Paris: CREDES/OECD; 2002.
- Research and Information Center For Health Economics, Organization for Economic Co-operation and Development. *OECD health data 2000*. Paris: CREDES/OECD; 2001.
- Association of the European Self-Medication Industry. Facts and figures: June 2001. Available from: <http://www.aesgp.be/Figures00/FFtable.html>. Accessed: June 13, 2002.
- Pharmig. Facts and figures 1999/2000. Vienna: Pharmig; 2000.
- Ganslandt M, Maskus KE. Parallel imports of pharmaceutical products in the European Union. Working paper No. 546. Stockholm: The Research Institute of Industrial Economics; 2001.
- Deeks J, Glanville J, Sheldon T, editors. Undertaking systematic reviews of research on effectiveness: CDR's guidance for those carrying out or commissioning reviews. 1st ed. CDR Report No. 4. York: National Health Service Centre for Reviews and Dissemination; 1996.
- Robinson R, Steiner A. Managed health care: US evidence and lessons for the NHS. Buckingham: Open University Press; 1998.
- Pelen F. Reimbursement and pricing of drugs in France: an increasingly complex system. *European Journal of Health Economics* 2000;0:20-3.
- Kanavos P. Overview of pharmaceutical pricing and reimbursement regulation in Europe. London: LSE Health and Social Care. Available from: pharmacos.eudra.org/F3/g10/docs/synthesis.pdf. Accessed: April 14, 2002.
- Heinesen B. Pharmaceutical pricing and reimbursement policies – Denmark. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.
- Abbott TA 3rd. Price regulation in the pharmaceutical industry: prescription or placebo? *J Health Econ* 1995; 14:551-65.
- Kanavos P. Pharmaceutical pricing and reimbursement – Austria. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.
- Eggermont M, Kanavos P. Pharmaceutical pricing and reimbursement – Belgium. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.
- Jommi C. Pharmaceutical pricing and reimbursement – Italy. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.

- 21 Sirkia T, Rajaniemi S. Pharmaceutical pricing and reimbursement policies – Finland. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.
- 22 Danzon P, Kim J. International price comparisons for pharmaceuticals. Measurement and policy issues. *Pharmacoeconomics* 1998;14 Suppl 1:115-28.
- 23 UK Department of Health. The government's response to the health select committee's first report on the cost and availability of generic drugs to the NHS. London: The Stationery Office; 2000.
- 24 De Vos CM. The 1996 pricing and reimbursement policy in the Netherlands. *Pharmacoeconomics* 1996;10 Suppl 2:75-80.
- 25 Le Pen C. Drug pricing and reimbursement in France. Towards a new model? *Pharmacoeconomics* 1996;10 Suppl 2: 26-36.
- 26 Mc Guinn T, Troy J. Pharmaceutical pricing and reimbursement – Ireland. LSE study on healthcare in individual countries: worldwide survey on pharmaceutical pricing and reimbursement structures. G10 Medicines 2001. Available from: <http://pharmacos.eudra.org/F3/g10/p6.htm>. Accessed: April 4, 2002.
- 27 Hill S, Henry D, Pekarsky B, Mitchell A. Economic evaluation of pharmaceuticals: what are reasonable standards for clinical evidence – the Australian experience. *Br J Clin Pharmacol* 1997;44:421-5.
- 28 Hoffmann C, Graf von der Schulenburg JM. The influence of economic evaluation studies on decision making. A European survey. The EUROMET group. *Health Policy* 2000;52:179-92.
- 29 Drummond M. Evaluation of health technology: economic issues for health policy and policy issues for economic appraisal. *Soc Sci Med* 1994;38:1593-600.
- 30 Lundkvist J. Pricing and reimbursement of drugs in Sweden. *The European Journal of Health Economics* 2002; 3:66-70.
- 31 UK Department of Health. Cost effective provision of disease modifying therapies for people with multiple sclerosis. Health Service Circular 2002/004. London: Department of Health; 2002. Available from: <http://ta.p.ccta.gov.uk/doh/coin4.nsf/page/HSC-2002-004?OpenDocument>. Accessed: May 2002.
- 32 UK Department of Health. The pharmaceutical price regulation scheme, 1999. London: Department of Health. Available from: <http://www.doh.gov.uk/pprs.htm>. Accessed: May 3, 2002.
- 33 Maynard A, Bloor K. Regulating the pharmaceutical industry. *BMJ* 1997;315:200-1.
- 34 Bloom N, Van Reenen J. Regulating drug prices: where do we go from here? *Fiscal Studies* 1998;19:321-42.
- 35 UK Department of Health. The pharmaceutical price regulation scheme report to parliament, May 1996. London: International and Industry Division and Department of Health; 1996.
- 36 Borrell JR. Pharmaceutical price regulation. A study on the impact of the rate-of-return regulation in the UK. *Pharmacoeconomics* 1999;15:291-303.
- 37 Earl-Slater A. Regulating the price of the UK's drugs: second thoughts after the government's first report. *BMJ* 1997;314:365-8.
- 38 Mossialos E. An evaluation of the PPRS: is there a need for reform? In: Green DG, editor. Should pharmaceutical prices be regulated? The strengths and weaknesses of the British pharmaceutical price regulation scheme. London: Institute of Economic Affairs, Health and Welfare Unit; 1997. p. 48-71.
- 39 Giuliani G, Selke G, Garattini L. The German experience in reference pricing. *Health Policy* 1998;44:73-85.
- 40 Rigger H. Recent public policies in The Netherlands to control pharmaceutical pricing and reimbursement. *Pharmacoeconomics* 1994;6 Suppl 1:15-21.
- 41 Lopez-Casasnovas G, Puig-Junoy J. Review of the literature on reference pricing. *Health Policy* 2000;54:87-123.
- 42 Zweifel P, Crivelli L. Price regulation of drugs: lessons from Germany. *Journal of Regulatory Economics* 1996; 10:257-73.
- 43 Ulrich V, Wille E. Healthcare reform and expenditure on drugs: the German situation. *Pharmacoeconomics* 1996;10 Suppl 2:81-8.
- 44 United States International Trade Commission (US). Pricing of prescription drugs. Investigation No. 332-419. Publication 3333. Washington (DC): International Trade Commission; 2000.
- 45 Productivity Commission. International pharmaceutical price differences [research report]. Canberra: AusInfo; 2001.
- 46 United States General Accounting Office. Prescription drugs: spending controls in four European countries. GAO/HEHS-94-30. Washington (DC): General Accounting Office; 1994.
- 47 Jonsson B. Pricing and reimbursement of pharmaceuticals in Sweden. *Pharmacoeconomics* 1994;6 Suppl 1:51-60.
- 48 Garattini L, Salvioni F, Scopelliti D, Garattini S. A comparative analysis of the pharmaceutical market in four European countries. *Pharmacoeconomics* 1994;6:417-23.
- 49 Rovira J, Darba J. Pharmaceutical pricing and reimbursement in Spain. *The European Journal of Health Economics* 2001;2:39-43.
- 50 Reekie WD. How competition lowers the costs of medicines. *Pharmacoeconomics* 1998;14 Suppl 1:107-13.
- 51 Danzon PM, Chao L. Cross-national price differences for pharmaceuticals: how large, and why? *J Health Econ* 2000;19:159-95.

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