

“Analysis of differences and commonalities in pricing and reimbursement systems in Europe”

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Table of contents

A.	Introduction.....	20
	I. Scope and purpose of the study	20
	II. Methodological issues in assessing the impact of policy practices	21
	III. Sources and methodology	24
	A. Literature.....	25
	B. Questionnaire	25
B.	Overview of pharmaceutical policy practices in EU MS	27
	I. A classification and definition of pharmaceutical policy practices	28
	Supply side practices.....	28
	Demand side practices.....	30
	II. Selection of 6 policy practices for detailed analysis	35
C.	Selected practices	36
	Price control.....	36
	I. Introduction.....	36
	Description.....	36
	Modalities	37
	Purposes	37
	Theory/rationale.....	38
	II. Application in Europe	38
	Overview.....	38
	Individual replies to the questionnaire.....	41
	III. Impact.....	51
	Experiences reported by countries.	51
	Literature	51
	IV. Discussion.....	53
	Key messages	53
	Risks.....	54
	Key success factors	55

Cost-sharing.....	56
I. Introduction.....	56
Description.....	56
Modalities	56
Purposes	56
Theory/Rationale.....	57
II. Application in Europe	58
Overview.....	58
Individual replies by countries	59
III. Impact.....	69
Overall experiences reported by countries.....	69
Individual replies by countries	70
Literature review.....	79
IV. Discussion.....	81
Key messages	81
Risks.....	81
Key success factors	82
Reference pricing	83
I. Introduction.....	83
Description.....	83
Modalities	83
Purposes	84
Theory/ Rationale.....	84
II. Application in Europe	85
Individual replies by countries	87
III. Impact.....	93
Overall experiences reported by countries.....	93
Individual replies by countries	94
Literature	100
IV. Discussion.....	103
Key messages	103
Risks.....	103
Key success factors	104
Payback.....	105
I. Introduction.....	105
Description.....	105
Purposes	105
Theory/rationale.....	106
Modalities	106
II. Application in Europe	107
Overview.....	107
Individual replies provided by MS'	107

III. Impact.....	111
Experiences reported by countries	111
Individual replies by countries	111
Literature	113
IV. Discussion.....	114
Key messages	114
Risks.....	114
Key success factors	115
Incentives for good prescribing practices	116
I. Introduction.....	116
Description.....	116
Modalities	117
Purposes	117
Theory/Rationale.....	117
II. Application in Europe	119
Overview.....	119
Individual replies by countries	119
III. Impact.....	130
Overall experience reported by countries.....	130
Individual replies by countries	130
IV. Discussion.....	142
Key messages	142
Risks.....	142
Key success factors	142
Generics Policies	143
I. Introduction.....	143
Description.....	143
Modalities	143
Purposes	144
Theory/Rationale.....	144
II. Application in Europe	144
Overview.....	144
Individual Country Replies.....	145
III. Impact of Generics policies	157
Overall experiences reported by countries.....	157
Individual replies by countries	158
Literature review	167
IV. Discussion.....	170
Key messages	170
Risks.....	171
Key success factors	171

D. Global perspective on pricing and reimbursement policies	173
I. Similarities and dissimilarities in EU MS pharmaceutical policies	173
II. Evidence of impact	174
III. Interactions/interdependence between practices	177
IV. Conditions for application.....	179
List of references	182

Tables

Table 1	Overview Supply Side
Table 2	Overview Demand Side
Table 3	Pharmaceutical Price Regulation in Europe
Table 4	International Price Reference
Table 5	Overview of reimbursement categories in Belgium
Table 6	Reimbursement Rates in Denmark in 2007
Table 7	Sweden - Reimbursement rates and patient co-payment rates, 2006
Table 8	Expenditures for pharmaceuticals non hospital (in Million Euro)
Table 9	Total expenditures for pharmaceuticals per class ATC and per category (%) of reimbursement by patients (out-of-pocket payment)
Table 10	Reference Pricing in Europe
Table 11	Payback systems in Europe
Table 12	Types of interventions aimed at changing doctors' prescribing behaviours
Table 13	Effectiveness of improved prescription instruments

Graphs

Graph 1	Countries used as international references
Graph 2	Evolution of the expenditures for pharmaceuticals for non-hospital patients (contribution health insurance versus contribution patients)
Graph 3	Expenditure for pharmaceuticals. Belgium
Graph 4	Price index in Germany
Graph 5	Evolution over time of price per DDD for 2 ATC-4 classes
Graph 6	Evolution of expenditures and use (DDD) of generics
Graph 7	Cost per prescription in Germany (Euro)
Graph 8	Prescription of Pharmaceuticals in Germany
Graph 9	Sales of Pharmaceuticals in Germany

List of annexes

Annex I	List of pharmaceutical policy practices
Annex II	Methodology of specific structured literature reviews
Annex III	Questionnaire on the impact assessment of pharmaceutical policy practices

Glossary of acronyms

AESGP	European Self-Medication Industry
APMI	Association of Pharmaceutical Manufacturers of Ireland
ATC	Anatomic Therapeutic Chemical Classification
CADIME	Centro Andaluz de Documentación e Información del Medicamento (Andalusian Center of Drug Documentation and Information)
EASP	Escuela Andaluza de Salud Pública (Andalusian School of Public Health)
EC	European Commission
EFPIA	European Federation of Pharmaceutical Industries and Association
EFTA	European Free Trade Association
EU	European Union
GDP	Gross Domestic Product
GIRP	Groupement International de la Repartition Pharmaceutique (The European Association of Pharmaceutical Full-line Wholesalers)
HSE	Health Services Executive - Ireland
LSE	London School of Economics and Political Sciences
MS	Member State
NHS	National Health Service
OECD	Organisation for Economic Co-operation and Development
OTC	Over-the-counter

PF	Pharmaceutical Forum
PPRI	Pharmaceutical Pricing and Reimbursement Information project
PPRS	Pharmaceutical Price Regulation Scheme
R&D	Research and Development
RP	Reference Pricing
UB	University of Barcelona
US	United States of America
WGP	Working Group on Pricing
WHO	World Health Organization

Country acronyms

AT	AUSTRIA
BE	BELGIUM
BG	BULGARIA
CY	CYPRUS
CZ	CZECH REPUBLIC
DE	GERMANY
DK	DENMARK
EE	ESTONIA
ES	SPAIN
FI	FINLAND
FR	FRANCE
EL	GREECE
HU	HUNGARY
IE	IRELAND
IT	ITALY
LT	LITHUANIA
LU	LUXEMBOURG
LV	LATVIA
MT	MALTA
NL	NETHERLANDS
NO	NORWAY

PL	POLAND
PT	PORTUGAL
RO	ROMANIA
SE	SWEDEN
SI	SLOVENIA
SK	SLOVAKIA (Slovak Republic)
UK	UNITED KINGDOM

Informants' data

Country	Organisation / Ministry	Unit
Austria	Gesundheit Österreich GmbH	ÖBIG
Belgium	RIZIV	General Directorate
Cyprus	Health Insurance Organization	
Denmark	The Danish Ministry of the Interior and Health	The Pharmaceutical Unit
Estonia	Ministry of Social Affairs	Pharmaceutical Policy
Finland	Ministry of Social Affairs and Health	Pharmaceuticals Pricing Board
France	Ministry of Health	Directorate of social security
Germany	Ministry of Health	Pharmaceuticals
Greece	Ministry of Development	
Hungary	National Health Insurance fund (Országos Egészségbiztosítási Pénztár)	Pharmaceutical Department
Ireland	Dept of Health and Children	Primary Care II
Italy	Italian Medicines Agency (AIFA)	Centre for Studies
Latvia	State Medicines Pricing and Reimbursement Agency	
Lithuania	Department of Pharmacy under the Ministry of Health	Division of Pharmacoeconomics
Malta	Ministry for Health, the Elderly and Community Care	Medicines Authority
Netherlands	Ministry of Health	Division reimbursement and efficient Use of Medical Products
Norway	Norwegian Medicines Agency	Pricing and pharmacy section
Poland	Ministry of Health	Department of drug policy and pharmacy
Portugal	INFARMED- National Institute for pharmacy and medicines / Ministry of Health	Economic Direction for Medicines and Health Products (DEMPS)
Romania	Ministry of Public Health	Pharmaceutical Directorate
Slovak Republic	Ministry of Health	Pharmacy department
Slovenia	Agency for Medicinal Products and Medical Devices	Sector for Pharmacoeconomics
Spain	Ministry of Health	General Directorate of Pharmacy and Medical Devices
Sweden	Pharmaceutical Benefits Board	
UK	Department of Health	Medicines Pharmacy and Industry Group

Executive Summary

Analysis of the pharmaceutical sector's performance is a complex task, due to the convergence of often conflicting social and health goals on the one hand and industrial goals on the other. While innovation and access are usually welcomed by all stakeholders, high prices and growing expenditure are perceived as bad news from the payer's perspective (consumers and health insurers) but as good news for suppliers, since for them it translates into higher revenues and profits. A comprehensive pharmaceutical policy has to make trade-offs between these conflicting goals.

Building a coherent EU pharmaceutical policy is a difficult task because pharmaceutical budgets, as well as decisions regarding pricing and reimbursement, are responsibilities of individual Member States. EU Member States differ greatly in their priorities regarding pharmaceutical policy: providing incentives for innovation, supporting domestic (generics or innovative) industry and employment, ensuring and improving access to drugs, limiting public expenditures on drugs, etc. Although concern over limiting public expenditures is rather common and growing in most countries, differences in priorities persist. Differences are obviously related to the pharmaceutical sector's diverse characteristics and levels of development, to the general level of income, and to the varied characteristics of health policies and health systems, among other factors.

Many countries have established a number of practices to control costs while maintaining the balance between equitable access and industry goals. There are significant differences in these practices, particularly in the rules for pricing and reimbursement of medicines in the EU Member States. These differences can be found not only due to the presence or absence of certain practices (price control, cost sharing, reference pricing, etc.) but in differences within the very practices themselves. Policy practices also change rapidly in MS, as do the responses of economic agents, adapting to and often reducing a policy's intended effects. This rapidly changing regulatory environment makes it difficult to assess the impact of policies on expected goals, or even to obtain an up-to-date picture of the EU's regulatory landscape.

Nevertheless, because of rising concerns over cost containment and the need to strike a balance, Member States have an increased need to grasp the substance of different practices and their impact. Since parts of this understanding are available in other

Member States, it is significantly valuable to promote the exchange of experiences, practices, and policies among the Member States.

The purpose of this study is, therefore, twofold. First, to obtain an updated, overall picture of the application of pharmaceutical policies and practices in European countries. Second, to build an in-depth understanding of certain selected practices as implemented in different countries, particularly regarding set-up, risks, success factors and impact on expenditure, reward for innovation and patient access.

The methodology of this study is based on two main instruments: a review of the literature on the impact of policy practices and a survey with country representatives in the Working Group on Pricing of the Pharmaceutical Forum (which ran in parallel to this study).

The report is structured in four parts:

The first, Part A, is an introduction that lays down the study's objectives, justification and methods.

Part B, the overview, presents an overall picture of a variety of pricing and reimbursement practices, presenting a structured overview of those currently in use. It focuses on supply-side mechanisms, such as price controls, expenditure and industry profits, as well as demand-side mechanisms aimed at physicians, patients and pharmacists, and also includes practices focused on financing/reimbursement. The questionnaire revealed that, on the supply side, most countries focus on control of prices although several focused on control of expenditure. On the demand side, practices aimed at physicians usually consist of guidance, education and monitoring; those aimed towards patients focus on education and cost-sharing and for pharmacists (generic) substitution is the most common practice.

Part C, assessment or evaluation of impact, offers an in-depth assessment of 6 practices and policies, and looks for evidence on the establishment and impact of selected practices in different countries.

Finally, part D highlights risk and success factors and looks for interactions between different practices within the framework of global pricing and reimbursement policies.

The evidence gathered in Part C leads to a set of tentative conclusions:

Direct product price regulation is losing ground in Europe, probably less the result of deliberate policy shifts than its decreased effectiveness within the new context of the Single European Market. Direct product price control can be difficult to implement in fair and efficient ways, and if it is effectively applied to lower the prices of innovative products beyond a certain level, is claimed to remove the incentives for innovation. Pricing based on a set of international prices in countries with similar characteristics looks quite reasonable for a small country that has no capacity to impose its own criteria and preferences. Cost-plus approaches to price control appear to be abandoned in favour of those based on international price-comparisons. Finally, pricing based on economic

evaluation and profit control makes a lot of economic sense, but it is complex to organise and its impact is not well assessed.

Cost-sharing has been maintained in most countries. It would appear reasonable to assume that cost-sharing is likely to have a disproportionately higher effect on mostly low-income patients who frequently need/use expensive services. These negative effects are often overcome by implementing safeguarding criteria, such as excluding some patient groups from cost-sharing or through sophisticated monitoring of patients' expenditures, as occurs in some Nordic countries.

According to responses obtained from the questionnaire, monitoring and follow-up of the effects of this practice in most countries has been limited, not going much beyond calculating the aggregate volume of payments by patients.

Reference Pricing is rapidly spreading across Europe. Most countries define the equivalent groups/clusters narrowly (active ingredient), but a few countries (Netherlands, Germany) have shifted to groups based on therapeutic equivalence. There are also broad differences in the way reimbursement prices are set and how exceptions are made. It is difficult to separate the effects of RP and generics policies, two policies which are often implemented together. Some in the industry claim that therapeutic RP reduces incentives for incremental innovation, which is assumed to pave the way – step by step – to major innovations over time. Some studies and experts have also concluded that RP does refrain price competition between generics. Savings were reported in the questionnaire by some countries (around 5%, Hungary and Italy). Changes in access are assumed to be limited, with some exceptions.

Payback is one of the most recent additions to pharmaceutical policies, and not much is known to date on how this practice is applied or what impact it might have. Some countries reported estimated savings between 10 and 800m EUR (between 0,3% and 7% of the pharmaceutical budget), depending on scope and set-up. Payback is not assumed to change access, given that patients are not affected. Impact on incentives for innovation differs, also depending on the specific exemptions taken into account or not for innovative medicines. Payback also offers an opportunity for low-price countries to accept higher prices, at the international level, while controlling final expenditures (taking also into account the difficulties in managing the money back).

Providing incentives for more efficient prescribing does not reflect a single practice but rather a large set of heterogeneous practices. Most countries provide guidelines, information and education, but only a limited number go beyond this “light” approach to monitoring and providing feedback and personal advice to prescribers. Financial and other incentives are very rarely applied. Some of the existing incentives for more efficient prescribing – especially, financial incentives - have a documented effectiveness, but most practices need to be considered as a group since they tend to reinforce each other.

Great variations are also found in generics' policies, particularly regarding leading elements of such policies: selective/priority financing, prescription by generic name, reference pricing, substitution by pharmacist, etc. Also, generics' policies are usually the result of a large combination of both demand and supply-side practices. The literature reveals a substantial number of studies on the impact of specific generics'

policy practices, such as generic substitution by the pharmacist. Generics' policies haven't been applied for a long time, accompanied by selective reimbursement, differential cost-sharing, patient and prescriber information and education. Recently, generics' policies have been complemented by RP and stronger financial incentives to pharmacists and prescribers. Few countries provide data on the impact of generic policies, although Sweden provides evidence to have attained ~760mEUR accumulated savings between October 2002 and December 2005. Most respondents assume no negative impact on innovation. It has also been noted that the impact of generics' policies cannot be evaluated independently from other related practices, particularly reference pricing.

Section D explains that each practice requires certain conditions for success, often depending on the application's scope and rigor, and that some carry potential risks, not only due to the way they impact on budgets but also how they effect patient access and reward innovation.

In conclusion, EU Member States share concerns for keeping several key issues in balance: controlling pharmaceutical expenditures, ensuring access for patients, rewarding industry for valuable innovations, and maintaining pharmaceutical production, which is associated with employment and income-generation. Most Member States employ a variety of practices as part of their national pharmaceutical policy and frequently introduce changes to counterbalance certain strategies adopted by the industry that might not necessarily coincide with Member States' own priorities.

To date, little evidence is available for key decision-makers on the impact of these different practices. This study summarizes some of the evidence obtained from the literature and has gathered and compared early findings from individual Member States. However, it is based on fragmented inputs and only reflects a situation that existed in one specific period, autumn 2006. It might, therefore, be interesting to consider adopting a more long-term approach, exchanging evidence on a greater number of practices among national authorities.

A. Introduction

I. Scope and purpose of the study

An analysis of the pharmaceutical sector's performance is a complex task due to the convergence of often conflicting social and health goals on the one hand and industrial goals on the other. While innovation and access are usually welcome by all stakeholders, high prices and growing expenditure are bad news from a payer's perspective (consumers and health insurers), but a desirable outcome for suppliers, since it translates into higher revenues and profits for them. A global pharmaceutical policy necessarily has to make trade-offs between these conflicting goals.

A widespread perception exists that the EU is losing leadership in pharmaceutical innovation in favour of other regions, basically the US and Japan (Gambardella et al, 2001). Other emerging economies, such as China, India or Brazil, are also seen as serious competitors to the EU in the future of pharmaceutical innovation. However, the EU is also concerned about issues related to access and equity in health and drug provision, both key elements in building a social Europe for its citizens. Additionally, underlying concerns exist regarding the continuing increase in health expenditures, above all the cost of medicines. Such concerns give rise to the need to strike a balance between ensuring that everyone has access to medicines at a sustainable cost while at the same time encouraging competitiveness, research and development (R&D) in the pharmaceutical industry.

The focus of this report is on assessing the impact of pharmaceutical policy practices, which is a requisite for designing and implementing "evidence-based policies". In order to carry out that task, however, it was necessary to obtain a detailed and comparable picture of present policy practices in EU MS. Pharmaceutical pricing and reimbursement policies are frequently modified, since many regulated parties often find it necessary to adjust their practices in order to reduce or eliminate the negative impact of previous policy decisions.

Pharmaceutical policies and strategies usually consist of a set of individual practices/mechanisms that often influence each other. For instance, a policy on the use of generic drugs often includes many practices to promote their use (generics' substitution, supply-side interventions such as fast-track registration and lower

registration fees, differential co-payments, information and education campaigns, prescription guidelines, reference pricing, financial incentives to physicians, and so on). Practices could either reinforce one another in attaining a desired objective or produce opposite effects. (e.g., both the promotion of generic prescribing and a reference price system are likely to increase competition and access by reducing prices and expenditure). However, some related practices - such as strictly regulated pricing for generics - might negatively affect expenditure and overall savings.

The purpose of this study is, therefore, double. First, to obtain an updated overall picture of how pharmaceutical policies and practices are being applied in European countries. Second, to build an in-depth understanding of selected practices as implemented in different countries, particularly regarding set-up, risks, success factors and impact on expenditure, reward for innovation and patient access.

There is value and need for Member States and authorities to obtain a clear picture of, among others issues, the multiple arrays of regulatory structures and policies currently in place; pricing and reimbursement mechanisms; and the impact of such factors on expected goals. Such information would enable countries to learn from each other when considering policy reforms and specific practices for improvements, and might also help them to predict and prevent conflicts derived from the mutual interaction between varying practices and policies. In turn, it could also help build awareness about what a certain practice might mean in terms of containing costs, rewarding innovation and ensuring patients' access to medicines.

The present study not only sets out to assess evidence on impact in accordance with the kind of relatively restrictive validity criteria employed by academics and researchers, but also to understand what decision-makers consider to be, and what they accept as a proof of, evidence of impact when choosing, implementing or evaluating policies and practices. It also seeks to identify the ways policy-makers monitor and assess the effects of their policies.

II. Methodological issues in assessing the impact of policy practices

Decision-makers draft and implement policies or design interventions in order to attain certain intended goals. They are, therefore, often interested in assessing *a priori* the likely impact of their decisions before they are implemented. They might be also interested in assessing *a posteriori* the actual impact of the decisions.

As this study understands the term, “impact” represents the intended and unintended effects on relevant outcome variables attributable to a given practice; i.e., evidence-based information that suggests a cause-effect relationship. Cause-effect relationships are often asserted or assumed in policy analysis, but are not easily verifiable because impacts are dependent on multiple causes and it is often difficult to allocate the part of

an effect that is attributable to each causal factor, or even to demonstrate that a given factor has any effect at all. Moreover, the impact of a practice might vary, depending on whether it is implemented on its own or as part of a broader set of measures. In any case, as long as policy practices continue to be implemented as parts of a package, assessing the impact of individual practices will be a difficult task at best, and impossible at worst.

A priori assessments can be done: a) in an intuitive, implicit form; b) using a formal, explicit theory; and c) by observing previous similar experiences. Usually a combination of “b” and “c” is likely to provide the strongest available evidence, since a theoretical approach alone cannot provide empirical proof. On the other hand, however, facts do not necessarily speak by themselves and their valid interpretation requires a conceptual or theoretical framework. In order to apply an evidence-based approach in making a specific policy decision it is necessary that:

1. the same or a similar decision has been made in the past, ideally repeatedly
2. the relevant data for assessing the impact has been recorded by a specific monitoring system or by general, well-established information systems, and
3. the data has been analysed validly and the results are available to the decision-maker,
4. and finally, the decision-maker will have to decide whether the evidence on impact is compelling enough (internal validity) and transferable, i.e. whether the intervention will work in the new setting where its application is being planned (external validity).

Monitoring and assessing policy decisions and programs are often assumed to be the responsibilities of those who implement them. This is especially true for monitoring: if it is not implemented as part of the policy, the possibility of obtaining appropriate information might be irreversibly lost. However – unless mandatory - incentives for monitoring are limited, for two main reasons: first, because it detracts resources that could otherwise be allocated to the program itself and second, because policy makers might perceive they get more risks than benefits if the impact is rigorously evaluated than if it isn't.

In economic terms impact assessment is, in fact, a public good. The benefits obtained from assessing health programs accrue to future decision-makers rather than to those responsible for the program in question. As with any public good, the level of provision without some form of public (in our case, international) financing or regulation is likely to be lower than the social (international) optimum.

A posteriori policy assessments can be carried out or sponsored by those responsible for making the decision, by other stakeholders particularly interested in the results, or by independent researchers. Assessments are subject to unintended methodological errors and data limitations, but in many policy areas exists the additional risk of intended bias in order to obtain “scientific” support for specific political interests.

To avoid bias and obtain the best evidence available at a given point in time, there is a growing movement to support appropriate methods for systematic literature reviews and

synthesis of the evidence. The Cochrane Collaboration has played a key role in promoting evidence based on the systematic review of literature and meta-analyses in the field of medical technologies and programs. Regarding health policy issues we found five sources of methodological guidance and current reviews:

1. The Campbell Collaboration
2. The Cochrane Effective Practice and Organisation of Care Group (EPOC), a Collaborative Review Group of the Cochrane Collaboration
3. The Canadian Health Services Research Foundation
4. The Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre)
5. The NHS Centre for Review and Dissemination

It is beyond the scope of this report to enter into a detailed discussion of the procedures involved in systematic reviews and syntheses or the criteria for inclusion or exclusion of studies in the reviews but, generally speaking, the evidence on impact is assumed to be more compelling when it derives from controlled experiments (such as clinical trials), even though such designs are seldom feasible in the field of policy analysis. Natural experiments and/or quasi-experimental studies provide a second quality level of evidence. Retrospective/observational time series analysis might provide acceptable evidence if the appropriate data are available and there is enough variation in the relevant variables and, especially, when a control group is available. Before-after studies without a control group are assumed to provide a weaker type of evidence, although it might still provide some useful information if the data permit modelling an adequate counterfactual. Dowd and Town (2002) attempt to present, in language that is not excessively technical, the basic kind of help senior-level decision-makers need to better understand how findings from health policy studies might be used to inform policy discussions, focusing on the issue of evidence on the causal relationship between measures and effect. Puig-Junoy (2005) adopts a much more focused approach in discussing what is required to evaluate the impact of pharmaceutical reference pricing. He developed a comprehensive check-list of stringent criteria and requirements for study selection in order to review the existing literature, and only 10 papers survived the scrutiny, basically coinciding with those selected by Aaserud et al (2006). He found that most studies refer to therapeutic RP and only one to generic RP. One of the conclusions is that non-experimental approaches require a credible basis for comparison, a counterfactual, which is not easy to construct.

The world of politics and management functions, obviously, under different criteria and constraints. Good evidence to inform policy decisions is probably valued and sought, but decisions are not likely to be postponed until appropriate evidence is available, nor would such behaviour be desirable from society's point of view. (Note that postponing a decision is, in itself, a decision as well). However, it is probably a good practice for decision-makers to: 1) look for the best available evidence, taking into account the cost of getting this evidence and the opportunity costs of delaying the decision, and 2) to ensure that policies and programs are appropriately monitored (at least) end evaluated. Such practices would help generate evidence on impact while at the same time assisting current and future policy-makers in the decision making process.

III. Sources and methodology

As stated earlier, this study aims to bring together academic and policy views on different pricing and reimbursement practices. We have, therefore, decided to base the study on a double set of sources: 1) available literature and 2) inputs provided by authorities and decision-makers in different EU countries.

The glossary¹ developed by the Pharmaceutical Pricing and Reimbursement Information (PPRI) project² has been used sometimes as a reference to ensure consistency and coordination in terminology with other pricing and reimbursement projects.

¹ Any reference to the glossary will appear as a footnote to facilitate comprehensive reading of the document.

² <http://ppri.oebig.at/>

A. Literature

First, a comprehensive review of the literature was undertaken in order to identify and synthesize the most important technical literature available on each practice. This structured review of the literature applied predetermined inclusion and exclusion criteria, critically appraised relevant literature, and extracted and summarized evidence-based data into findings (detailed review and methodology are described in Annex III).

The databases consulted are generally well-known and included: *Medline*, *Web of Knowledge* and *Ovid*. In addition, a specific search in specialized journals was done in the following publications: the *European Journal of Health Economics* and the *Journal of Health Economics*, *Health Policy* and *Health Economics*. The terms used for the search are available in the dictionary of health terminology (Medical Subject Headings of the National Library of Medicine - MeSH terms). It also included key words directly related to pharmaceutical policies, although some of them were not included among MeSH terms. The search strategy was carried out combining Boolean operators with all the descriptors. Links to "related articles" were only considered when the review specifically mentioned an evaluation of pharmaceutical policies in Europe.

The selection was carried out independently by three researchers; differences were resolved through consensus. Data collection and analysis focused on the following aspects: Study Reference, Objectives, Policy Evaluations, Impact/Effect Evaluations, Applied Methodology, Data Used (nature, source, countries, period, etc.), Results, Conclusions and Recommendations.

The researchers then identified a set of studies containing current systematic reviews that assessed the effects of policies for pricing and reimbursing pharmaceuticals. A comparison was done on the criteria applied for selecting the studies which, in the researchers' view, provide acceptable evidence.

Obviously, the more restrictive the criteria applied, the smaller the resulting body of evidence. An extremely restrictive example is provided in a recent review by the Cochrane Collaboration (Aaserud et al, 2006) aimed at determining the effects of pricing and purchasing policies on drug use, health care utilization, health outcomes and costs (expenditures). That review found only eleven studies that satisfied the selection criteria, ten on reference pricing and one on index pricing. Moreover, most of the reference pricing studies referred to senior citizens in British Columbia. This evidence can hardly be generalised to other settings and, as a consequence, the guidance the whole exercise provides to policy makers is quite small.

B. Questionnaire

This study included a questionnaire that, on the one hand, allowed researchers to construct a general picture of different pricing and reimbursement practices used in Member States and, on the other hand, shed light on a selected number (6) of practices and policies currently in application: actual set-up, experiences related to impact (particular those related to budget), patient access and reward for innovation.

The parallel timing of this study with the 2006/2007 sessions of the Working Group on Pricing of the Pharmaceutical Forum allowed the direct involvement of participants of most EU Member States, as well as of some EFTA countries represented in this Working Group.

This questionnaire was presented and distributed to the members of this Working Group in the course of August 2006³. National representatives either filled in the questionnaire themselves or did so with input provided by experts in their administrations. This study is based on their personal responses to that questionnaire and, therefore, does not necessarily reflect official positions of the MS.

We received answers from 25 European countries. In several cases, additional contacts were established between the study team and the national representatives. All replies were obtained during autumn 2006 and are assumed to reflect the situation at that time (some extra information after this period has been sometimes included and referred in a footnote).

Participants attending the Working Group in representation of other organisations and stakeholders (GIRP, EFPIA and AESGP) also had the occasion to answer the questionnaire and to provide their suggestions, comments and additional documentation and information. Some of the answers received by members of the GIRP association defer from the ones received by representatives from the Ministry of Health. On the one hand, this situation proves the complexity of the pharmaceutical terms used in this study and could justify a future single and agreed glossary made by academia and international organizations involved in pharmaceutical issues. On the other hand, the different answers to the same questions could understand as a lack of clearness in the national regulations that gives rise to confusion. Moreover, EFPIA prepared an extensive document that collects the main cost containment measures implemented by some European countries between 2003 and 2005 (by chronological order). Nonetheless, responses mentioned in this study are based exclusively on inputs provided by Member States and the other documentation has been used to verify some of the comparative information (for example, implemented year of one practice) provided by Member States.

³ The questionnaire was sent by electronic mail. Enclosed with it was an attached document titled, “*Overview of Pharmaceutical Policy Practices*,” to help informants to fill out the questionnaire in accordance with the same generally accepted terms and to help avoid misunderstandings regarding certain terminology (for example, reference pricing and international reference price).

B. Overview of pharmaceutical policy practices in EU MS

In most countries, the pharmaceutical market is one of the most heavily regulated. The rationale behind governmental regulation of the pharmaceutical market involves the existence of market failures, concerns regarding equity and accessibility, cost containment, expenditure control, etc. Policy-makers can influence the performance of markets through different types of interventions⁴. They might set up incentives (economic or otherwise) for different actors (manufacturers, wholesalers, physicians, patients, third-party-payers), set up or remove existing constraints to their behaviour, provide certain goods, such as information, finance or subsidies, etc.

Interventions in the pharmaceutical market can be classified according to several criteria: the nature of the intervention (providing information and incentives, setting constraints, etc), stated or assumed purposes, the groups of actors targeted, the organization in charge of the intervention, and so on.

Most interventions have more than one effect and might, therefore, be associated with more than one objective. The focus of our study's impact analysis is on three effects:

- a) ensuring (efficient and equitable) access⁵ to medicines,
- b) providing adequate incentives for innovation, and
- c) expenditure control.

These are often conflicting objectives. Whether and to what degree these conflicting objectives are attained by a given intervention is often a matter of analysis and empirical evidence.

There are other potential objectives, such as supporting domestic production, along with different ways to formulate them. For instance, expenditure control might refer only to pharmaceutical expenditure or to global health expenditure. Improving the effectiveness, safety and quality of pharmaceuticals, or promoting their rational use, are

⁴ Various terms are often used as synonyms for intervention, such as, practice, mechanism, measure, etc.

⁵ PPRI: Access: The ability to obtain health care, as determined by factors such as the availability and affordability of **goods** and services.

often formulated as self-standing policy objectives, but it can also be assumed that they are implicit in the objective of attaining efficient access.

I. A classification and definition of pharmaceutical policy practices

We will use the term “practice” as a synonym for intervention, measure, mechanism or regulation to refer to well-defined, structured and systematic actions by regulators and large third-party payers that affect the rules and functioning of a market or agents’ behaviour.

The usual distinction between supply and demand-side interventions refers to the two basic economic units of a market: suppliers and demanders. In the case of pharmaceutical markets, demand is usually not determined by a single decision-making unit but by, at least, three of them: the patient/consumer, the prescriber and the pharmacist. Moreover, the consumer does not directly pay for medicines (out-of-pocket) in most developed countries since they are often partially, or completely, financed by a third party payer, either a public or a private insurer. In the EU the share of pharmaceutical expenditure paid by third-party payers accounts for over 75% of the total market (Mrazek 2002). This subsidisation obviously affects the demand for pharmaceuticals, which becomes larger than it would if consumers had to pay for pharmaceuticals exclusively from their disposable income. The supply side of pharmaceutical markets refers mainly to drug manufacturers, although all economic units involved in the life cycle of a drug are also part of that group. The distinction between supply and demand-side units and interventions is, to some extent, a conventional one. For instance, it is not perfectly clear whether pharmacists should be classified in the demand or in the supply side of the market. Here for this exercise we will consider pharmacists as demand side.

Supply side practices

Price regulation.

This can also be referred to as product price control, administrative or statutory pricing⁶, and price cap⁷.

It usually consists of a fixed or a maximum price that applies to the manufacturers’ price (direct manufacturers’ price regulation, price cap). Different pricing procedures

⁶ PPRI: Statutory pricing: Pricing system, where pharmaceutical prices are set on a regulatory basis (e.g. law, enactment, decree).

⁷ PPRI: Price cap: a cost-containment measure that fixes ex-ante the maximum price of a pharmaceutical, e.g. taking into consideration inflation rates and production costs. Companies are allowed to choose any price below this threshold and, in exchange, authorities refrain from further control of company data (profit margins, sales etc.).

exist: regulation may apply to the initial price when the product is marketed (*initial price*) and/or to *posterior price changes*, which allow regulators to set *price freezes*⁸.

- 1) The price might be calculated on the basis of costs, plus a certain profit margin (*cost-plus pricing*⁹),
- 2) It can also be based on the prices for the same product in other countries, which is often referred to as “external price referencing¹⁰”, cross-country referencing and “international price comparison”
- 3) It might also be based on the cost of similar treatments for the same indication (*internal price referencing*¹¹ or *reference pricing*).
- 4) Finally, price and reimbursement decisions might derive from economic evaluations that compare the new treatment with existing therapies (*based on cost-effectiveness analysis*¹² and other forms of economic evaluation).

Some countries list several of the former criteria as the basis for price setting.

Direct Expenditure Control

Price control policies are often unable to contain pharmaceutical expenditures because utilization grows without control. Therefore, some old and new practices directly point to price control as one variable that impacts pharmaceutical expenditure¹³.

- 1) *Discounts*¹⁴ are mandatory or negotiated reductions in the drug’s final price for certain institutional payers, while
- 2) *Rebates* are returns of a specified proportion of the sales made by a manufacturer to an institutional purchaser over a given time period (as, for example, in Germany, Ireland and Spain’s newly proposed system).
- 3) *Payback* is a risk-sharing mechanism that requires manufacturers (either individually or collectively, e.g. via their industry association) to return a certain part of their “excess” revenue to a purchaser if sales exceed a previously determined target.
- 4) Price-volume agreements¹⁵ are usually applied to single new products, where the price agreed is conditional to the expected number of units sold (France, Spain).

⁸ PPRI: Price freezes: a popular cost-containment method. The price of a pharmaceutical is fixed at a given level, mostly for a predetermined period of time. Price freezes are sometimes based on agreements between the pharmaceutical industry and authorities, but in most cases it is done by law.

⁹ PPRI: Cost-plus pricing: pricing procedure which take not only take into account the production cost of a pharmaceutical product but other costs as well, such as promotional expenses and especially a profit margin for fixation of the price into account. This share is usually expressed as a percentage of the cost.

¹⁰ PPRI: External price referencing: the practice of comparing pharmaceutical prices across countries. Various methods are applied and different country baskets are relevant.

¹¹ PPRI: Internal price referencing: a method to compare prices of pharmaceuticals in one country with the price of identical pharmaceuticals (ATC 5 level) or similar products (ATC 4 level) or even with therapeutically equivalent treatment (not necessarily a pharmaceutical) in another country. Often performed in the course of a reference price system.

¹² PPRI: Cost-effectiveness analysis: compares the cost-per-unit of outcome of various alternative therapies in order to identify the most efficient one. Determines the cost incurred to obtain an increase in health benefit.

¹³ Expenditure = Price * Quantity

¹⁴ PPRI: Discount: a price reduction granted to specified purchasers of a pharmaceutical.

A posterior increase of the units sold and, hence, on the expenditure on the product, might lead to either a return of the excess expenditure or to a posterior price reduction.

Profit Control

This refers to a system applied in the UK for the sales of branded medicines to the NHS. It can be defined as an indirect price control mechanism.

Tax benefits

They might be linked to investment in R+D or in manufacturing capacity (Belgium, for example).

Demand side practices

Demand side practices are aimed at changing the behaviour of agents that jointly determine the demand for medicines, i.e. physicians, patients and pharmacists. It could certainly be argued that reimbursement mechanisms are also demand side practices, since reimbursement by a third party payer clearly affects the demand.

Aimed at Physicians

Physicians' behaviour might be affected by:

1. *Clinical practices' guidelines and prescription guidelines*
2. *Educational and information methods* (such as prescribing advice, computerized decision support, etc.),
3. *Monitoring of prescribing patterns*, and
4. Establishment of *prescription quotas* (e.g., percentage of generic prescribing in Spain) and *pharmaceutical budgets*¹⁶.

All these mechanisms might be reinforced by *financial or non-financial incentives* for good prescribing practice in an attempt to reinforce behavioural changes, stimulate cost-consciousness, and promote a more rational use of medicines (maximize effectiveness, minimize risk, minimize cost).

Aimed at Patients

¹⁵ PPRI: Price-volume agreement: Similar to a framework agreement, a volume control tool. An agreement is reached between public authorities and a manufacturer regarding the price of a pharmaceutical based on a forecast of its sales volume. If the actual sales volume exceeds the forecast, the price of the pharmaceutical is usually revised downwards.

¹⁶ PPRI: Pharmaceutical budgets: Pharmaceutical budgets are a cost-containment measure of third party payers. The maximum amount of money to be spent on pharmaceuticals in a specific region or period of time is fixed ex-ante.

Cost-sharing is the most widespread and traditional mechanism aimed at patients/users. *Cost-sharing* might take the form of 1) a (*fixed*) *co-payment*¹⁷ or fee, 2) a *co-insurance or percentage co-payment*¹⁸ (a fixed or variable % of the price) and 3) a *deductible*¹⁹, etc. Patient behaviour might also be affected by *information and educational campaigns*.

Aimed at Pharmacists

Substitution²⁰ is the (mandatory or voluntary) capacity of pharmacists to change a brand prescription for a cheaper (generic) medicine, in order to reduce the cost of prescribed treatments while maintaining a standard quality.

The traditional pharmacy mark-up²¹ or fixed *pharmacy margin*²² system of retribution for pharmacists is often seen as providing inadequate incentives to pharmacists; it appeals to their financial interest in selling higher-priced drugs and, in general, to increase sales. *Other financial incentives for dispensing practices* might include any alternative system or remuneration scheme (salary/lump sum, capitation, dispensing fee²³, differential mark-ups, e.g. higher mark-up for generics or lower-priced products, etc.) that removes incentives to sell more and at higher prices.

*Claw-Back*²⁴ refers to discounts of pharmacies' dispensing fees that accrue to the third party payer (UK) or discounts on pharmacy purchase costs of drugs (The Netherlands).

Financing / Reimbursement²⁵

¹⁷ PPRI: Fixed co-payment: an out-of-pocket payment in the form of a fixed amount (for example, a prescription fee) to be paid for a service, a pharmaceutical or a medical device.

¹⁸ PPRI: Percentage co-payment: cost-sharing in the form of a set proportion of a service or product's cost. The patient pays a certain fixed proportion a service or product's cost, while the social health insurance / national health service pays the remaining proportion.

¹⁹ PPRI: Deductible: out-of-pocket payment in the form of a fixed amount which must be paid for a service or of total cost incurred over a defined period by a covered person beforehand a social health insurance / national health service, then all or a percentage of the rest of the cost is covered.

²⁰ PPRI: Generic substitution: practice of substituting a pharmaceutical, whether marketed under a trade name or generic name (branded or unbranded generic), by a pharmaceutical, often a cheaper one, containing the same active ingredient(s). Generic substitution may be performed by prescribers (doctors) and in some countries also by dispensers (pharmacists).

²¹ PPRI: Pharmacy mark-up: The gross profit of pharmacies expressed as a percentage of the pharmacy purchasing price

²² PPRI: Pharmacy margin: The gross profit of pharmacies expressed as a percentage of the pharmacy retail price.

²³ PPRI: Dispensing fee: pharmacists' payment of fees for the service of dispensing a pharmaceutical.

²⁴ PPRI: Claw-back: A system allowing third party payers to recoup (part of the) discounts/rebates granted in a reimbursement system involving various stakeholders, e.g. wholesalers and pharmacists.

²⁵ PPRI: Reimbursement: Reimbursement is the cost percentage (of a service or a pharmaceutical) paid for by the social health insurance / national health service. A 100% reimbursement means that the social health insurance/national health service accepts 100% of the costs for a pharmaceutical or service. Pharmaceuticals eligible for reimbursement are often grouped according to selected characteristics, e.g. route of administration (oral, etc.), main indication (oncology, paediatric, etc.), ATC level, classification (hospital-only, etc.). In many countries different reimbursement rates are determined for different reimbursement categories.

Most third party payers apply the principle of selective financing, meaning that not all products are equally reimbursed. This principle might be implemented at the product or group level by means of *positive lists*²⁶ and *negative lists*²⁷. (Sometimes the reimbursement status is defined not exclusively by the product itself, but also by this indication). A negative list can be also being seen as 100% cost-sharing.

*Reference pricing systems*²⁸ set a fixed reimbursement level for all products in a given group or cluster of products. Since it defines the amount of the price to be paid by the third-party payer for the drug (and consequently by the user, in addition to possible co-payment), reference pricing could also be considered a form of cost-sharing, particularly if manufacturers do not lower drug prices to the reference price level and leave consumers the option to pay the difference²⁹.

Finally, some countries use *economic evaluations* to assist in their decisions on reimbursement (and, implicitly, pricing) of new products.

The following two tables give an overview of which European countries use which of these particular practices, based on the replies received to the questionnaire.

²⁶ PPRI: Positive List: List of pharmaceuticals that may be prescribed more or less without further conditions at the expense of a social health insurance / national health service.

²⁷ PPRI: Negative List: List of pharmaceuticals which cannot be prescribed at the expense of the social health insurance/ national health service.

²⁸ PPRI: Reference Price System: The social health insurance / national health service determines a maximum price (= Reference Price) to reimburse certain pharmaceuticals. When an insured person purchases a pharmaceutical product for which a fixed price has been established (~ the so-called reimbursement price), he or she must pay the difference between the fixed price and the actual pharmacy retail price of the product in question, in addition to any fixed co-payment or percentage co-payment rates that might apply. Usually the reference price is the same for all pharmaceuticals in a given ATC 4 level and/or ATC 5 level group.

²⁹ Reference price systems should be clearly differentiated from the external and internal price referencing practices indicated above; the former practice being a means of financing/reimbursement, and hence a demand-side measure, with the latter being a form of direct price control, hence a supply- side measure.

Table 1: Overview Supply Side³⁰

	Product price regulation							Control of expenditure					Industry regulation			Product reimbursement				
	Initial price decision based on clinical performance	Initial price decision based on economic evaluation	Initial price decision based on cost of existing treatments	Initial price decision based on cost-plus calculations	Initial price decision based on international prices	Controlled price updates	Other	Use of discounts / rebates	Payback	Price-volume agreements	Use of price-freezes and cuts	Other	Profit control	Tax benefits	Others	Reference Price System	Positive lists	Negative lists	Based on economic evaluation	Other
AT	ü	ü	ü		ü		ü		ü			ü					ü		ü	
BE	ü	ü	ü		ü	ü					ü					ü	ü		ü	
CY				¼	ü								¼	ü			ü			
DE									ü							ü		ü		
DK							ü			¼	ü					ü			ü	
EE		ü	ü		ü					ü						ü	ü		ü	
EL				ü ¼	ü	ü			ü		ü					ü	¼		¼	
ES	ü		ü	ü	ü	ü			¼	¼	ü			ü		ü	¼	¼	ü	
FI	ü	ü	ü		ü	ü	ü			ü	ü						ü	ü	ü	
FR	ü		ü		ü				ü	ü	ü						ü	ü	ü	
HU			ü		ü				ü	ü	ü			ü		ü	ü	ü	ü	
IE	ü	ü	ü		ü				ü	ü						ü	ü	ü	ü	
IT	ü	ü	ü		¼	ü			ü					ü		ü	ü		ü	
LT					ü	ü										ü	ü		ü	
LV	ü	ü	ü			ü										ü	ü		ü	ü
MT																	ü		ü	
NL					ü						ü					ü	ü		ü	
NO					ü					ü	ü					¼	ü	ü	ü	
PL	ü				ü											ü	ü		ü	
PT	ü	ü	ü		ü	ü	ü			ü	ü			ü		ü	ü		ü	ü
RO					ü	ü			ü		¼			ü		ü	ü	¼	ü	
SE	¼	ü	¼		¼		ü		¼							¼	ü		ü	
SK	ü	ü			ü	ü			ü							ü	ü		ü	
SI		ü			ü	ü	ü									ü	ü		ü	ü
UK						ü	ü				ü			ü	ü		ü		ü	ü

ü Currently applied

¼ Once applied but discontinued

Source: Data from EASP's questionnaire.

³⁰ Some countries use the product price regulation only for reimbursable pharmaceuticals. Please see details in the overview preceding table 3.

Table 2: Overview Demand Side

	Physicians							Patients			Pharmacists			
	Clinical practices /prescriptions Guidelines	Educational and information	Monitoring of prescribing patterns	Prescription quotas	Pharmaceutical budgets	Financial incentives	Other	Information education campaigns	Cost sharing	Other	Generic substitution	Financial incentives	Claw-back	Other
AT	ü	ü	ü			ü		ü	ü				ü	
BE	ü	ü	ü	ü		ü		ü	ü				ü	
CY											ü			
DE	ü	ü	ü	ü		ü		ü	ü		ü			
DK	ü	ü	ü					ü	ü		ü			
EE	ü	ü					ü	ü	ü					
EL			ü					¼	ü					
ES	ü	ü	ü	ü	ü	ü		ü	ü		ü	¼		ü
FI	ü	ü	ü					ü	ü		ü			ü
FR	ü	ü	ü					ü			ü	ü		
HU	ü		ü						ü		ü			
IE		ü	ü			¼		ü	ü			ü		
IT	ü	ü	ü					ü	ü		ü	ü	ü	
LT	ü			¼		¼			ü					
LV	ü	¼	ü	ü	ü			¼	ü		ü			
MT	ü	¼	¼							ü	ü			ü
NL	ü	ü	ü			ü		ü	ü		ü	ü	ü	
NO	ü	ü	ü	ü					ü		ü	ü		
PL		ü						ü	ü		ü		ü	
PT	ü	ü	ü				ü	ü	ü	ü	ü			ü
RO		ü	ü		ü			ü	ü		ü			ü
SE	ü	ü	ü		ü	ü		ü	ü		ü			
SK	ü	ü	ü	¼	¼			ü	ü		ü			
SI	ü	ü	ü								ü			ü
UK	ü	ü	ü		ü	ü		ü	ü			ü	ü	

ü Currently applied

¼ Once applied but discontinued

Source: Data from EASP's questionnaire

II. Selection of 6 policy practices for detailed analysis

A subset of six practices was selected for detailed analysis. The aim of the selection was to include relevant practices in accordance with several criteria. One criterion was to include practices from both the supply side (such as a price control and payback) and the demand side (such as cost-sharing and incentives for good practices), traditionally used for controlling public pharmaceutical expenditure. Some relatively new practices were also included (such as a payback, which could prove to be of special interest because it has not been previously studied in detail), and reference pricing, for which a large number of studies are available. The final criterion was also to select policies that include several practices; for example, generics' policies that include different practices such as generic substitution by pharmacists, financial incentives for physicians, fast-track registration or incentives for good prescribing, which include education, prescription guidelines, financial incentives, etc

Accordingly, the following practices and policies were selected:

- Price control
- Cost-sharing
- Reference pricing
- Payback
- Incentives for good prescribing practices
- Generics' policies

C. Selected practices

Price control

I. Introduction

Description

Price control is a form of market regulation that limits the capacity of the supplier to set the price of a product. Price control usually takes the form of a maximum price (ceiling), which means that the supplier is allowed to set a lower price.

Price control usually affects the ex-factory (manufacturer's) price, but other price components, such as wholesaler's and pharmacist's mark-ups, might also be regulated. Although the initial price is set product-by-product, posterior updates to compensate for inflation are usually applied to the whole market.

Price control is probably the oldest form of trying to control pharmaceutical expenditures and improve drug affordability. Many countries use it, with the most relevant exception being the US. In Europe it is used by Denmark, Germany, Malta, Sweden and the UK. Some European countries have replaced direct price control by indirect control modalities (profit control, cost-sharing, reference pricing) and alternative forms of expenditure containment and competition. Curiously, price regulation is less prevalent among developing countries, where it has been often removed as a consequence of the requests and recommendations of developed countries and international development organisations, but has often not been substituted by alternative cost-containment measures.

Pharmaceutical products are protected by patents and other forms of market exclusivity during their first years in the marketplace. This allows innovators to have a temporary monopoly that impedes price competition. European countries frequently decide to regulate the prices of pharmaceutical products because their governments are increasingly involved in financing them.

In order to control public spending on pharmaceuticals and ensure the population's access to medicine (price control as social welfare), governments use different types of price regulation. Such practices consequently result in different prices for the same medicines in different countries. If the prices are not directly regulated, they are often restricted by reimbursement policies.

The mechanics of price-control usually differ from country to country, but the end result is normally the same: the pharmaceutical companies are prohibited from charging a market-based price for the products they manufacture.

Modalities

In this chapter we focus on what is often called administrative price control, product price control or direct price control, where the maximum selling price of each product is directly set by the regulator.

Other forms of regulation can indirectly affect the price of pharmaceuticals. One of the most well-known examples can be found in the UK's system, the Pharmaceutical Price Regulation Scheme, which limits the profits of manufacturers who supply branded medicines to the NHS, requiring either the return of excess profit and/or a reduction of prices. Under that system manufacturers are, however, free to set the (relative) prices of single products and the effects are very different from direct price control systems.

One of the most important differences among direct price control systems is the way the (maximum) price is determined. According to a particular country's regulations, the price might be set by one or more of the following criteria:

- § Clinical performance
- § Economic evaluation (cost-effectiveness ratios)
- § Cost of existing treatments for the same condition or disease
- § Cost-plus calculations (cost of production plus a certain profit margin)
- § International prices of the product
- § Innovative character of the product

Purposes

The main purpose of price control is to limit (control, contain) private and public pharmaceutical expenditure in order to ensure the affordability of patient treatment and the financial sustainability of the health system.

In Europe, the average share of public pharmaceutical expenditure is approximately 75% of total pharmaceutical expenditure. Clearly, States are interested in having a sustainable public pharmaceutical budget and in ensuring that they get good value for money spent.

Theory/rationale

From an economic perspective price control is justified when the market does not lead to an optimal price, i.e., the minimum price required to compensate suppliers in order to maintain the production that meets society's demand. In the case of an innovative industry which is expected to recover the investment on R&D from the price of the products it sells, the price should be high enough not only to cover the current costs of production, but also to recover over time the previous expenditure on R&D and to earn a profit with an appropriate premium to account for the inherent risks of the innovation activity. Intellectual Property Rights (IPR), trade marks and other market exclusivity privileges are some of the main tools used in many countries to provide the needed incentives, by temporarily protect the innovator from competition.

The legal monopoly provided by IPR (besides other causes of market exclusivity, and the lack of or the limited price sensitivity of the demand) is one of the main justifications of pharmaceutical price regulation, as governments are usually concerned by the problems of affordability of the population to medicines and by the expenses borne by the public health systems.

II. Application in Europe

Overview

1. Price control used only for reimbursable pharmaceuticals: Austria, Finland, France, Ireland, Italy, Latvia, Lithuania, Poland, Slovenia, Spain
2. Price control used for all products: Belgium, Cyprus, Hungary, Greece, Slovakia
3. Price control used for all products (except OTC): Norway, Portugal, Romania
4. No (direct) product price regulation: Denmark, Germany, The Netherlands, Malta, Sweden, UK

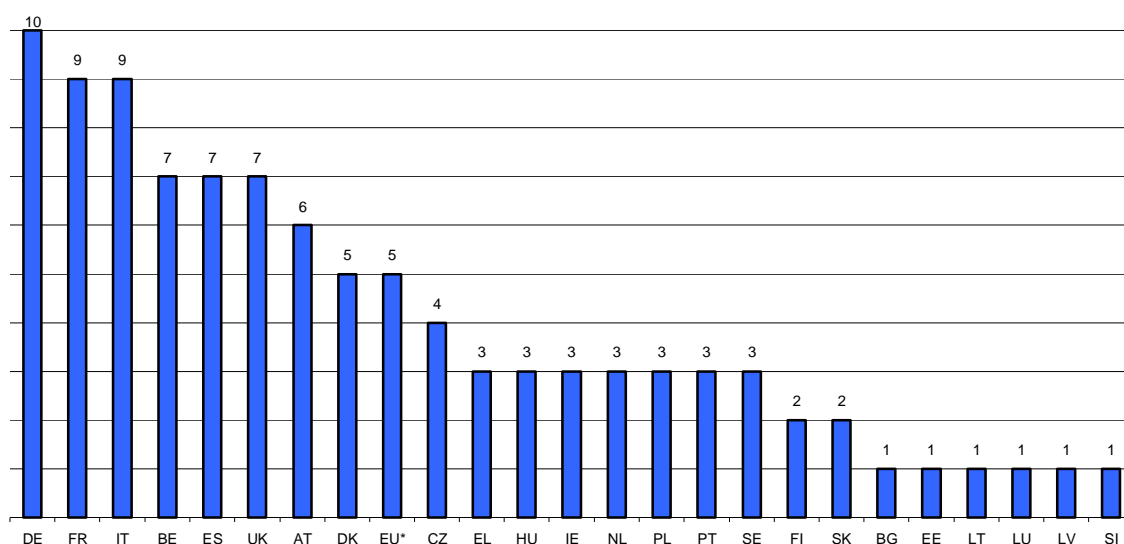
Table 3: Pharmaceutical Price Regulation in Europe

	Product price regulation						
	Initial price decision based on clinical performance	Initial price decision based on economic evaluation	Initial price decision based on cost of existing treatments	Initial price decision based on cost-plus calculations	Initial price decision based on international prices	Controlled price updates	Other
AT	ü	ü	ü		ü		ü
BE	ü	ü	ü		ü	ü	
CY				¼	ü		
DE							
DK							ü
EE		ü	ü		ü		
EL				ü ¼	ü	ü	
ES	ü		ü	ü	ü	ü	
FI	ü	ü	ü		ü	ü	ü
FR	ü		ü		ü		
HU			ü		ü		
IE	ü	ü	ü		ü		
IT	ü	ü	ü		¼	ü	
LT					ü	ü	
LV	ü	ü	ü			ü	
MT							
NL					ü		
NO					ü		
PL	ü				ü		
PT	ü	ü	ü		ü	ü	ü
RO					ü	ü	
SE	¼	ü	¼		¼		ü
SK	ü	ü			ü	ü	
SI		ü			ü	ü	ü
UK						ü	ü

ü Currently applied
¼ Once applied but discontinued

Source: Data from EASP's questionnaire

Graph 1: Countries used as international references



*EU as one country

Source: Data from EASP's questionnaire

Table 4. International Price Reference

	AT	BE	CY	EL	ES	FI	FR	HU	IE	LT	LV	NL	NO	PL	PT	RO	SK	SI
CRITERIA	Average	Average and Minimum	Average	Average	Minimum	Others	Others	Minimum	Average	Average (95%)	Others	Average	Average (three lowest)	Other	Minimum	Minimum	Average (not exceed 10 % three lowest)	Average
COMPARE	Ex-factory and wholesale level	Ex factory and retail	Wholesale	Ex-factory	Ex-factory	Wholesale s	Ex-factory	Ex-factory	Ex-factory	Ex-factory	Ex-factory	Ex-factory	Pharmacy purchase s	Ex-factory	Ex-factory	Exfactory	Ex-factory	Wholesale
COUNTRIES REFERENCE	AT	BE	CY	EL	ES	FI	FR	HU	IE	LT	LV	NL	NO	PL	PT	RO	SK	SI
AT			X			X		X	X				X			X	X	
BE			X		X	X		X	X				X					
BG																X		
CY																		
CZ								X		X						X	X	
DE			X			X	X	X	X			X	X			X	X	X
DK			X			X			X				X			X		
EE										X								
EL			X			X		X										
ES			X			X	X	X	X						X		X	
FI									X				X					
FR			X		X	X		X	X			X			X		X	X
HU										X						X	X	
IE						X		X					X					
IT			X		X	X	X	X							X	X	X	X
LT																X		
LU						X												
LV										X								
MT																		
NL						X			X				X					
NO																		
PL										X						X	X	
PT			X			X		X										
RO																		
SE			X			X							X					
SK								X		X						X		
SI								X										
UK					X	X	X		X			X	X			X		
EU*	X	X		X							X			X				

* EU as one country

Source: Data from EASP's questionnaire

Individual replies to the questionnaire³¹

Austria

In Austria, the pricing and reimbursement systems are very closely linked, since there are separate pricing rules for pharmaceuticals still awaiting approval for inclusion into the Reimbursement Code (EKO). Pharmaceuticals included in the Reimbursement Code (EKO) have to be priced either at the EU average price, as established by the Pricing Committee (PK), or below this price. The EU average price serves as a maximum price.

The overall framework for pricing builds the Price Act (Art.3.1 Price Act 1992), and, in addition to this Act, the Federal Chamber of Labour (BAK) and the Federal Chamber of Commerce (WKÖ) have agreed on a system of price notification.

A price notification system for all pharmaceuticals (on- and off-patent, POM or OTC) exists at the manufacturer's price level, while the Federal Ministry of Health and Women's Issues (BMGF), advised by the Pricing Committee (PK), calculates the EU average price, applicable to all pharmaceuticals eligible for reimbursement. Furthermore, there are statutory wholesale and pharmacy mark-ups for all pharmaceuticals.

In Austria, external price referencing is used to calculate the EU average price of reimbursable pharmaceuticals. The EU average price is set according to regulations on procedural rules for calculating the EU average price (Art. 351c.6 ASVG).

Pharmaceutical companies applying for reimbursement must provide information on, among other things, the ex-factory and the wholesale price of their product in all of the other 24 EU Member States. Pharmaceutical companies need to use a standard form, which was developed by the Price Committee, *Gesundheit Österreich GmbH*. Geschäftsbereich ÖBIG is responsible for checking the prices submitted by the industry. Prices are compared per piece with the same strength, same package size and same dosage. Prices are compared at the ex-factory and wholesale level. The formula used to set the price reflects the average price per unit of all 24 EU Member States.

Cyprus

Pricing decisions are made independently from reimbursement decisions in Cyprus, and price regulation is applied to all products.

The countries used as references are Sweden, Austria, France and Greece; alternative countries used include Denmark, Germany, Italy, Belgium, Portugal and Spain. The wholesale price is compared and the main criterion used to set the price is the average price of specific products in selected countries.

³¹ The text included in sections under the heading of "*Individual Replies to the Questionnaire*" has been based on the responses to the questionnaire. The authors have only edited their replies for clarity. Any additional information included by the authors to help in understanding the text will be marked as "*Authors' note*".

The cost-plus method is used for locally manufactured products; however, the final wholesale price cannot exceed 80% of the original. The “plus” is 3% for shipping and handling and the resulting price is the wholesale price.

Denmark

Free pricing is the norm in Denmark. However, reimbursement may be denied if the price is found to be too high in comparison to other pharmaceuticals or alternative treatments for the same disease.

Companies can change their prices every two weeks. However, in December 2006 the Danish Association of the Pharmaceutical Industry (Lif) and the Danish Ministry of Health and the Interior agreed that until the end of 2008 the price of prescription medicines in receipt of a general reimbursement, including general restricted reimbursement, could not be raised above the individual package price in effect on August 30, 2006.

For the period covering 2000-2005 Denmark used a “basket” of countries to assess the reimbursement price, i.e. the figure from which the reimbursement was calculated, cf. section on cost-sharing/Denmark.

Finland

Price and reimbursement decisions are made jointly except for the application of price increases, which only affects prices. Price regulation applies only to reimbursable products.

The following criteria are used to assess the reasonableness of a proposed wholesale price:

- treatment costs incurred from use of the medicinal product and benefits that accrue from its use, including both the patient and the total costs of healthcare and social services
- benefits and costs incurred from other available treatment alternatives
- prices of comparable medicinal products in Finland
- prices of medicinal products in other EEA countries
- manufacture, research and product development costs of medicinal products and
- funds available for reimbursement³².

The Finnish wholesale price is calculated on the basis of prices in other countries. The countries taken into account when assessing the reasonableness of the wholesale price are: The Netherlands, Belgium, Spain, Ireland, Iceland, United Kingdom, Italy, Austria, Greece, Luxemburg, Norway, Portugal, France, Sweden, Germany and Denmark. None of the individual countries has a special status in price comparison.

³² <http://www.stm.fi/Resource.phx/eng/orgis/board/pharmaboard/legislation.htx>
<http://www.stm.fi/Resource.phx/eng/orgis/board/pharmaboard/legislation.htx.i201.pdf>
<http://www.stm.fi/Resource.phx/eng/orgis/board/pharmaboard/legislation.htx.i209.pdf>
<http://www.stm.fi/Resource.phx/eng/orgis/board/pharmaboard/legislation.htx.i212.pdf>

Since 1999, whenever a medicinal product contains a new active substance, all applicants seeking confirmation of a wholesale price are required by law to include a pharmacoeconomic evaluation in their application. Those pharmacoeconomic evaluations are assessed by the Pharmaceuticals Pricing Board and utilised in the decision-making process. The guidelines for preparing a pharmacoeconomic evaluation are provided by the Ministry of Health and Social Affairs. Therapeutic practices and costs used in the evaluation should be adjusted to correspond to Finnish treatment practices and cost structures. A *maximum willingness to pay threshold* (cost per QALY) is not explicitly set.

If the applicant wants the medicine's R&D expenses and manufacturing costs to be considered, a statement of those costs is required. The figure the applicants usually submit is the average sum of R&D and manufacturing costs published by EFPIA. Product-specific figures are seldom presented.

If the applicant has shown the relative effectiveness and benefits to be gained from the use of a product compared to other available treatment alternatives, a higher price may be confirmed. The cost-plus is determined on a case-by-case basis.

A higher price may be approved for the most highly demanded pharmaceutical form than for other pharmaceutical forms. The cost-plus is maximum +20 %. In special cases a higher cost-plus may be approved.

The applicant submits information on manufacture, research and product development costs to the Pharmaceuticals Pricing Board, as well as a justification for the cost-plus request.

France

In France price and reimbursement decisions are taken together, but only reimbursable products are price controlled.

The countries used as a reference for international prices are the UK, Germany, Spain, and Italy, using ex-factory price for comparisons (products that are at least ASMR³³ III). For others products, it is mostly comparison with existing drugs (IV-VI). To obtain an ASMR V, the price needs to bring savings to the system.

The criteria used to set prices is "coherent price" similar with selected countries

³³ Authors' Note: In France, there are six different levels of ASMR (*l'amélioration du service médical rendu*) according to the level of innovation. The levels are:

I = innovative product of significant therapeutic benefit

II = product of therapeutic benefit, in terms of efficacy and/or reduction in side effect profile

III = already existing product, where equivalent pharmaceuticals exist; moderate improvement in terms of efficacy and/or reduction in side effect profile

IV = minor improvement in terms of efficacy and/or utility

V = no improvement but still granted recommendations to be listed

VI = Negative opinion regarding inclusion on the reimbursement list

(http://news.investinfrance-nordic.org/old/2/download/how_to_be_reimbursed_2000.pdf)

Greece

In Greece, price and reimbursement decisions are made independently and all pharmaceutical products are regulated.

The price of new medicinal products is established according to a figure calculated on an average of the three lowest prices among EU-25 countries (two EU-15 countries + Switzerland and one among the 10 new access countries). Ex-factory prices are compared. The formula used to set prices is based on the average price of a given drug in selected countries

The cost-plus formula is used only for locally developed and manufactured products, taking into account R&D and industrial cost. The plus added covers administration, promotion, and distribution costs.

The sources of information used to define the cost-plus price are the *"Indices from the Ministry of Development-General Secretariat for Commerce,"* among others.

Hungary

Price decisions are independent from reimbursement decisions. The National Health Insurance Fund (NHIF) makes the decision on reimbursement – which depends on the price offered - but the NHIF is not entitled to negotiate the price.

The Minister of Health Regulation has declared three price control practices:

1. International price control - the ex-factory price of the product cannot be higher than the lowest price of drugs with the same active substance in the European Economic Area. The countries used as reference are France, Ireland, Germany, Spain, Portugal, Italy, Greece, Poland, Czech Republic, Slovenia, Slovakia, Belgium, Austria, Cyprus, Denmark, United Kingdom, Estonia, Finland, Iceland, Netherlands, Latvia, Lichtenstein, Lithuania, Luxembourg, Malta, Norway, Sweden, Bulgaria and Romania.
2. The first generic price must be 70% lower than the original drug's price;
3. Within an existing fixed reimbursement reference price group a new generic drug's price cannot be higher than the group's reference price. Reference price groups and reference prices (prices per unit, daily therapeutic costs) are re-evaluated 4 times a year.

A price-freezing system operates in Hungary that does not allow manufacturers to raise the price of reimbursable products during a 2-year period, which enters into effect once the reimbursement decision is made. Exceptions to this system can be made if:

- The drug is recommended for first line treatment and
- The manufacturer is able to prove that his manufacturing cost is higher than the recently established price.

Ireland

Prices are determined within the reimbursement application and approval process. Price control is only for reimbursable products³⁴.

The countries used as a reference are Belgium, Denmark, France, Germany, Netherlands, Spain, UK, Finland and Austria. The price used for comparisons is the ex-factory price with the criteria of average price of selected countries, as available. Prices reviewed against reference countries at two and four years.

³⁴ Authors' Note: Article 5 (Pricing) of the Agreement between the Association of Pharmaceutical Manufacturers of Ireland and the Health Services Executive on the supply terms, conditions and prices of medicines supplied to the health services (i.e. the GMS and other community drugs schemes), the HSE, state-funded hospitals and state agencies whose functions normally include the supply of medicines.

5. PRICING

5.1 Price Freeze

The price to wholesaler of each item of medicine covered by this Agreement will not be increased for the term of the Agreement (save as might be required under Clauses 5.3, 5.4 and 11.3)

5.2 Price of New Medicines

The price to wholesaler of any new medicine introduced to Ireland following the commencement of this Agreement shall not, on the date of initial price notification to the HSE, exceed the currency adjusted average price to wholesaler in the nominated EU member states.

If any new medicine is not available in all nominated EU states on the date of initial price notification to the HSE, the Irish price to wholesaler shall not exceed the currency adjusted average price to wholesaler in the nominated EU States in which the new item of medicine is available.

If a new medicine is not available in any of the nominated EU States, the Irish price to wholesaler will be agreed between representatives of the manufacturer or importer concerned and the HSE within 60 days of the date of the reimbursement application.

5.3 Price Monitoring and Review

The price to wholesaler of any new medicine introduced to Ireland under this Agreement shall be realigned to the currency-adjusted average price to wholesaler in the nominated EU member states in which the medicine is then available, two years and four years following the commencement of the Agreement.

Price changes (if any) resulting from these realignments will be implemented within 60 days of the realignment date. No realignment will be required within 12 months of the date of reimbursement approval.

5.4 Price Modulation

Product price modulation will be permitted under this Agreement, on an exceptional basis and in condition that any such product price modulation will be demonstrably cost neutral for the State in each year of the Agreement.

The HSE may require audited documentation of any price modulation and shall have the sole discretion to accept, reject or seek variation in any modulation application and to seek an appropriate refund if the terms of this clause are not adhered to.

5.5 Applicable Exchange Rates

The applicable exchange rates for initial price notification of medicines will be the exchange rates published by the Central Bank of Ireland, on the date of price notification or realignment.

5.6 VAT

Prices referred to in this Agreement are VAT exclusive prices.

5.7 Nominated EU States

The nominated EU States are Belgium, Denmark, France, Germany, the Netherlands, Spain, the UK, Finland and Austria.

5.8 Price Adjustment

The prices of existing branded or other generic products, which will change as a result of the price reduction in patent-expired medicines provided for in clause 6 of the IPHA Agreement, must be notified to the HSE by 1 February 2007 and again by 1 December 2008. Should such notice not be received, the HSE may reduce the reimbursement price of such products in line with the reductions provided for in the IPHA Agreement.

The new industry agreement allows, for innovative, ex-factory repricing in order to retain low cost and low volume products in the market (e.g. flat, non-dosage related pricing structures. The State may also allow price modulation, i.e., offsetting a price increase against a cut for another product, with budget neutrality.

Italy

In Italy, pricing and reimbursement decisions are strictly linked and are AIFA's – the Italian Pharmaceutical Agency's- responsibility (*Commissione Prezzo e Rimborso*). Prices are only regulated for reimbursable products.

Italy used an external reference pricing system until 2001 (Spain, France, UK and Germany). Then, because of its ineffectiveness in containing pharmaceutical expenditures, the system was replaced

The price of pharmaceuticals in Italy is the result of a negotiation between the Italian Pharmaceutical Agency (the *Commissione Tecnico Scientifica*, the *Commissione Prezzi e Rimborso*) and the pharmaceutical companies. The negotiation takes into consideration several elements, including: the social relevance of the disease for which the medicine is indicated, the effect of the medicine on the disease (substantial improvement, symptomatic improvement, etc.), expected utilisation and financial impact, prices in other countries, prices in of similar medicines in Italy, etc

Latvia

In Latvia, price decisions are made along with reimbursement decisions, and price regulation is only applied to reimbursable products.

International price comparison is not compulsory, but is done for decisions on reimbursement price. Prices in all European countries are part of the information submitted by the company to the MPRA (The Medicines' Pricing and Reimbursement Agency)

The price used as reference is the ex-factory price, and the price should not exceed the price in other countries with similar socio-economic factors.

Lithuania

In Lithuania price decisions are made independently from reimbursement decisions and price control is only applicable to reimbursable products.

For international reference pricing the countries used as references are Poland, Latvia, Estonia Hungary, Slovakia, and Czech Republic. The price used for comparison is the ex-factory price. Reimbursed prices cannot be higher than 95 percent of the average of prices in reference countries

Malta

In Malta there are no direct pricing decisions, although reimbursement decisions do take price into consideration. There is no (direct) product price regulation and the tendering system is an indirect way to control prices for the NHS, but no price controls apply to the private market. When considering whether to include a medicine on the Government Formulary List, its costs and benefits are weighed (cost/benefit analysis).

Netherlands

In the Netherlands pricing is typically free, within the limits of a maximum price scheme. For products that cannot be included in the reference pricing system, the price is considered together with the reimbursement decision.

The pharmaceutical prices (ex-factory prices) of Germany, UK, Belgium and France are used to calculate the maximum price scheme. The Netherlands does not use international prices to make its reimbursement decisions.

The criterion used to set the price is the average price of selected countries (based on lowest price per pack). A maximum price is set for each product with a given active substance, strength and formulation.

Norway

In Norway price decisions and reimbursement are more or less independent. The industry can lower prices in order to gain reimbursement.

Pharmaceutical product price is regulated for all products except OTC

Prices are based on the average of the three lowest pharmacy purchase prices in Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands, Sweden and the UK.

Poland

Price approvals and reimbursement decisions are taken together under public regulation, but only for reimbursable products.

When submitting an application form, manufacturers have to fill in information related to existing prices in other EU countries (after that, Ministry make a comparison on those prices). Comparisons refer to ex-factory prices.

The following criteria are taken into consideration:

- 1) price level in countries having similar Gross National Product per capita,
- 2) price competitiveness,
- 3) influence of the medicine on direct cost of treatment,

- 4) volume of supply in the period preceding the application's submission and volume forecast for the following period,
- 5) production costs,
- 6) proved effectiveness of the medicine,
- 7) significance of the medicine in combating diseases carrying high epidemiological and social risk.

Cost-plus is applied to all products.

Portugal

In Portugal, the initial price decision is made independently from the reimbursement decision. Prices are set up by the Directorate General for Enterprise (DGE) according to the Regulation n°29/90 of 13th January. Pricing is a two-step process: DGE agrees to a maximum price for all new medicines (except hospital-only specialities and OTC) and reimbursement applications are then processed by INFARMED, which can suggest the applicant lower this price in order to obtain reimbursement status.

Spain, France and Italy are the reference countries. The criteria used to set the price is the minimum price of selected countries

Manufacturers/importers maximum selling prices (PVA) at introduction are strictly based on the lowest ex-factory price found for identical or similar pharmaceutical specialities containing the same active ingredient. Price comparisons are made by taking into account identical or similar specialities in the countries of reference, country of origin and Portugal, and comparing prices for each country. The active substance and pharmaceutical form must be identical, as too - ideally- should be both the strength and the pack size. If the pack size differs, the smallest one is used. If the strengths differ, the most approximate strength is considered and calculation is made.

Romania

In Romania price decisions are taken independently from reimbursement decisions. All prescription medicine prices are regulated (prices for OTC are not regulated).

The countries used as references for international prices are Czech Republic, Bulgaria, Hungary, Poland, Slovakia, Austria, Italy, Lithuania, Denmark, UK and Germany. The price used for comparison is the ex-factory price and the criterion is the minimum price in selected countries.

Slovakia

In Slovakia price decisions related to drugs used for outpatients are taken together with reimbursement decisions. Price decisions on drugs used only for inpatients are taken independently from reimbursement decisions. All products have price regulation.

The countries used as international references are: Czech Republic, France, Hungary, Austria, Germany, Spain, Italy, and Poland. The price used to compare is the ex-factory price.

The proposed price should not exceed more than 10 % of the average price of the drugs in the three countries listed above, taking into account the lowest prices.

Slovenia

In Slovenia price decisions are taken independently in two institutions (Pricing decisions at the Agency for Medicinal Products and Medical Devices and Reimbursement decisions at the Health Insurance Institution). Pharmaceutical price regulation is only for reimbursable products.

The countries used as a reference are Italy³⁵, France, and Germany. The price used to compare is wholesale price³⁶, with the criteria of average price of selected countries (Note: formula also includes setting the maximum price level as a percentage of the above listed average, e.g. 85% for originator drugs³⁷)

With regard to cost-plus, 0.5% of the wholesale price is added for third-country imported medicines (not local and EU-MS produced).

The prices are formed on the basis of negotiations with the National Health Insurance Institute (ZZZS). Exceptional changes in the price of a certain drug prompted by institute members' needs will be possible only with the minister's consent³⁸. The Minister recognizes the justification of the importance of the product for the maintenance of public health on the basis of data presented by the marketing authorization holder.

Sweden

There is no (direct) product price regulation.

Spain

Reimbursement decisions are made prior to price decisions, since only reimbursable products have a regulated price.

International price referencing is based on France, Italy, Belgium, and the United Kingdom, but this may change with the new law (October 2006), which will take all EU countries' prices into account. The prices taken into account are ex-factory prices. Normally, the criterion used is minimum price of selected countries

³⁵ From January 2007, Austria has replaced Italy

³⁶ From January 2007, also ex-factory

³⁷ From January 2007, the maximal price level is 100% for originators, and 85% of the mean of the cheapest and most expensive generic on the comparative countries.

³⁸ <http://www.ukom.gov.si/eng/slovenia/publications/slovenia-news/4209/4233/>

Cost-plus is applied for all products. Overall manufacturing cost, including R&D and marketing, make up to 12%-16% of the fixed industrial price, while benefits make up 12%-18% of the invested costs. The sources of information are cost accounts provided by the applicants and international chemical prices to evaluate a substance's price.

United Kingdom

In the United Kingdom there are no separate pricing and reimbursement decisions. Once the NHS list price of a branded medicine has been set under the PPRS, it is automatically reimbursed at that price.

Reimbursement prices for generics are set and published monthly in the Drug Tariff (DT). The DT has three main categories, namely category M, A and C. Reimbursement prices of category M medicines are set quarterly based on manufacturers' prices after discount. Category M covers 84% by net ingredient cost of generics reimbursed in the NHS. Category A prices are based on list prices of a basket of 2 main full-line wholesalers and 3 manufacturers. Category C products are not readily available and their prices are based on a particular brand or manufacturer.

The prices of all prescription medicines supplied to the NHS are controlled, branded medicines through the Pharmaceutical Price Regulation Scheme (PPRS) and generic medicines through the Drug Tariff. The retail prices of medicines sold over the counter (OTC) direct to the public are not controlled.

The prices of branded prescription medicines and the profits that manufacturers are allowed to make on their sales to the NHS are controlled by the Pharmaceutical Price Regulation Scheme (PPRS).

Under the scheme, which has existed in various forms since 1957, the profits made by pharmaceutical companies from their sales to the NHS are regulated. If a company's profits exceed its target profit, it is required to reduce its prices or make a repayment to the Department of Health. There is no guarantee that the target profit will be achieved. On market entry, companies have freedom of pricing for major new products i.e. new active substances within the constraint of their profit target. Also for line extensions relating to such new products, granted on the basis of an abridged application within five years of the grant of the original authorisation of the new product.

Where a new product has not been subject to a new active substance marketing authorisation, companies must seek the Department's agreement to the price of the new product. In reaching a decision on the acceptability of a price for a new product that is not introduced following the granting of an EU or UK new active substance marketing authorisation, the Department may take into account factors such as the following:

- § the price of other presentations of the same medicine or comparable products
- § forecast sales and the effect on the NHS drugs bill
- § the clinical need for the product
- § any exceptional costs

The NHS list price of existing products may only be increased with the Department's agreement if the criteria for price increases set out in the agreement are met.

The PPRS seeks to achieve a balance between reasonable prices for the NHS and a fair return for the industry to enable it to research, develop and market new and improved medicines.

III. Impact

Experiences reported by countries.

The impact of price control does not appear easy to assess. Therefore, no questions on the evidence of its impact were included in the questionnaire. However, prices seem to be higher in countries with no price control and with indirect modalities of price control, such as US, UK and Germany. Moreover, removal of price controls in some developing countries seems to have been followed by price increases, although there is little documented evidence, especially on its long-term effects.

Price control, in particular when based on cost-plus formula or on discretionary, non-predictable decisions of the regulators, has often been criticised by the industry and by pro-market experts. Price control is assumed to create arbitrary distortions of resource allocation and to reduce the incentives for R&D and innovation.

It has also been stated that industry might compensate price control by forcing the increased consumption of pharmaceuticals. This assumption is difficult to prove and it is not even supported by theoretical considerations: a profit-maximising supplier would not have less incentive to promote consumption with higher prices than with lower prices.

Literature

Although most of the European countries set a maximum price on their pharmaceutical products, little literature exists in Europe on this topic. Most of it comes from the US and tries to assess what would happen if price regulation was applied there and how it would affect R&D. The International Trade Administration -U.S. Department of Commerce- carried out a study in 2004 on the impact of the deregulation of prices of eleven countries of the OECD, from a theoretical point of view, and one of the conclusions formulated by that study was that in the absence of price controls revenues available for R&D could be significantly higher (U.S. Department of Commerce, 2004). Other studies (Kessler 2004, Santerre 2004, Calfee 2001) also conclude that price controls limit investment in R&D because they make it more difficult for companies

(despite their entitlement to patents) to recover their investment and, therefore, do not provide incentives to invest more.

Some of these studies (Vernon 2005, Giaccoto *et al* 2005, U.S. Department of Commerce 2004) carry out theoretical simulations that attempt to determine the negative consequences of price control. However, as Vernon points out, among the studies' limitations is the fact that their predictions are speculative and thus don't also take into account the social welfare perspective. In this same sense, the Giaccoto study points out that only costs were taken into account when, in fact, other elements, such as social policy, need to be kept in mind (for example, compensating economic benefits through greater access to prescription medications subject to U.S. drug price control policies).

Another topic that has raised considerable debate recently is the relationship that exists between "launch delays" and pharmaceutical price controls. Danzon *et al* 2005 pointed out that countries with low prices have fewer launches and longer launch delays (sometimes as a way for companies to avoid the effects of parallel trade). However, some reactions have raised this study that try to question the direct relationship among those two elements. Garattini *et al* 2007 pointed out that any interpretation of results stemming from the literature on "launch delay" should be cautiously considered and that a better understanding is needed of the reasons behind their delays. As many countries use international price referencing, it is logical for companies to want to launch their products in high price countries first. Also, countries might not necessarily consider a "launch delay" to be a strictly negative outcome, since it could save them money in terms of the often questionable opportunity cost of foregone health benefits for patients.

Therefore, the literature's main conclusions regarding the effects of price controls on innovation have been that:

- § Adverse consequences and negative effects of price regulation are often alleged, but little or no compelling evidence is provided.
- § Some of the studies are financed, directly or indirectly, by the pharmaceutical industry (Calfee 2001, Kessler 2004), thus posing possible conflict of interest problems. Industry is obviously interested in convincing regulators that price control should be removed because, irrespective of its impact on R&D and innovation, the lack of price regulation in their usually monopolistic markets allows higher profits.
- § It must be accepted that it is very difficult to find compelling evidence on either positive or negative effects of price regulation on R&D and innovation due to the multiplicity of factors involved and the long causality chain linking non-regulated pricing to innovation.

Diverse initiatives exist, such as the OECD's Project on Pharmaceutical Pricing Policy, that seek to improve the basis for informed policy-making, principally in the area of pharmaceutical pricing, and that consider global and cross-national impacts of pharmaceutical pricing policies.

IV. Discussion

Key messages

- § Most countries do not allow free pricing of new products, unless they have alternative indirect tools to control them, such as, a RP systems, profit control, generic policies, etc. In spite of its shortcomings, direct price control seems to be the most used option in cases where a product enjoys a real monopolistic position and other policy practices are of little value.
- § Price control might anyway fail even in the objective of controlling expenditure, if the amount of units sold grows out of control.
- § Price control is in particular a policy practice to consider by small countries with a small publicly funded drug market, where practices based on third-party financing is a small proportion of total expenditure.
- § Industry generally criticizes direct administrative price control, as it often limits the income and profits that might otherwise be attained and lobby for a free market (i.e. for a non-regulated non-competitive market on the grounds that price controls lead to low prices that discourage R&D and innovation.)
- § Administrative price control is usually criticised on theoretical grounds, as well. Most health policy-makers are aware of the limitations and negative side effects (distortions in resource allocation, scope for discretionary behaviour and potential for corruption, etc.)
- § However, the causal link between price level and innovation is complex and far from clear, both from a theoretical and an empirical perspective. The fact that countries with a strong, innovative industry usually have a relatively high price level does not prove that high prices lead to more R&D and innovation; the causal relationship might go the other way round: a strong industry might be able to impose high prices and the government might be inclined to accept them because high costs to patients and the health systems are compensated by positive effects on the balance of trade. A key aspect of administrative price control is how the price is determined. Cost plus approaches, very widespread in earlier times, are being replaced by other criteria: international prices, cost of alternative or similar treatments and, more recently, cost-effectiveness criteria that theoretically provide sounder alternatives for setting administrative prices. Setting prices based on pharmaceutical and economic criteria – at least for innovative, publicly-funded medicines – is one way to reward innovations that provide society with added value.
- § Removal of administrative price control might be introduced in markets where competition is feasible, for instance, when the market exclusivity of an originator has expired and generics enter the market. In fact, however, most EU MS control the price of generics as well, which suggests that institutional decisions influence the demand for medicines, making it less price sensitive, at least, in the view of many policy makers

- § Patients might be positively affected by price controls in the short-term, since lower prices lead to lower premiums and co-payments, but negatively affected in the long-term if claims regarding their negative impact on innovation are true.

Risks

- § Inappropriate price controls systems might introduce distortions in the allocation of resources and unfairly discriminate some suppliers. They might also negatively affect productive activity and innovation. Given the global scope of pharmaceutical markets, the effect on innovation is not likely to be relevant except for large countries.
- § Price controls, if applied where competition is possible, e.g. on product categories where generic products are available in larger markets, might artificially increase the total spending on these product categories and limit savings opportunities.
- § Price control might lead to parallel trade, as it happened in the EU. However, this is not likely to happen with new drugs, as companies can and tend to avoid it by not accepting to market a product in a given country at a price significantly below other EU countries.
- § There is a risk that countries trying to set low prices by means of price regulation will experience delays and even non-availability some new products while they are under market exclusivity conditions.
- § Setting prices based on the prices of other countries is a relatively simple strategy, probably a good option for a small country, although it might lead to countries with strong price control systems to be the last ones to access new medicines, as companies will choose to get market approval in countries that allow high prices or have no price control at all.
- § If prices of pharmaceuticals are freezed in a situation of high inflation, the result can be an irreversible damage to some industries and a strong incentive to launch “false” innovations at up-dated, profitable prices
- § Price and profit control is more likely to be feasible if applied to a relatively small number of the most economically relevant products and companies.
- § Globalization of the pharmaceutical market – and in the EU, the establishment of the Single Market - has greatly eroded the power of national price regulators and this trend is likely to continue in the future, unless double pricing becomes an accepted practice and the holders of market exclusivity rights find it again more profitable to accept price differentials across EU MS.

Key success factors

- § Countries with a substantial amount of public funding of pharmaceuticals are in a stronger position to negotiate relatively low prices, as the threat of no market access implies a larger opportunity cost for the supplier.
- § Availability of appropriate information on costs of production is essential for properly running a cost-plus or profit control system. Brazil apparently obtains this kind of information thanks to its own public manufacturing units. The UK uses auditors in order to check the information provided by the companies. Similarly, price regulation based on economic evaluation requires a certain administrative culture and a certain level of technical capacity and know-how by the regulatory bodies.

Cost-sharing

I. Introduction

Description

Cost-sharing is a provision of health insurance or third-party payment that requires the individual who is covered to pay part of the cost of the medical care received. Cost-sharing may be in the form of deductibles, co-insurance or co-payments (OECD definition). Cost-sharing is a form of splitting the cost of health care services in order to reduce public expenditure on the service.

Modalities

The most usual pure modalities of cost sharing are:

- § *Co-payment*: the user pays a fixed amount for a given service. It is also known as a user fee.
- § *Co-insurance*: the user pays a proportion of the cost of the service. The percentage of the cost to be paid by the user can be fixed or decrease with the amount.
- § *Deductible or excess*: the user must pay a fixed amount for a service before any payment of benefits can take place.
- § *Residual payment*: the user has to pay a proportion or the full amount of the cost of a service beyond a certain ceiling. Reference pricing is actually a form of that type of cost-sharing.

In practice, systems often combine several pure modalities. For instance, reference pricing might be added to a general cost-sharing scheme.

In order to avoid or minimize unwanted effects on access, cost-sharing systems include exclusion criteria for some user categories (pensioners, widows, indigents, etc). Caps may exist on the amount a user has to pay for a service or on the cumulative payments made within a certain time period.

Moreover, proposals have been put forth to set up cost-sharing systems where the amount to be paid by the users is related to their income or ability to pay.

Purposes

Declared objectives of cost-sharing include:

Cost containment:

- To generate income or reduce expenditure for the third-party-payer
- To reduce administrative costs (deductibles)
- To make users cost-conscious
- To promote competition (reference pricing)

Access:

- To reduce abuse and inefficiency (reduce use of unnecessary drugs or unnecessary quantities)
- To facilitate access where needed

Innovation:

Cost-sharing is not claimed to affect innovation.

Theory/Rationale

Cost-sharing is aimed at making users more economically responsible for their behaviour and avoiding or reducing moral hazards. Economic theory assumes that a rational consumer will bring consumption up to the point that the last unit consumed has the same marginal utility than the money he/she pays for it (its marginal costs), which is assumed to lead to an efficient allocation of resources. Moral hazard means that an insured individual that does not have to pay for a service at the time of consumption (including someone receiving goods or services for free) will change his/her behaviour and use a larger amount of the service than would be the case should he/she have to pay for it, a rational behaviour that leads to social inefficiency.

From the point of view of economic analysis, a key aspect of cost-sharing arrangements is the resulting marginal cost for the consumer. For instance, in the case of a deductible, the marginal cost to the user is 100% of the actual cost, and at some point it falls to 0.

From this perspective, the forms of cost-sharing can be classified as:

1. Fixed payment
2. Variable payment
 - a. Linear pricing
 - b. Fixed plus linear
 - c. Non-linear
 - full marginal price
 - partial marginal price

Effects on access:

According to economic theory, setting or increasing the amount users have to pay for a good or service is expected to reduce the number of units consumed, as demand curves are normally assumed to have a negative slope.

Some authors discuss the rationale and fairness of cost-sharing on the grounds that (except for first contacts with the health system) it is usually the health professional, not the user, who decides medical consumption.

It has also been noted that the supposed effects of cost-sharing might be nullified by a complementary cost-sharing insurance.

Effects on cost-containment:

The immediate impact is a reduction in overall spending on the good or service. Public/third-party spending on the drug or service is expected to decrease because fewer units will be consumed and because part of the cost is shifted to the consumer.

However, the overall effect on expenditure is uncertain, as it depends on whether and how the reduced consumption is substituted and on the administrative costs of collecting the fees. Cost-sharing is expected to have a larger impact on the consumption of lower-income individuals, as the price-elasticity of their demand is assumed to be greater than for higher-income individuals.

Innovation:

The effects on innovation are uncertain, but other things equal, it is likely to reduce the suppliers' revenues, which might negatively affect innovation.

II. Application in Europe

Overview

1. No co-pays: The Netherlands and Malta
2. Flat rate: Austria, Italy, UK (with implicit ceiling: prescription pre-payment certificate)
3. Percentage rates: Belgium, France, Greece, Estonia, Finland (with annual ceiling), Latvia, Lithuania, Poland, Portugal, Slovakia, Slovenia and Spain
4. Uniform %: Cyprus, Germany, Norway
5. Co-insurance, with % decreasing with accumulated expenditure over a given period and with a ceiling: Denmark and Sweden.
6. Deductible: Ireland, Sweden
7. In many countries there are specific exemptions for certain products as well as for some patient and socio-economic groups.

Individual replies by countries

Austria

In Austria, when receiving a prescription from a doctor contracted by the Austrian Social Insurance System, patients have to pay a flat rate prescription fee. In 2006, the prescription fee amounted to € 4.60 (it's legal basis is in Art. 136.2 and 3 of the Austrian Social Insurance Law (ASVG) 1955). Additionally, patients have to pay for over the counter drugs and non-reimbursable pharmaceuticals out-of-pocket. The Austrian Social Insurance Law (ASVG) lists all pharmaceuticals that are not listed in the reimbursement list (EKO). (Art. 351c.2 ASVG)

Socially disadvantaged persons, e.g. elderly pensioners with an income below a certain threshold (around € 690 for 1-person-households) and persons with communicable diseases, such as tuberculosis or HIV, are exempt from the prescription fee. (Art. 136.4 and 5 ASVG 1955). There are no out-of-pocket maximums in Austria.

Certain pharmaceuticals are not included in the reimbursement list (EKO). Nevertheless, patients may apply for individual reimbursement under very special circumstances (e.g. for hospital products in cases when the patient re-enters primary care settings, such as is often the case with oncology drugs). This individual reimbursement requires an ex-ante approval of a "head physician". In 2005 an average of 45,000 prescriptions per month were approved via this individual reimbursement procedure.

Belgium

In Belgium the preferred system for financing patients' pharmaceutical costs is for them to obtain reimbursement through a third party payment (= Co or Out-of-Pocket-Payment). Under this system patients with prescriptions for reimbursable medicines pay only part of the total cost of medicines when they go to the pharmacy. The prescription is then sent on to the patient's insurance fund, which pays the remaining cost to the pharmacist.

Co-payment is equal for everyone, except for patients with a preferential reimbursement status (widows, orphans, retired and disabled persons, low income ...), who benefit from a preferential reimbursement. Co-payment is limited to a percentage of the real cost, and limited to a 'ceiling'-fee.

The percentage of the cost that is reimbursed, as well as the maximum, depends on the category assigned to the pharmaceutical in question: category A, B, C, Cs or Cx. The Minister of Social Affairs, following recommendations from the Commission for Reimbursement of Medicines, assigns those categories.

Medicines pertaining to the categories A, B and C are considered "necessary" medicines and they are classified as a function of their specific medical and therapeutic importance.

Category A is reserved for vital medicines, such as medicines to treat diabetes or cancer, while other therapeutically important medicines are placed in category B (antibiotics, for example). Medicines intended for symptomatic treatment (mucolytic agents to treat chronic bronchitis) are classified in category C.

The categories Cs and Cx are reserved for medicines used to treat influenza vaccines and antihistamines (Cs) and contraceptive medicines (Cx).

Table 5: Overview of reimbursement categories in Belgium

Reimbursement categories	Preferentially insured patients (non-hospitalized)	Regularly insured patients (non-hospitalized)
Category A	100% reimbursed No personal contribution	100% reimbursed No personal contribution
Category B	85% reimbursed Personal contribution: 15%, with a maximum of €7,00	75% reimbursed Personal contribution: 25%, with a maximum of €10,40
Category B – large package	85% reimbursed Personal contribution: 15%, with a maximum of €10,40	75% reimbursed Personal contribution: 25%, with a maximum of €15,70
Category B – ATC 4 th level group	85% reimbursed Personal contribution: 15%, with a maximum of €10,40	75% reimbursed Personal contribution: 25%, with a maximum of €15,70
Category B – large package & ATC 4 th level group	85% reimbursed Personal contribution: 15%, with a maximum of €15,70	75% reimbursed Personal contribution: 25%, with a maximum of €23,50
Category C	50% reimbursed Personal contribution: 50%, with a maximum of €10,40	50% reimbursed Personal contribution: 50%, with a maximum of €17,40
Category C – ATC 4 th level group	50% reimbursed Personal contribution: 50%, with a maximum of €15,70	50% reimbursed Personal contribution: 50%, with a maximum of €26,10
Category Cs	40% reimbursed Personal contribution: 60%, no maximum	40% reimbursed Personal contribution: 60%, no maximum
Category Cx	20% reimbursed Personal contribution: 80%, no maximum	20% reimbursed Personal contribution: 80%, no maximum

Source: Belgium. Ministry of Health (EASP questionnaire)

A large-sized package is defined as one that contains more than 60 units. Medicines that belong to a therapeutic group of medicines (ATC 4th level) with at least one (reimbursed) generic drug are subjected to a higher personal contribution. This governmental measure was introduced in November 2005 to encourage patients to switch –wherever possible – to generic alternatives.

On top of this personal contribution, however, the reference reimbursement system also makes it possible to charge a supplementary amount. The Belgian reference reimbursement system was introduced on June 1, 2001 and aimed to stimulate the prescription of less expensive medicines. If a (cheaper) generic reimbursed medicine is available which contains the same active component (or components), the original medicine enters the reference reimbursement system. This means that its reimbursement basis is diminished by 30% (ex -factory level), while its applied price remains the same.

Although the reimbursement basis of the original medicine is diminished, the personal contribution increases, with the difference between the applied price and the new reimbursement basis (the so-called "supplement") being charged to the patient. However, pharmaceutical companies do have the option of lowering their applied price in order to reduce, or even eliminate, the patient's supplement.

If a patient is hospitalized, a fixed daily amount of €0.62 is charged (irrespective of the number of units of the reimbursed medicines he/she receives).

Remark: Differences exist within the social security system depending on whether the persons are salaried or self-employed. The system for salaried persons is the most widely extended. Salaried persons are insured both for high risk care (hospitalisation, etc.) and low risk care (pharmaceuticals in an ambulatory setting, etc.). Self-employed people are insured only for high risk. This does not include reimbursement for medication, except, for instance, when oncological therapy and treatment of AIDS is involved.

Regarding exclusion criteria for some categories of users or products, there is a provision to limit the expenses for patients called "MAF" or "maximum invoice", i.e. the maximum co-payment to be paid by a family for health care, including medicines. For patients below certain income levels, this system sets the annual maximum amount of co-payment for all health care interventions for which the social security system provides partial intervention. This maximum is linked to a family's income. Medicines reimbursed by the social security system in categories A, B and C are also included in this system; those listed in categories Cs and Cx are not included. Neither are non-reimbursed medicines (the so-called medicines of category D)."

The patient cost for non-reimbursed pharmaceuticals, or for pharmaceuticals used for non-reimbursed indications, can exceptionally be covered by the Belgian Health Care System through the "Special Solidarity Fund". Its decisions apply to individual patients. The request is introduced through a patient's Health Insurance Fund, following its evaluation by a committee of expert physicians. This procedure is usually limited to expensive medications such as those required for rare disorders (e.g. chemotherapy for rare forms of cancer, not included in the general registration of chemotherapeutic agents).

Denmark

Denmark has co-payments for patients. On application from the doctor the Danish Pharmaceutical Agency may determine that for persons with an extensive, permanent, and well-documented need for medicinal products the reimbursement rate shall be

100% of that part of the total co-payment in excess of DKK 3,410 per year. A year co-payment of DKK 3,410 corresponds to a total purchase worth DKK 17,545 for the over 18-year-olds (corresponding to DKK 19,095 for the under 18-year-olds).

On application from the doctor, the Danish Pharmaceutical Agency can grant reimbursement of 100% of all medicinal products prescribed by a physician for patients who are terminally ill and who, according to a physician's prognosis, will not live much longer and will not benefit from hospital treatment.

It is also possible to obtain subsidies from the public sector for social motives. Some medicinal products available only by prescription and some OTC are not subsidized (except for terminally ill patients).

Below you can see the percentages of the reimbursement and the percentages of co-payment by patients. Rates differ depending on whether the patient is older or younger than 18 years of age.

Table 6: Reimbursement Rates in Denmark in 2007

Annual expense per person for medicinal products entitled to reimbursement before subtraction of reimbursement*	Reimbursement for people older than 18	Patient charge for people older than 18	Reimbursement for people younger than 18	Patient charge for people younger than 18
DKK 0-465	0%	100%	50%	50%
DKK 465-1,125	50%	50%	50%	50%
DKK 1,125-2,645	75%	25%	75%	25%
More than DKK 2,645	85%	15%	85%	15%

* The maximum amount allowed applies from 1 January 2007 and is adjusted 1 January every year. ** Calculated from reimbursement prices, cf. section on reference pricing.

Source: Denmark. Ministry of the Interior and Health (EASP' questionnaire)

Patients may choose to sign up to a private insurance scheme covering some of the co-payments.

Denmark is monitoring the general consumption of prescription drugs very closely. The maximum amount for reimbursement is adjusted once a year. The Danish Pharmaceutical Agency's web page (<http://www.dkma.dk>) provides up-dated statistics and information on medicine prices and reimbursement options.

Estonia

There is cost-sharing implemented in Estonia. There are exclusions for some categories: pensioners and children below 16 have lower out-of-pocket payment.

Finland

The Finnish reimbursement system consists of three reimbursement categories: basic refund (42 % reimbursed), lower special refund (72 %) and higher special refund (100 % after fixed co-payment EUR 3). A medicinal product can belong to one, but also to two or three, reimbursement categories at the same time. In addition, an extra refund is granted if the patients' co-payments for reimbursable products exceed an annual ceiling sum (EUR 617 in 2006).

The reimbursement categories are graded according to medical criteria based on the severity of the illness and the necessity of the drug treatment. A Government Decree defines the severe and chronic illnesses that entitle patients to reimbursement under the special refund categories³⁹. The higher special refund category covers 34 chronic illnesses where drug treatment is necessary and effective to maintain the patient's health status and where the drug restores or replaces normal bodily functions. The lower special refund category includes 10 chronic illnesses where drug treatment is necessary to maintain the patient's health status. In each reimbursement category, as well as in additional refund, the patient always pays a part of the medicinal costs.

The co-payment in reimbursement categories is as follows:

- § basic refund: 58 % of the costs,
- § lower special refund: 28 % of the costs,
- § higher special refund: EUR 3 per purchase of medicinal product
- § additional refund: EUR 1.50 per purchase of medicinal product.

In the year 2005 patients' share of total costs of reimbursable medicines was 33 %. This figure does not include social assistance paid by the local municipal authorities towards the cost of drugs, nor the drug costs taken into account in calculating the level of support paid to pensioners, children and people with disabilities. No figures on these compensations are available.

The rate of co-payment of reimbursable medicines is not dependent on a patient's age or financial standing. There are no reimbursable medicines that patients can obtain for free. However, in Finland schemes other than social health insurance also exist that often cover a patient's drug costs, e.g. social assistance paid to people with low incomes by the local municipal authorities and support paid to pensioners, children and people with disabilities.

An annual maximum has been set to limit the amount of co-payments a patient is expected to pay for his/her reimbursable medicines, basic topical ointments and clinical nutritional preparations. When the annual ceiling sum (EUR 617 in 2006) is reached, the patient is entitled to an additional refund. Subsequent costs of reimbursable products are reimbursed in full after EUR 1.50 co-payment per medicine per purchase.

The reimbursement is paid for a purchase equivalent to a maximum of three months' treatment at a time. The dispensing pharmacy must substitute the prescribed medicine with a cheaper generic product unless expressly denied by the prescribing doctor or the

³⁹ <http://www.stm.fi/Resource.phx/eng/orgis/board/pharmaboard/legislation.htx.i219.pdf>

customer. The reimbursement is calculated on a medicine's purchase price and the patient does not need to pay any extra amount, even if he/she rejects the generic substitution.

France

In France, strictly speaking, cost-sharing does not exist. 95% of the population has some kind of complementary health insurance (mandatory for the poor), so there is almost no out-of-pocket payment, except for those who purposely decide not to participate in an insurance plan.

The only existing cost-sharing is a 1€ flat fee for consultations. It can be raised for visits outside of the gate-keeping system (seeing a specialist first). It does not apply to any pharmaceutical products.

Greece

In Greece, patient co-payments do exist. The rate of co-payment for a reimbursable drug is uniform for all insurance funds and is set at 25%, except for several special patient groups (e.g. with chronic conditions), where the rate is either zero or 10%. There are no out-of-pocket maximums.

Hungary

There are two major types of reimbursement categories in Hungary; the first category refers to each indicated use of the drug described in the Marketing Authorization's Product Information. Pharmaceuticals listed in this group can be prescribed by any physician. Reimbursement levels are 0%, 25%, 55% and 85%.

The second reimbursement category refers to drugs with special indications. The cost of drugs included in this group can be reimbursed up to 50%, 70%, 90% or 100%. These indications for their use, and the specialists authorized to prescribe them, are listed in a Common Declaration prepared jointly by the Minister of Health and the Minister of Finance.

Drugs can receive both types of reimbursement simultaneously.

When a higher-priced brand-name drug is chosen, the patient must pay the difference between the fixed reimbursed rate and the sale price.

Ireland

In Ireland, patients who do not have full eligibility (i.e. receive free drugs and medicines), are required to co-pay the cost of their drugs and medicines. The Drug Payment scheme applies to Irish residents who do not have a medical card. Under this scheme no individual or family member has to pay more than €85 in any calendar

month for approved prescription medicines. Family expenditure covers the nominated adult, his/her spouse and children under the age of 18. Persons over 18 but under 23 and enrolled in a full-time education program may also be included as dependents.

Those with full eligibility under section 59 of the 1970 Health Act (persons with income below specified levels, over 70 years of age, or certain discretionary cases) receive approved items free of cost. Those with certain prescribed conditions may receive items free for the treatment of that specific condition. Certain people infected with Hepatitis C may also receive items free.

Italy

In Italy, some regions (9/22) have introduced a ticket (i.e. a small payment of between 1-2€ per receipt or per pack) aimed at making patients more sensitive to the cost of medicines.

Some low-income people are exempted from having to pay for these tickets. In some regions specific patients (i.e. diabetics) are exempted from paying a ticket fee for medications used to control diabetes. The system differs significantly from region to region.

Latvia

Four reimbursement levels exist in Latvia (100%, 90%, 75% and 50%), depending on the severity and chronic nature of the disease. All drugs containing the same indications for use are reimbursed at the same level.

Pregnant women or children (who may have to use an insulin pump or inject insulin 3-4 times a day) are excluded from co-payment for test strips for diabetes.

Lithuania

This country has four levels of reimbursement – 50%, 80%, 90%, and 100%. The level is determined according to diseases in the *List of Diseases and Medicinal Products* (List A).

Children up to 18 years of age and disabled persons are eligible to receive medicinal products published in the *List of Diseases and Medicinal Products* (List A), as well as medicinal products included in another list (List B), which are 100% reimbursable at the official price level. Pensioners can be reimbursed for 50% of the cost of products appearing in list B. Insulin (the only product without co-payment) is fully reimbursable.

Malta

In Malta there is no cost-sharing in terms of co-payment. Medicines supplied by the NHS are paid for through taxation and social security benefits. Specific population

groups/qualified patients⁴⁰ are entitled to receive certain basic medicines free of cost. All nationals who suffer from chronic diseases are qualified to receive medicines necessary for their treatment. Patients that are not qualified can purchase drugs through private pharmacies but must pay full cost. If a patient is not entitled or the drug is not on the Government Formulary List, the patient has to pay for the drug fully.

Norway

The standard patient co-payment for reimbursed drugs is 36%, up to an annual maximum spending level of NoK1 615 in 2006, with expenses above this threshold covered by the National Insurance Administration. The annual limit includes co-payments for physician consultations. Patients aged over 67 years and disabled people have been exempt from co-payment charges since 1 January, 2003. Children under the age of 7 are also free from payments.

Poland

In Poland, there are 3 types of cost-sharing:

- § Lump sum fee (3.20 PLN)
- § 30%
- § 50%.

Certain groups of patients with special needs are entitled to broader health care services: war invalids, as well as the financially dependent spouses, widows or widowers of soldiers, are entitled to a family benefit. This also applies to people who are entitled to receive free of charge drugs which are marked with the symbol “*Rp*”.

Portugal

The NHS functions with a percentage based co-payment system. There are five different levels of reimbursement in Portugal: 100%, 95%, 69%, 37% and 15%. In case of pensioners, whose income is lower than 14 times the minimum national wage, an extra 15% is reimbursed in case of non fully reimbursement categories, reaching a level of 100%, 84%, 52% and 30%. The inclusion of medicinal products in different reimbursement categories depends on their therapeutic classification. Some pathologies are also fully reimbursed (paramyloidosis, cystic fibrosis, lupus, haemophilia, thalassemia, Turner’s syndrome, HIV/AIDS...) Reimbursement is only applicable for prescription products. OTC products are not reimbursed⁴¹.

⁴⁰ According to income, diseases, professions....

⁴¹ New co-payments due to the recent approval of new legislation (applied since the beginning of February 2007)

Slovakia

In 2005, patient co-payments made up 13 % of the total drug budget for prescription drugs. There are different co-payment rates (but no fixed percentages rates) for reimbursable pharmaceuticals

Slovenia

In Slovenia, medicines on positive list are generally reimbursed 75% of the price or maximal attributed value by the obligatory, and 25% of the price by the voluntary insurance. Medicines on intermediate list are reimbursed vice versa 25% and 75% from the two sources, respectively.

Some patient groups - such as children/minors, students, the generally disabled - or patients needing specific treatments, e.g. mentally ill, diabetics, women in their child-bearing years who need birth control products, are entitled to receive full reimbursement under the obligatory insurance program.

Spain

In Spain, patients under the age of 65 have to pay 40% of their drug costs; patients over 65 years of age (pensioners) or patients disabled by industrial accidents do not have to pay anything. Patients under 65 years of age have to pay 10% of the cost (up to a maximum of 2.64 euros per package) for medicines used to treat chronic diseases and others, such as anti-cancer medicines. Patients do not have to pay any fees for hospital care or drug treatments received during their hospitalisation.

Sweden

The patient pays full price, up to a certain cost level (SEK 900/€96.96), for reimbursable prescription medicines. Once this level is reached, there are reductions in the additional cost. The maximum amount payable by the patient during a 12-month period is SEK 1800 (€193.91). The table below describes in more detail the different co-payment rates and the reimbursement rate that apply in certain situations.

Table 7: Sweden - Reimbursement rates and patient co-payment rates, 2006

Annual expenses for patients in terms of reimbursement price in SEK / €	Co-payment rate in %	Reimbursement rate in %
SEK 0-900 / €0-96.96	100%	0%
SEK 901-1700 / €96.97-183.15	50%	50%
SEK 1701-3300 / €183.16-355.52	25%	75%
SEK 3301-4300 / €355.52-463.25	10%	90%
SEK 4301- / €463.26-	0%	100%

Source: Sweden. Health Ministry (EASP's questionnaire)

A patient who refuses generic substitution will have to pay the difference between the reimbursement price of the patented drug and the pharmacy retail price of the cheapest available generic. Such costs are not included in the co-payment ceiling of SEK 1,800.- / €194.-.

For non-reimbursed medicines the patient bears the full cost, regardless of the reason for the medicine being excluded from the reimbursement system.

The Swedish reimbursement system contains no social clauses that cover private pharmaceutical expenses. However, individuals who use large amounts of medicines are protected from high costs as explained above. Children under 18 years of age within a family unit are considered as one beneficiary and their pooled co-payments are maximized to SEK 1,800/12-month period. Also, insulin is exempted from the reimbursement system and completely free of charge to the patient.

The Swedish system provides “free” drugs after crossing the last rung in the cost-sharing ladder. There is a certain risk that this might lead to over-dispensing of high-cost drugs to patients.

UK

In England a flat rate prescription charge is payable for each item dispensed via an NHS prescription. The charge is 9.73 euros from 1 April, 2006. This system of charging has been in existence since 1968.

The exemption⁴² is based on one of a number of factors: the method of delivery, the type of medication, the age of the patient, the patient’s condition, or the patient’s income.

⁴² The basis of exemption from prescription fees in England

(1) No charge for medication for the patient (regardless of patient’s status or income):

- supplied to hospital inpatients
- supplied on discharge following inpatient treatment
- supplied and administered personally by a GP
- supplied by a GP for immediate treatment (and no prescription form is used)
- administered at a hospital or walk in centre
- supplied for personal administration by person making the supply in accordance with a patient group direction
- supplied for the treatment of a Sexually Transmissible Infection (and no prescription form is used, eg supply is by a hospital)
- which is a prescribed contraceptive (oral or listed appliances)

(2) No charge for any prescriptions for patients who are in one of the following categories:

- Children under 16
- Young people aged 16, 17 18 receiving qualifying full-time education
- Men and Women aged 60 and over
- Pregnant women and women who have had a child in the previous twelve months who hold a valid exemption certificate
- People who hold a valid exemption certificate for an accepted disablement (but only in respect of medication for the accepted disablement)
- People suffering from the following conditions who hold a valid exemption certificate
 - Permanent Fistula (including caecostomy, colostomy, laryngostomy, or ileostomy) which requires continuous surgical dressing or requires an appliance

There is no specific maximum applied to out-of-pocket expenses. However, a patient may effectively cap the prescription fees payable by purchasing a prescription pre-payment certificate (PPC). PPCs are available for 4 months for a fee of 52.14 euros or for 12 months for a fee of 139.37 euros (from 1 April, 2006). No further prescription fee is payable at the point of dispensing and the patient may obtain an unlimited number of prescribed items during the period of the certificate. A patient may specify the start date of a PPC as up to one month before, or one month after the date of application.

III. Impact

Overall experiences reported by countries

1. Most countries report they do not to have a monitoring system or carry out impact evaluations. Some Scandinavian countries report a detailed monitoring system, at the patient-level, which is the basis for specific cost-sharing measures with threshold-levels for private or public spending per patient (Denmark,

-
- forms of hypoadrenalism (including Addison's disease) for which specific substitution therapy is essential
 - diabetes insipidus or other forms of hypopituitarism
 - diabetes mellitus (except where treatment is by diet alone)
 - hypoparathyroidism
 - myasthenia gravis
 - myxoedema
 - epilepsy requiring continuous anti-convulsive therapy
 - continuing physical disability which prevents the patient from leaving his residence without the help of another person.

- (3) No charge for any prescriptions for patients who are not in any of the above groups but who have a low income.

(a) The patient is named on an HC2 charges certificate for full help under the National Health Service Low Income Scheme. Either partner (including civil partners from December 2005) may make the claim. The level of help is based on a comparison between income and requirements of the individual/couple at the time a claim is made (or a charge was paid). "Requirements" are the same as income support applicable amounts plus housing costs and council tax the individual/couple is liable to pay. The level of income at which help ceases will depend on the individual's/couple's circumstances. No help is available when capital is more than 30,710 euros for people living permanently in a care home or 23,400 euros for anyone else. Or

- (b) Recipients of the following who do not need to make a separate Low Income Scheme claim:

- § Income Support (capital ceiling 23,400 euros)
- § Jobseekers' Allowance Income-based (capital ceiling 23,400 euros)
- § Pension Credit guarantee credit (for partners under 60, recipient will be entitled on age grounds) (no capital ceiling)
- § Tax credit awarded and family's annual gross taxable income (from 6 April 2006) is 22,000 euros or less (no capital ceiling) with:
 - § working tax credit and child tax credit, or
 - § working tax credit with a disability, or severe disability, element, or
 - § child tax credit and not eligible for working tax credit

(and the patient is named on a tax credit exemption certificate)

Finland, Sweden). Some countries report an amount of aggregate co-payment, on a national/regional level (often as part of expenditure and consumption statistics).

2. No assessment has been reported on the impact of cost-sharing on expenditure and utilization/access in comparison to a potentially free-of-charge alternative.

Individual replies by countries

Austria

In Austria, prescription fees are only used for financial contributions to the pharmaceutical budget. Prescription fees are not deliberately used as a controlling mechanism.

In 2005, prescription fees made up 3% of total health insurance revenues and 14% of the pharmaceutical expenditure.

Insofar as the impact on patient access to drugs is concerned, for certain old-age pensioners with an income just above the threshold (of €690 for 1-person-households) prescription fees might present an impact on their access to pharmaceuticals.

Austria has a long tradition of using the lump-sum system. Over the years the lump-sum figure has gradually risen. The advantage of a lump-sum system is its low administrative workload; however the danger exists that it may discriminate against certain social groups or people with specific diseases.

As an experience, in the beginning of this practice the financial impact target of 3-4% annual growth of pharmaceutical expenditure could be achieved.

Belgium

Belgium has no formal monitoring system on the budgetary impact of pharmaceuticals. However, since 1999 the Social Security authorities have organized a data collection system called "*Pharmanet*" to obtain better insight into the consumption trends of pharmaceuticals and their impact on the country's overall drug expenditures, including spending across various therapeutic categories. *Pharmanet's* data can permit prescriptions to be linked to a variety of variables, including the prescriber, age, gender and concomitant medication. At this point in time it is not possible to link the data to disease or indicated use. The data is used to evaluate consumption trends, down to the lowest ATC-level. *Pharmanet* is permanently used to monitor the system (Social Security expenditure and patient spending) and, when necessary, to adjust, refine or adapt the system.

Data on evaluation monitoring is presented below:

Graph 2: Evolution of the expenditures on pharmaceuticals for non-hospital patients (contribution health insurance versus contribution patients)

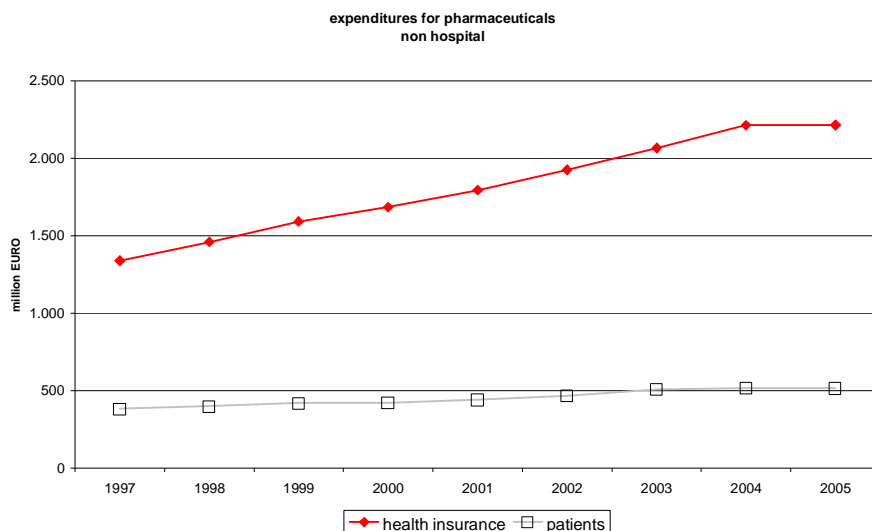


Table 8: Expenditures for non-hospital pharmaceuticals (in Million Euros)

expenditures for non-hospital pharmaceuticals (in Million EUROS)

	1997	1998	1999	2000	2001	2002	2003	2004	2005
health insurance	1337,2	1458,0	1589,9	1682,5	1792,8	1923,2	2063,7	2211,8	2212,4
patients	379,9	397,5	417,5	421,8	439,2	465,8	506,9	516,6	513,5
total	1717,1	1855,5	2007,5	2104,3	2232,0	2388,9	2570,7	2728,3	2725,8
patients (in % of total)	22,1	21,4	20,8	20,0	19,7	19,5	19,7	18,9	18,8

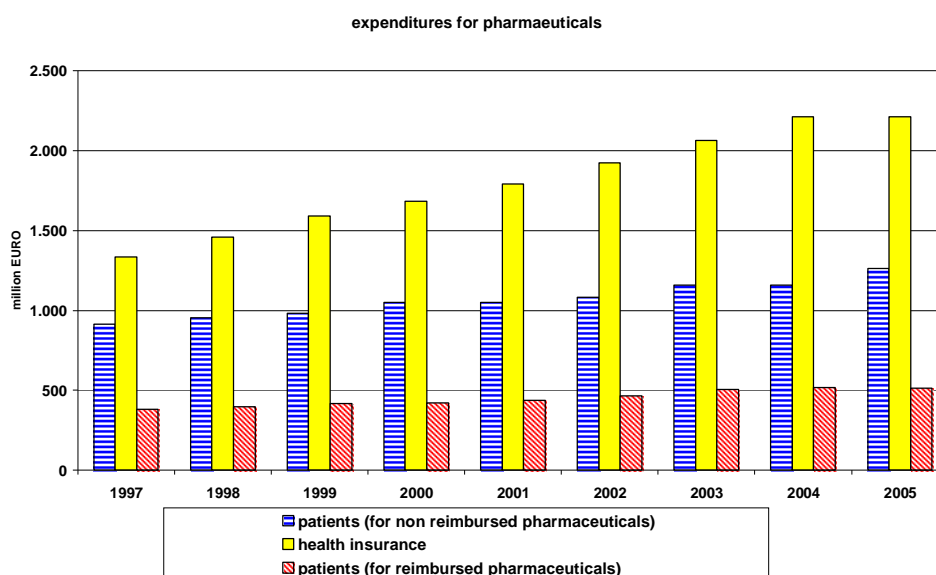
Table 9: Total expenditures for ATC pharmaceuticals per class and per category (%) of reimbursement by patients (out-of-pocket payment)

2005 expenditures for non-hospital pharmaceuticals per ATC class (in Million EUROS)

ATC		Total	% paid by patients
A	ALIMENTARY TRACT AND METABOLISM	294.63	17.15
B	BLOOD AND BLOOD FORMING ORGANS	144.10	13.09
C	CARDIOVASCULAR SYSTEM	715.10	21.52
D	DERMATOLOGICALS	42.14	18.10
G	GENITO URINARY SYSTEM AND SEX HORMONES	62.31	26.63
H	SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	64,7	8.24
J	ANTIINFECTIVES FOR SYSTEMIC USE	263.98	22.14
L	ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	225.28	0.77
M	MUSCULO-SKELETAL SYSTEM	136.90	24.05
N	NERVOUS SYSTEM	456.59	20.09
P	ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS	0.87	26.98
R	RESPIRATORY SYSTEM	259.11	26.39
S	SENSORY ORGANS	34.52	19.81
V	VARIOUS	24.63	1.45
Z	unknown	1.39	0.35
		2.725.82	

Insofar as patient access is concerned, cost is generally not considered to be a hurdle for patients who need access to pharmaceutical care since health insurance covers more than 50 % of the costs for all pharmaceuticals. Moreover, a mechanism called “MAF,” or “maximum invoice”, i.e. the maximum co-payment to be made by families below a certain income level for health care (including medicines) limits patients’ expenses by establishing an annual maximum amount of co-payment for all health care interventions; the rest is paid for by the social security system.

Graph 3. Expenditure for pharmaceuticals. Belgium



The key success factor is the availability of a high-performance monitoring system (type Pharmanet) that provides a detailed evaluation and, when necessary, permits rapid intervention.

The system’s major benefit is the possibility it provides for making distinctions between different types of therapies, as well as making patients more co-responsible (through higher out-of-pocket payment for less vital medicines, for medicines with less expensive alternatives...). The experience is recommendable and successful.

Denmark

The reimbursement system is based on individual need and the rate for reimbursable medicinal products depends on a given patient’s prior consumption of pharmaceuticals within a one-year period. E.g., the amount to be reimbursed to any given patient will depend on the total cost – calculated on the basis of reimbursement prices – of all eligible medicinal products purchased by that patient within a one-year period. The goal of this system is to ensure that the neediest patients get their costs reimbursed through the public system.

The system's management is decentralized, with local counties and regions overseeing patients' expenses and reimbursements in accordance with financial parameters established annual financial framework by the Danish government.

To run a reimbursement system such as the Danish one, a central IT-system that links all the pharmacies in the country is essential. The Danish system might differ from other European systems where reimbursement is often handled through private health insurance companies.

Experts from Denmark recommend this practice. However, the decision of whether to choose between publicly-funded or privately funded health insurances it is clearly a question of national health policy to be made by each country.

Finland

Pharmacies must transmit information on all dispensed medicines that have been reimbursed to the Social Insurance Institution in Finland (Kela). This information is then fed into the prescription register at Kela. The register includes the following information:

- § *Patient*: identification number, age, sex, and diseases entitling the patient to special reimbursement
- § *Doctor*: sickness insurance code => speciality
- § *Medicine*: the Nordic code number, ATC group, brand name, package size, strength, number of packages, dosage and indication as written by the doctor, coded indication for special reimbursements, cost, reimbursement, date of prescription and date of purchase.

Based on the above information, Kela continuously follows the accumulation of a patient's co-payments. When the annual ceiling sum of co-payments (EUR 617 in 2006) is reached, the patient is entitled to an additional refund. Kela reports regularly on the number of patients entitled to an additional refund and the budgetary impact of additional refunds.

Data on reimbursement cost and drug utilisation based on the prescription register at Kela is published annually in the *Finnish Statistics on Medicines* and on the Kela website⁴³.

In the year 2005 patients' share of total costs of reimbursable medicines was 33 %. In the basic refund category patients' share of the costs was on the average of 57.9 %, while in the lower special refund category it was 30.1 % and in the higher special refund category, 2.7 %. The figures do not include social assistance paid by the local municipal authorities towards the cost of drugs, nor the drug costs taken into account in calculating the level of support paid to pensioners, children, and people with disabilities. No figures on these compensations are available.

⁴³ <http://www.kela.fi/research> – Reimbursement of medicine costs – Statistics

Patients, patient organizations, pharmaceutical companies and doctors claim that when changes in legislation occur these often affect patient's co-payments, increasing the patient's share of the costs (and possibly, patients' access to medicines). In their opinion the patients' share of medicinal costs is too high in Finland and it might affect treatment compliance.

Several comments follow concerning the Finnish experience:

§ Reimbursement categories are graded according to medical criteria based on the severity of an illness and the necessity of drug treatment. Severe and chronic illnesses that entitle patients to reimbursement under the special refund categories are defined in a Government Decree ³². To change the status of an illness listed in a decree is politically difficult because of strong opposition by patients and public opinion. The higher the reimbursement status, the more difficult it is to effect a change downwards.

§ Generic substitution is in effect in Finland. The consumer can deny the substitution without any penalties. When a medicine is granted a higher special reimbursement status, patients seem to deny its substitution more often. In the higher special reimbursement category the patient pays only a fixed co-payment of EUR 3 per purchase, per medicine and seems not to take any financial interest in substitution. It can be concluded that substitution does not work effectively in this higher special reimbursement category.

§ The structure of patient's co-payment in different reimbursement categories was changed early on in the year 2006. Prior to that change the patient's co-payment included, in addition to a co-payment percentage, a fixed co-payment per purchase of all medicinal products included in the same reimbursement category. Because of the fixed co-payment scheme, many patients found it more economical to buy all the products belonging to the same reimbursement category at the same time – often up to a three-month supply. As a result, unnecessary purchases were observed. Currently, the co-payment is calculated as a certain percentage of the medicine's cost or a fixed co-payment per medicine. The actual model does not encourage patients to buy large amounts at the same time or to concentrate their purchases. Less waste and improved compliance are expected to be gained.

§ Early in the year 2006 a fixed co-payment per medicine was also introduced into the additional refund. Prior to that, once the annual ceiling of co-payments was reached, medicines were free - thus increasing the consumption and/or purchase of drugs. One challenge is to determine the patients' share on a level that won't hinder purchases but will act to restrain unnecessary purchases.

Experts have commented that when patients bear a greater share of the costs, their awareness is increased so measures that stimulate that awareness are to be recommended. The Finnish reimbursement system is based on the principle that reimbursement rates for severe and chronic illnesses should be higher than for acute and temporary illnesses. This principle has been largely accepted in Finland.

Hungary

Concerning impact on access to patients, poor patients can get the medications that are reimbursed for free. The patients have a limit of (12.000 HUF/month calculated upon the co-payment).

Ireland

The Drug Payment scheme first introduced in 1999 is acknowledged to be consumer-friendly and a significant improvement on the systems that existed heretofore. Once the individual/family reaches the €85 threshold in the calendar month on approved prescribed medicines the State covers the balance. The medical card scheme ensures that patients who are unable to afford their drugs/medicines receive them free of charge.

Italy

Regional expenditure is monitored by the National Observatory on Utilisation of Medicines (Osmed). Ticket methodology does not seem to be very effective because regions with tickets may have higher pharmaceutical expenditures than the national average and regions without tickets appear to have their pharmaceutical expenditures well-controlled (under the national average)

The ticket system may impact on access; for this reason only a limited number of regions use it.

Industries would like to see a higher co-payment, but such a policy would probably be very difficult to implement because of the nation's expectations on universal coverage by the National Health Service and possible issues related to equity of access.

Latvia

Patients claim that they cannot afford to make the co-payment for drugs with high prices. On the positive side, say experts from Latvia, this encourages more rational use of drugs.

Lithuania

On the issue of access, Lithuanian experts cite the availability of better access to medicinal products for children, disabled persons, and pensioners. They state that it is difficult to evaluate the impact on innovation.

Poland

Concerning evaluation of budget impact, experts from Poland indicate that the practice of cost-sharing increases the availability of reimbursed medicines, but that country's budget is limited in that regard. There is no data on budget impact

Impact on patients' access to medicines is more difficult to measure and depends on the level of co-payment. The main difficulty is how to classify medicines to relevant level of co-payment.

Portugal

Every year *Infarmed* publishes an annual statistical report with information on its activities, particularly on the marketing of medicines in Portugal. It analyses the sales growth of pharmaceutical specialities in terms of total market share and impact on the amount consumed by the NHS. On its website, *Infarmed* also publishes information on a monthly basis regarding the evolution of the NHS's pharmaceutical expenditures.

The Portuguese reimbursement system was evaluated for the period 2004-2005 by an independent consulting group (Europe Economics). The study's conclusions, "*Sistema de Comparticipação de Medicamentos e a sua Adequação à Reforma da Saúde, incluindo o Regime de Preços dos Medicamentos a Participar pelo Estado,*" are available on Infarmed's site⁴⁴.

⁴⁴ The study's recommendations on the Portuguese co-participation system were:

(a) High priority reforms —

– The reference price system should be widened and based on protocols, allowing it to include in-patent drugs. Under this scheme the co-participation rate would be based on therapeutic protocols devised and put forward by a central committee and designed to achieve better therapeutic value. The co-participation regime for chronic diseases would be included under this system.

– Prices of generics should be liberalised. In particular, the existing regulation, which hinders the movement of generic prices, and which limits the price of the first generic in the market at 65 per cent of the reference branded products, should be removed.

– The reference pricing system for generics should be changed so that the reference price is defined on the basis of the price of lowest or second-lowest price generic.

(b) Lower priority reforms —

– Once the generic market has achieved a sufficient level of maturity (one may use a penetration level of 20 per cent as a measure), the additional 10 percentage points currently given in the co-participation of generics should be removed.

– The additional 25 percentage points that are added into the calculation of the reference price for users under the Special Regime should not be extended beyond December 2005, when the existing law expires.

– New medicines used for the treatment of diseases covered under the protocol-based reference price system should not have to negotiate with Infarmed about the co-participation price; these medicines should be allowed to have any price, provided it is below that calculated by DGE.

– The parallel import of generic medicines should be encouraged.

– Survey-based systems of gathering information on prescription habits should be adopted.

– Once the extent of use of the protocols is clarified, and once it is possible to obtain a clear view on the levels of the expenditure of medicines borne by patients, it is recommended that consideration should be given to setting a threshold for that expenditure, above which the co-participation of the State would be greater.

Slovakia

Evaluation of drug consumption is made every three months by health insurance companies.

Concerning budget impact, in some areas it is possible to evaluate drug consumption. Some impact might occur on access to patients in the group using me-too drugs, e.g. statins, ACE inhibitors.

Impacts on reward for innovation are claimed mainly by the generic industry and their affiliated organisations.

Slovenia

Health insurance institutions monitor drug consumption on a regular basis and produce and publish quarterly analyses and reports on consumption.

Voluntary insurance represents approx. 15-20% of the national market's value.

Voluntary insurance is practically ubiquitous; therefore relative impact is unseen from the side of the patient. Currently, as a consequence, patients do not have any out-of-pocket co-payments. Access to medicines is therefore very high, because it can be expected that people would be hesitant to pay 25% or 75% of a product's price from their own pockets, because this is not in the local tradition.

The system rewards innovation, as more than 60 % of the market value corresponds to originator products. If large co-payments were necessary, people would turn even more to generics, or else do without the product.

The system is stable and functions well. Gradual increase of burden of newer medicinal products, which frequently come to reimbursement list on the intermediate list, raises the pressure towards higher premiums, which are currently independent from a person's income (approximately 20 € per month). In practice, this system has proven successful and is recommendable.

Spain

Spanish authorities perform a periodic review of the impact of cost-sharing on the total amount of pharmaceutical expenditure. The percentage that corresponded to cost-sharing was approximately 6% in the year 2005.

Concerning impact on access to patients, past abuses of pensioners' prescriptions (which are free of cost-sharing) by citizens who would otherwise have to pay their fair share for such medications, is avoided through the use of a health ID card and inspections.

Sweden

Monthly evaluations examining patient co-payments over time and as a percentage of total drug costs are performed at the country as well as at county council level.

Co-payments amount to approximately 20% (corresponding to 4 billion SEK) of the total annual costs for reimbursed medicines.

The first deductible within an annual period is perceived as too costly by certain individuals (pensioners, people with low incomes, etc). However, it is possible to make payments on an installment plan.

No changes are foreseen regarding practices that are currently in use. It has been claimed that co-payments could help limit unnecessary use of medicines and increase compliance.

UK

There is no formal monitoring system in place.

Published data shows that the revenue from prescription charges and pre-payment certificate fees was £422m for England in 2004-05. Additional revenue is also raised by an NHS Trust or Hospital when a charge is paid by a non-exempt patient.

The policy means that no one should be unable to obtain prescribed items on the basis of affordability, as those on a low income are exempt from charges. Citizens' representatives claim that those whose income is just above the threshold for free prescriptions cannot afford multiple prescription charges or a lump sum for a pre-payment certificate. Groups representing patients with medical conditions that are not included in the list argue that the list is not in line with modern medicine and that "their" condition should be included.

This system has been in place since 1968 and set up costs are not available. It is based on arrangements for paying pharmacists centrally for items supplied to patients. It permits pharmacists to collect charges at the point of supply and the flat rate charge means that the patient knows what he/she will have to pay regardless of the cost of the item to the NHS, where the patient lives or who is providing the treatment. The fact that all items are free to an exempt patient means that a doctor's clinical judgement is not dictated by patient charges. This also means that a patient does not need to seek one exemption route for one type of medication and a second route for other items.

The present arrangements for patients' charges sit with arrangements for paying pharmacists and have done so since their inception. They permit charges to be collected at the point of supply at a level that is the same nationally and within a system funded by taxation. Any evaluation of the success of systems applied elsewhere would depend on a number of factors, for example how it is funded, arrangements for paying pharmacists and if the same arrangements should apply in the UK.

Literature review

The RAND experiment (Manning et al, 1988), carried out between 1974 and 1977, is still often quoted as the benchmark study on the effects of cost-sharing in health care. It consisted of a randomised trial of over 7,700 individuals designed to assess the effects of cost-sharing on health services' utilization and health outcomes. Individuals were offered the choice of among 15 plans, with varying levels of co-insurance, and an expenditure limit of US\$1,000. The results showed that co-insurance reduced the use of both appropriate and inappropriate health care. They also showed the negative effects of co-insurance on equity, as poorer individuals – especially poor children – were more affected than those with higher incomes. The study did not provide any evidence of any significant impact of cost-sharing on overall health care utilization or health status.

In 1995, Rubin and Mendelson reviewed 19 studies on cost-sharing, most of them in the US. Their findings supported the RAND results: reduction in overall demand of appropriate and inappropriate care.

Hughes and McGuire (1995), reviewed the price elasticity of the demand for drugs in the UK's NHS and did their own analysis. Demand elasticities ranged from -0.01 to -0.02 in an early study by Lavers (1983) up to -0.37 in their own study. All studies showed reductions in consumption and in expenditure on pharmaceuticals, but they did not analyse the potential effects on overall health expenditure and on health.

The two most comprehensive reviews on cost-sharing in pharmaceuticals are those done by Lexchin and Grootendorst (2004) and Gibson *et al* (2005).

Lexchin and Grootendorst reviewed studies, regardless of the methodology, that assessed changes in prescribing behaviour, drug cost utilization, overall health care costs or utilization or changes in health status. They then expressed their results in quantitative measurements in English and French from 1-1-1977 to 31-12-1999 in OECD countries.

59 studies were initially selected, but 5 were later excluded because of lack of controls (3), extremely small groups (1) and post-only time series (1). Of the remaining 54 papers, 43 referred to the US or Canada, 7 to the UK and 6 to other EU countries. It is worth noting the apparently limited amount of research done on this topic in the EU, although this might be partially due to language bias and the disregard of grey literature.

Authors discuss the potential population bias in the selection: the bulk of the studies comes from the US Medicaid (mainly low-income, non-elderly and elderly with chronic diseases), US Medicare (elderly), Canadian provincial drug programs (mainly elderly and those receiving social assistance), and the UK's NHS (total population). They also discuss the types of study designs found (experimental time series variations in drug fees, cross-sectional variation in drug fees) and the potential methodological problems in quantitatively assessing the impact of prescribing fees (sample selection bias, endogenous policy changes, omitted confounding variables and regression to the mean). They present the results by population group, finally concluding that "In general, in all of the different population groups, supplemental insurance increased drug use and fees

reduced use” and that “consistent with predictions of economic theory, the degree of price sensitivity was higher the larger the share of income spent on prescription drugs. Hence those with low income were particularly price sensitive”. They note that nearly all co-payments are under US\$8 and that for larger co-payments the relative impact would likely be higher. In their conclusions they state that given the potential implications for accessibility and equity, “Whatever policy changes are made in this area need to be closely evaluated. In the past, changes have been made without any prior objective research evidence and without plans to study downstream effects of policy changes” (Lexchin and Grootendorst, 2004).

The most recent comprehensive review on the effects of prescription drug cost sharing is Gibson et al (2005), although it was restricted to studies in English on populations from the US and Canada. The authors identified 30 studies, of which, according to the authors, eleven had not been addressed in previous reviews. Their results point to the fact that besides confirming the conclusions of previous reviews that cost-sharing usually reduces consumption of prescription drugs and induces a switch to generics, high levels of cost-sharing have other troublesome, although not consistently reported, unintended effects, namely, treatment disruptions such as lower levels of treatment adherence, continuation and initiation

IV. Discussion

Key messages

- § Most insurance systems worldwide have extensively applied various modalities of cost-sharing policies on pharmaceuticals.
- § Establishing exemptions and ensuring that they are appropriately enforced, requires quite sophisticated mechanisms of control in order to avoid fraud.
- § An income-related cost-sharing mechanism probably requires a well-developed income tax system that allows setting up and enforcing means-tested payments.
- § Cost-sharing is not assumed or claimed to affect innovation

Risks

- § Cost-sharing has usually been shown to have negative effects on access and equity (unless user income and other considerations are taken into account in the formula for determining the amount to be paid by the user). Traditional exemptions have been often inappropriate, leading to criticism and the discredit of the system and often to fraud. It might lead to non-compliance and discontinuation of treatments and impose a too heavy financial burden to low-income, heavy users
- § Setting up, broadening the scope or introducing changes in cost-sharing often face strong social opposition, as the citizens concerned, especially in countries with well-established publicly funded health systems are very sensitised to that issue. This might restrict the ability and willingness of policy makers to establish or modify this practice.
- § The effects might be compensated by complementary insurance.
- § Cost-sharing increases administrative costs (in relation to a free access system), which might be larger than the amount of user payments collected if fees are relatively small. This is especially relevant for drugs delivered at health centres that do not charge other services, as it will require devoting some resources to collecting and processing the fees. The administrative cost is likely to be negligible when drugs are delivered through independent retailers and reimbursed by the third-party payer.
- § Cost-sharing does not seem to discriminate according to therapeutic effectiveness, and hence, it might not improve efficiency nor reduce abuse, just shift costs from the insurer to the patient.

- § Cost-sharing might delay the first contact with the health system to a time when the disease process is more advanced, the intervention more costly and some irreversible health losses might have occurred.
- § Cost-sharing might promote fraud (e.g. regular users obtaining drugs through an cost-sharing exempt user)
- § If not applied to all alternative treatments for a condition it might distort the efficient allocation of resources (e.g. users might be hospitalised without clinical need for it, only in order to allow them free access to a drug treatment)
- § A fixed co-payment per prescription or package might be compensated by physicians prescribing larger packages.

Key success factors

- § Cost-sharing is relatively easy to implement when drugs are distributed through private retailers (pharmacies), paid by the consumer and later reimbursed by the third-party payer.
- § A difficult balance has to be found if cost-sharing has to play a relevant role in expenditure containment while not disproportionately affecting people at risk (low income individuals and heavy drug consumers).
- § The Nordic countries have recently introduced sophisticated cost-sharing arrangements that seem to adequately address these concerns by establishing varying amounts for cost-sharing and setting time limits to cost-sharing. These approaches, however, require appropriate data recording systems and the use of new ITs, such as, individual magnetic health cards, etc.

Reference pricing

I. Introduction

Description

Reference pricing (RP) is a financing mechanism that consists in establishing a maximum level of (third-party) financing/reimbursement for a group of drugs assumed to be therapeutically equivalent. The share of the price above the reference price is borne by the consumer.

Modalities

RP mechanisms differ in two basic ways:

1. The criteria *for defining* the therapeutic equivalence and, consequently, the grouping of drugs into clusters, and
2. The criteria *for computing* and up-dating the reimbursement price

Regarding therapeutic equivalence, the criteria for defining RP groups (or clusters) can be either very narrowly (including only products with the same active substance, form of administration, dosage, etc.) or very broadly defined (including products for a given indication with similar efficacy/effectiveness). There might be additional criteria for the inclusion/exclusion of certain drugs from the reference price system; for instance, drugs under patent protection are often excluded.

The Cochrane Collaboration Review on Pharmaceutical Policies (Aaserud et al, 2006) defines three levels of drug groups for RP:

- Level 1. Grouping of drugs that have identical bioactive ingredients and therefore are considered therapeutically interchangeable i.e. generic groups. Examples are Canada (Ontario), Denmark, Italy, Norway, Sweden and the USA (Medicaid).
- Level 2. Drugs pooled in analogue groups, i.e. slightly different chemically but in related groups with comparable or identical indications (e.g. the analogue group of ACE inhibitors). This is, for example, used in British Columbia.
- Level 3. Grouping of all drugs used to treat a particular condition (e.g. all hypertension drugs). This is, for example, used in the Netherlands and Germany.

The reference price value is based on the prices of a subset of the products included in the cluster; for instance, it might be the average price of three products with the lowest price, or the price of a single product with the lowest price, etc. The value of the reference prices is regularly up-dated, for instance, annually.

Purposes

The immediate purpose of RP is to generate or reinforce price competition in pharmaceutical markets. RP is often considered a component of or complement to a generics policy (although, strictly speaking, RP does not imply the existence of generics). The final aim of reference pricing is to reduce pharmaceutical prices and expenditure for third party payers while maintaining a product's standard quality.

Theory/ Rationale

In a perfect competition scenario, and assuming products were homogeneous, all products would be priced the same, since no consumer would pay a higher price for the same good. Price differences would only be possible as a result of differences in quality.

However, when manufacturers differentiate products or attempt to promote consumer loyalty to a given brand, homogeneous products might have different prices. In pharmaceutical markets, firms often compete by marketing and advertising, not by prices. This situation is partly driven by the fact that consumers are not perfectly informed on the characteristics of medicines and health professionals who influence the demand for drugs are often not economically accountable for their decisions and, hence, insensitive to prices.

RP has an impact on demand because it provides an element of price-sensitivity. The payer sets a single price for all products that it considers to be equivalent. If the doctor and the patient choose to consume a brand whose price is higher price than the reference price, the patient will have to pay the difference.

RP forces manufacturers of branded products to choose between two strategies: (1) to reduce prices to bring them in line with the reference price or (2) to maintain prices above the reference price and, therefore, capture a brand-premium for its efforts in marketing and sales and, eventually, for real differences in quality.

The rationale of RP is based on the assumption that products in a single price group are equivalent and homogeneous for a well-informed consumer.

II. Application in Europe⁴⁵

Overview

- § Most MS use RP (17); 2 eliminated it (NO, SE)
- § RP usually applies to all product categories when generics are available. Some exemptions exist for specific products (anti-HIV in NL, dermal products & anti-arrhythmia in SL, central purchased in LT)
- § Grouping of medicines is usually narrow, per active substance and form (a). HU and IT have mixed systems and broader groups (ATC4-5), particularly when no generics are available. NL and LV compare treatments.
- § The reference level is usually established as a function of the lowest price.
- § Experts are the main source for setting up the system. Other Member States and literature are referred to as well.

Table 10: Reference Pricing in Europe⁴⁶

COUNTRY	DATE	GROUP	STANDARD CLASSIFICATION	REIMBURSEMENT LEVEL
BE	June 2001	Drugs that have the same active ingredient(s)	ATC5	Is determined for each individual (new) reference speciality.
DE	1989	Drugs that have the same active ingredient(s)	ATC4	Fixed at the lower 30 % of the Price Range within the Group.
DK	1993	Drugs in the RP system on the basis of active ingredient(s), form(s) and strength	ATC5	The lowest drug price in the group.
EE	2003	Drugs that have the same active ingredient(s) and form(s)	ATC5	The second lowest price in the group.
EL	Over 20 years	Drugs that have the same active ingredient(s) and form(s)	ATC5	A Reference Price per therapeutic category and a Rebate Price per medicinal product are established.
ES	1999	Drugs that have the same active ingredient(s)	ATC5	The average of the 3 lowest prices, calculated by cost of treatment/day.
HU	1993	Drugs that have the same active ingredient(s) and form(s) -1993- Medicines chemically slightly different but related - 2003-.	ATC5	In a RP group (ATC5), the lowest price per unit (PPU).

⁴⁵ Authors' note: Although Cyprus and Malta stated that they have reference pricing, their systems do not coincide with the definition used in this study.

⁴⁶ Authors' note: Although the classification WHO ATC/DDD states that there are five official levels (from ATC-1 to ATC-5) - www.whocc.no/atcddd/atcsystem.html#2-, some countries answered that they used ATC-7. We have edited ATC7 to read as ATC 5.

COUNTRY	DATE	GROUP	STANDARDCLASSIFICATION	REIMBURSEMENT LEVEL
IT	2003	Drugs that have the same active ingredient(s) and form(s) , are bioequivalent and have the same therapeutic indications (when generics are available). Medicines that are slightly different chemically, but related (without generic competitors)	ATC 4	The lowest drug price in the group (which, by law, must be at least 20% cheaper than the originator). Calculation of the average cost per DDD (expenditure in mil €/ utilisation in mil DDD) and the % of utilisation and expenditure in the group.
LT	1996	Drugs that have the same active ingredient(s) and form(s)	ATC 5	Reimbursement level is determined according to the disease.
LV		Drugs that have the same active ingredient(s) and form(s). Drugs that have the same active ingredient(s). Medicines that are slightly different chemically, but still related.	ATC 3, 5	The lowest drug price in the group.
NL	1991 (current reimbursement levels from 1999).	Drugs with a (more or less) similar indication, route of administration, targeted age group and for which no clinically relevant differences in outcomes apply.		Before 1999: The weighted average price of the group based on prices After 1999: Cost-effective products - the price of the first product becomes the reimbursement limit of the cluster in which both products will be placed.
PL	1999.	Drugs that have the same active ingredient(s) and form(s). Drugs that have the same active ingredient(s). Medicines slightly different chemically, but still related.	ATC4	The lowest drug price in the group.
PT	March 2003.	Drugs with the same active ingredient, pharmaceutical form and dosage (cluster).		Reference price corresponds to the highest generic price for each cluster on the market.
RO	1997	Drugs that have the same active ingredient(s) and form(s)		The lowest drug price in the group.
SE	1993 to 30.09. 2002	Drugs that have the same active ingredient(s) and form(s) Drugs that have the same active ingredient(s) , if the form was considered clinically relevant.		The lowest drug price in the group.
SK	1996	Drugs that have the same active ingredient(s) and form(s).	ATC5	The lowest drug price in the group.

COUNTRY	DATE	GROUP	STANDARD CLASSIFICATION	REIMBURSEMENT LEVEL
SI	November 2003	Drugs that have the same active ingredient(s) and form(s) and the same strength (dose of active substance) and are bioequivalent (strict implementation of generic definition in the Directive 2001/83)	ATC5	The lowest drug price in the group.

Source: Data from EASP's questionnaire

Individual replies by countries

Belgium

Reference pricing has been used in Belgium since June 1, 2001. The groups are development with drugs that have the same active ingredient(s). Neither the pharmaceutical form, mode of delivery, nor the strength of its active component(s) is taken into account to determine whether or not an original speciality enters the reference reimbursement system. However, some exceptions are contemplated:

- § An injectable, original speciality does not enter the reference reimbursement system if the reimbursed generic alternative is a non-injectable speciality;
- § Original specialties can temporarily obtain the status of exception if they have an ATC code (WHO) different from the generic alternative; however, this temporary status must be confirmed. In such cases, the pharmaceutical company can submit an application to the Commission for Reimbursement of Medicines (if not, the original speciality enters the reference reimbursement system anyway); the original speciality loses its status of exception when a generic alternative with an identical ATC code is added to list;
- § A pharmaceutical company can also obtain the status of exception for some original specialties via an application, submitted to the Commission for Reimbursement of Medicines. If the request is found acceptable, the original speciality will be allowed to enter the reference reimbursement system; if the Commission accepts their arguments the reimbursement basis will later be restored.

The standard classification is ATC5.

The reference reimbursement system is reviewed every six months (on January 1st and on July 1st). Three months prior to those dates, a determination is made regarding new "reference specialties" (original medicines that will enter the system). An original speciality enters the reference reimbursement system if a (cheaper) generic, reimbursed speciality is available which contains the same active component(s). This means that its reimbursement basis is diminished by 30% (ex-factory level), while maintaining the applied price. Consequently, a new reimbursement basis is determined for each individual (new) reference speciality. Three months ahead, the new "reference

specialities” are determined or the maintenance of the status of exception is checked. This gives the pharmaceutical industry the opportunity to submit applications to obtain the status of exception or applications for price reduction.

Reference pricing is only applied on (post-patent) specialities with generic alternatives (same active component).

The Belgian reference pricing system was elaborated by economic experts, based on other countries’ experiences.

Denmark

The existing system entered into force in Denmark on the 1st of April 2005. Different kinds of reference pricing have been used since June 1993. Denmark groups the drugs in the RP system on the basis of active ingredient(s), form(s) and strength and assigns the ATC5 level. The reimbursement level is based on the lowest drug price in the group, defined as the same active substance, the same or similar pharmaceutical form, the same strength and the same package sizes (allowing for a maximum of 25% deviation between package sizes within a group). It is applied to all groups of medicines, providing a substitution with the same active ingredient (synonymous products) is available, i.e. medicinal products that compete in parallel with imported products and/or generic products.

The reimbursement groups for reimbursable products are identical to the substitution groups, cf. section on Generics Policies/Denmark.

Estonia

In Estonia, reference pricing has been used since 2003. It is applied to drugs that have the same active ingredient(s) and form(s), to level ATC5 and reimbursement is based on the second lowest price in the group. Reference pricing is used for all groups which have generic competition.

Germany

Reference pricing started in 1989 in Germany. The standard grouping is all active ingredient(s) in ATC-Groups at level 4 ("Jumbo"-Groups), drugs with mayor therapeutic additional benefit in comparison with the other substance within the group are excluded. Special sub-groups may be established if therapeutically necessary. Grouping only for same active ingredients is also possible, if no "Jumbo"-Groups can be established. Different combinations of active ingredients can also be grouped if they are treating similar conditions. The standard classification used is ATC 4.

Reference prices is fixed at the lower 30 % of the Price Range within the Group

All drugs that can be grouped are covered by reference-prices. It will be only groups with comparable drugs. There are three different groups:

- (a) same ingredient (ATC5),
- (b) same class: pharmacologically and therapeutically comparable (and chemically related) drugs based on ATC-Level 4 ("Jumbo"-groups: regular grouping)
- (c) combinations drugs

All products that can be grouped are included. The German system allows the coverage of maximum 80 % of prescription / 50% of sales volume. There is no grouping of soloist.

The experience used to set-up this practice are HTA-reports for every grouping that are written on the base of international clinical studies. Reference prices are established only with prices in the German market.

Cost development for drugs under reference prices and outside is monitored on annual basis. Reasons for cost increase are monitored annually: prices, number of packages, cost per prescription/ share of high-cost pharmaceuticals

Greece

Reference pricing have been used in Greece over 20 years, grouping drugs that have the same active ingredient(s) and form(s) under standard ATC5 classification for all groups of medicines. It excludes products that are developed in Greece and no reference product exists in other EU states.

A reference price per therapeutic category and a Rebate Price per medicinal product are established. Should the weighted difference between the price of the product in a therapeutic category and that category's reference price be positive, the pharmaceutical company must then pay back to the insurance organisation the amount corresponding to that difference, multiplied by the quantities reimbursed by Social Insurance Organizations.

Hungary

In Hungary, reference pricing has been used since 1993. There are two major types of reference pricing:

- Drugs that have the same active ingredient and form (these are called substance fixed groups) - introduced in 1993 (based on ATC5), and
- Medicines that are slightly different chemically but related (these are called therapeutic fixed groups) - introduced in 2003 (based on ATC4).

Reimbursement level depends on ATC5 or ATC4 groups.

In substance fixed groups, the reference product is the drug with the lowest price per unit (PPU) and that:

- a. is not canceled from the register

- b. is a bioequivalent of the original product
- c. was marketed in the last 6 months of the previous year
- d. its degree of days on treatment (DOT) based on market share (MS) reached 1% in its RP group.
- e. package size: the amount of active ingredient – taking into account the relevant indication – can't exceed the prescribed monthly defined dose described in the "Summary of Product Characteristics."

In therapeutic fixed groups (ATC4), the reference daily therapeutic cost (DTC) calculation method is as follows:

1. Sort the products in ascending order by daily therapeutic cost.
2. Assign to every product its DOT-based market share (DOT MS of the last 6 months of the previous year).
3. The reference DTC is obtained by averaging the daily therapeutic cost of the lowest-priced products, in ascending order, which product's summarized MS reaches the 50% of the group.

The reimbursement = reference DTC * DOT * reimbursement rate.

The reimbursement level depends on the ATC4 group. ATC4 groups and maximum reimbursement levels are stipulated in the Ministry of Health's Regulations, and their norms follow the EU Directive on Transparency. Reimbursement levels can be 0%, 25%, 55%, 85% and, in special indications, 50%, 70%, 90% and 100%.

A reference pricing system based on the same active ingredient (substance fixed groups) is applied to each group of medicines that contain the same compound. A reference price system based on the same therapeutic indication (therapeutic fixed groups) is applied to those groups of drugs considered chemically related (ATC4) according to proposals made by the Chamber of Physicians. Every product category with reimbursement level higher than 0% is included in the system.

Italy:

In Italy two different systems for reference pricing exist, depending on whether generics are available or not.

For reimbursed medicines where generics are available

Functioning since 2003, this system applies to drugs that have the same active ingredient(s), bioequivalent form(s), and therapeutic indications.

The reimbursement level is set at the lowest drug price within that group (which, by law, must be at least 20% cheaper than the originator).

For reimbursed medicines without generic competitors

Reference pricing in this system is done by grouping medicines that are related but whose chemical composition may differ (the ATC4 category is used). The average cost

per DDD is calculated (expenditure in million €/ utilisation in million DDD) and the % of utilisation and expenditure in that group is then calculated. If the average price per DDD of the group's top-selling medicines is excessive then companies are asked to cut their prices according to a formula. If companies do not agree, then the product is excluded from reimbursement.

Input to set up the practices was obtained from the expertise of experts, literature, and past experiences in the classification of medicines.

This methodology was extensively used in 2003 (National Form 2003) and resulted in a broad reduction in prices

Latvia

In Latvia, reference price grouping is applied if the drugs are interchangeable according to four criteria:

- 1) same indication;
- 2) same patient group;
- 3) no differences in efficacy or side effects; and
- 4) the same route of administration. The categories used are ATC 3 and 5; for reimbursement purposes, the lowest drug price in the group is used.

Lithuania

Reference pricing has been applied in Lithuania since 1996. The reference price group includes drugs that have the same active ingredient(s) and form(s), with standard classification ATC 5. Reimbursement level is determined according to the disease (for example, Captoprilum is reimbursed at the 50% level for cardiac insufficiency (I-II function class), but for ischaemic heart disease or hypertension it is reimbursed at the 80 % level).

Reference pricing is used for all medicinal products produced by more than one producer (when products are produced by only one producer, they become centrally purchased products).

Netherlands

Reference pricing has been used in the Netherlands since 1991 (current reimbursement levels originate from 1999). The system groups together drugs with mostly similar indications, routes of administration, targeted age groups and for which no clinically relevant differences in outcomes apply.

The reimbursement level is obtained from the group's weighted average price, based on 1999 prices.

Products introduced after 1999 can get a premium price if the manufacturer can show cost-effective medications with added therapeutic value; once a second and

therapeutically similar product arrives, the price of the first product becomes the reimbursement limit of the cluster in which both products will be placed.

Typically, RP is applied to all products except for products that cannot be grouped by drugs with mostly similar indications, route of administration, targeted age group and for which no clinically relevant differences in outcomes apply

Generally, there is no explicit policy that excludes certain product categories from reference pricing; in practice and implicitly, anti-HIV products are excluded.

Norway

A reference pricing system was used in Norway from 1993 to 2001

Poland

Reference pricing has been used in Poland since 1999. The system groups together drugs that have the same active ingredient(s) and/or form(s), and medicines that are related, although their chemical composition may differ slightly.

The standard classification used to group the drugs is the ATC4 level, but this is not a general rule. Each medicine is evaluated specifically.

The reimbursement level is set in accordance with the lowest drug price for all medicines in the same related group.

The opinions of experts were used to set up these practices.

Portugal

Reference pricing has been used in Portugal since March 2003. It is applied only to medicines with generics on the market (that contain the same active ingredient, pharmaceutical form and dosage) and is grouped in clusters, or drugs with the same active ingredient, pharmaceutical form and dosage. Reference price corresponds to the highest generic price on the market, for each cluster. Generics refer to INN generics with proven bioequivalence, not to branded generics (copies).

Romania

Reference pricing has been used in Romania since 1997. The system groups together drugs that have the same active ingredient(s) and form(s). ATC coding is used, but reference price is established based on INN and pharmaceutical form. The reimbursement level is set in accordance with the lowest priced drug in the group.

All medicines on the positive list have reference prices. Non-prescription medicines are only reimbursed for certain categories of patients (i.e. pregnant women, children); in

those cases, a “reimbursement price” is applied, one that is established differently from the reference price.

Experts’ opinions were the main source used to set-up the practice.

Slovakia

Reference pricing has been used in Slovakia since 1996. The system groups together drugs that have the same active ingredient(s) and form(s) (ATC5) and reimburses them at the rate of the lowest priced drug in the group. It includes individual drugs and “me-too” drugs but largely excludes orphan drugs.

Slovenia

Reference pricing has been used in Slovenia since November 2003. The system groups together drugs that have the same active ingredient(s) and form(s) (ATC5) and reimburses at the lowest drug price in the group. This system is applied only to some groups of medicines organized in clusters having the same active principle, strength and formulation. Medicines are selected from groups based on bioequivalence; dermal products and antiarrhythmic agents are excluded.

To set up the practice, experts and other countries’ experiences were used.

Sweden

In Sweden, reference pricing was used from 1993 until September 30, 2002. Drugs were grouped according to active ingredient(s) and form(s), and also drugs with the same active ingredient(s), if the form was considered clinically relevant. The reimbursement level was the lowest drug price in the group. Reference pricing was applied to all groups where generic competition was available.

II. Impact

Overall experiences reported by countries

§ Savings reported: HU: -5% in 6 months; IT: basis for price cut in 2004 with 500-600M EUR savings (around 5%); LV: -0.6MEUR in 6 months; DK: 100M DKK (around 1,5 %)

§ Impact on access: generally limited; some increase in out-of-pocket expenses reported; some supply problems reported.

§ Impact on reward: limited, as only off-patent products were involved; claims that incremental innovation was not rewarded.

§ Risks/Success factors:

- Need to win the confidence of MD's, patients, use of media (SL)
- Watch out for limitation of price-competition (NL, SE)
- What to do with new innovations/biotech?

Individual replies by countries

Belgium

Every six months the budgetary impact of new reference prices is evaluated (see table below):

Table 11: Budgetary impact of Reference Pricing in Belgium

Year	Measure	Applicable	1st estimation of budgetary impact (in euro) (1)	Last estimation of budgetary impact (in euro) (2)*	degree of realisation of the 1st estimation (3) [= (2)/(1)]
2003	1. Percentage (**) is increased from 20% to 26%	01/01/2003	-17.700.000	-17.019.521	96%
	2. New reference specialities (26%)(January)	01/01/2003	-6.752.203	-5.867.347	87%
	3. New reference specialities (26%)(July)	01/07/2003	-29.585.905	-37.201.907	126%
2004	4. New reference specialities (26%)(January)	01/01/2004	-4.907.065	-4.423.250	90%
	5. New reference specialities (26%)(July)	01/07/2004	-10.792.274	-11.637.546	108%
2005	6. New reference specialities (26%)(January)	01/01/2005	-26.284.498	-26.551.983	101%
	7. Percentage (**) is increased to 30%	01/07/2005	-15.662.178	-17.592.788	112%
	8. Extended reference pricing is introduced (30%) (molecule level)	01/07/2005	-28.114.345	-23.833.777	85%
	9. New reference specialities (30%) (July)	01/07/2005	-20.510.683	-18.856.980	92%
TOTAL :			-293.318.654	-290.014.318	99%

* The estimations of measures 5 to 9 are not final

(**) The percentage the reimbursement bases is lowered with when entering the reference reimbursement system

Source: Belgium. Health Ministry (EASP's questionnaire)

Reference pricing mechanisms were responsible for a drop in expenses in retail/2005 of > 30 million Euros in the first three ATC-4 classes (statins, acid inhibitors, anti-depressive agents).

The methodology used to estimate the drop in expenses was to calculate expected expenses by forecasting historical data, giving greater weight to recent data.

It had no impact on innovation because the system was only applied on post-patent specialities.

The main difficulties detected were in cases where an original speciality entered the reference reimbursement system for the first time (January 1st or July 1st) and only one generic alternative exists at that moment, supply problems can occur during the first months following that date.

This practice is recommended because it has results in prices competitions, which create room for innovation.

Denmark

In Denmark, evaluation takes place on an *ad hoc* basis, but there is no formal monitoring system.

The expenditure on public reimbursement was approximately DKK 100 million lower per year when compared with the level of the previous reference price system.

Insofar as patients' access to medicines is concerned, the Danish National Health Service issues a general reimbursement to patients for some of their pharmaceutical costs. Patients can receive a reimbursement when they spend more than DKK 480 a year on reimbursement-eligible medicines. Patients can also obtain another, more specific, kind of reimbursement known as the single reimbursement. In such cases, however, a doctor must make an application on the patient's behalf. The amount to be reimbursed is calculated on the basis of the least expensive medicine in the substitution group. The least expensive medicine is also used as the basis for calculating the total amount a patient is eligible to receive as a reimbursement for the medicines he or she has purchased.

Regarding the impact on reward for innovation: if the product's price is considered reasonable in relation to its therapeutic value and the product itself meets other qualifying criteria, general reimbursement is normally granted by the Danish Pharmaceutical Agency. The price is solely the pharmaceutical company's decision.

Estonia

In Estonia budgetary impact is evaluated on a quarterly basis. Reference pricing has generated price decreases which stabilized during a two-year period. A slight increase has been noted in out-of-pocket payments.

There is no impact on reward for innovation, since patented drugs are not covered by the reference price.

There were no major obstacles if there is political will to rationalize drug consumption by encouraging the use of generic drugs.

Reference pricing was successful in reducing drug prices and continues to encourage generic drug use. Price decreases should not be expected to continue unless further changes are undertaken within the system.

Germany

In Germany there are no relevant restrictions for access to new medicines.

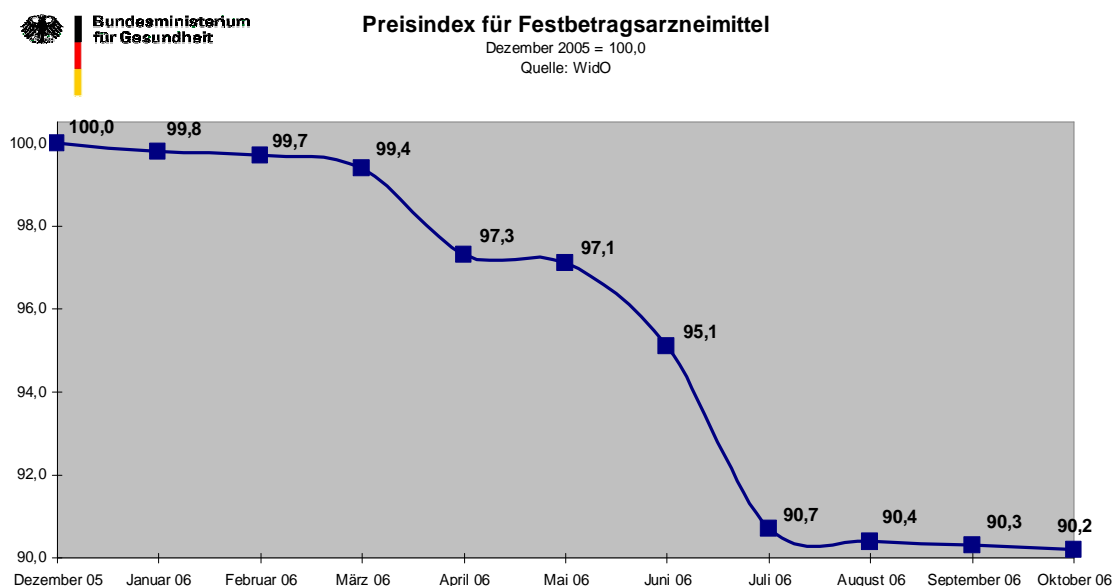
On the issue of reward for innovation, drugs that can prove they offer major therapeutic advantages in comparison with other drugs included in the group are not subject to reference prices. No restrictions for coverage or prescription are placed on high potential drugs (biologicals for treatment of cancer, HIV, EPO etc.) Cost coverage for high potential cost drugs is already more than 20 % of drug expenditure.

The main difficulty posed by a reference price system is how drugs should be grouped. Their classification should be based strictly on medical evidence.

In the German reference price system price controls do not exist; only reimbursements are limited. Patients' willingness to pay for additional costs is very limited. Hence, the market share of products with prices higher than the reference price is also limited. The reference price system is very successful in holding the line on prices but does not prevent doctors from prescribing more expensive drugs; they can still switch from low-cost drug-groups to high-cost drug-groups to treat similar conditions without any consequences. Reference pricing should, therefore, be combined with prescription guidelines.

Price regulations and prescription guidelines can be combined in a model based on competition, in which the single health insurance funds establish its own drug formulary on the base of tendering drugs. Also the doctors should take part in the contracts between sickness funds and pharmaceutical companies. Newly drafted legislation is currently under discussion in the German Parliament.

Graph 4: Price index in Germany



Source: Germany. Health Ministry (EASP's questionnaire)

Greece

Greece expects to introduce mechanisms to analyse budget impact in early 2007.

The main difficulty lies in the lack of qualitative data on prescriptions. The application of bar coding on medical packages and prescription packs will facilitate the extraction of data.

Hungary

Hungary reports the results of its reference pricing system twice a year, first in January and then in July. An evaluation of possible cost-containment effects is carried out prior to implementation and six months after implementation.

In the first half of 2005 Hungary spent 95 B HUF (1/3 of the total amount) on drugs that were involved in the RP-system. In the second half the expenditure on these medicines decreased by 5%.

The impact on reward for innovation only affects those medications that included in the RP-system at the ATC5-level, which do not have generic substitutes.

Italy

For reimbursed medicines when generics are available

With regard to its budgetary impact, reference pricing has produced substantial savings mainly by reducing the originator's price to a value equal (or very near) the generic's price. Smaller savings have been obtained by the use of "pure" generics.

It has no impact on patients' access to drugs because they can obtain the medicines they need free of charge. If they don't agree to use the generic version, they have to pay the difference.

For reimbursed medicines when no generics are available

Impact on pharmaceutical expenditure is monitored on a monthly basis by the National Observatory on the Utilisation of Medicines (OsMed) at AIFA. In the year 2004 this methodology resulted in a savings of between 500-600 mil €.

Concerning patients' access to medicines, studies showed that the methodology had no impact on access (= the difference between reference price and actual price was paid by pharmaceutical companies through price reductions).

One of the main difficulties encountered in the early phase was that companies resisted cutting their prices. Policy makers must be strong enough to "impose" price cutting mechanisms.

Latvia

In Latvia the impact of reference pricing is monitored every six months. In the last half year an evaluation of budgetary impact showed savings of approx. 570,000 €

Impact on innovation and on patient access is not monitored.

One of the system's main difficulties is the lack of comparative clinical data available on the relative efficacy and effectiveness of pharmaceuticals. Experts recommend that the same price be paid for pharmaceuticals with the same efficacy.

Netherlands

Budgetary impact, level and growth of pharmaceutical expenditure in the Netherlands is relatively low compared to other countries. This results from a mix of measures, including the therapeutic reference system, international price referencing (maximum price), claw-back and the covenant (a agreement between the Ministry of Health, Welfare and Sport, the Royal Dutch Pharmaceutical Society (Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie, KNMP), Dutch Health Insurers (Zorgverzekeraars Nederland, ZN) and the Trade Organisation of the Generic Medicines Industry in the Netherlands (Bond van de Generieke Geneesmiddelenindustrie Nederland, Bogin))

In isolated cases the system may contribute to restricting patients' access to drugs; such is the case when product prices are higher than the reimbursement limit and high co-payments apply. Typically, the system incurs very few co-payments since, in almost all cases, the product's price is not higher than the limit.

Isolated cases of impact on innovation may exist since some manufacturers claim that the added value of their products are not accepted and the product is assigned a reimbursement limit that is much lower than the product's cost, incremental innovation is not rewarded in case there the products brings no added therapeutic value. However, in case a new innovative product shows to have an added therapeutic value, the product is not included in the reference price system and a reimbursement limit is not assigned. In these cases, very often the price claimed by the manufacturer is awarded. In the NL, each month innovative products are included in the reimbursement scheme at prices claimed by the manufacturer.

Norway

In Norway reference pricing was discontinued because the system led to higher co-payments for patients and generated delivery problems for cheaper medicines that were the basis for the reference price.

Poland

Budgetary impact is always included in the application form. This impact statement is contrasted with analyses prepared by the Ministry of Health and helps control expenditure.

Impact for innovative medicines is impeded because of patients' co-payment. For innovative medicines prices are set on higher level than generics.

As a risk of this practice is stated that new generics appearing on the reimbursement list lead to a lower reference price and to higher co-payment.

Portugal

The reference price system in Portugal is reviewed four times a year and the values of the reference prices are reviewed (as well are included new homogeneous groups), but the basic mechanism has remained the same since the system was first created. The reference price system represents 40.1% of the NHS expenditure.

One advantage of using reference prices is that it encourages the industry to lower drug prices; another is that it makes patients more sensitive to the price of medicines.

One limitation in the Portuguese price reference system is the fact that the reference price corresponds to the highest generic medicine.

Because the industry continually introduces new adaptations to the system, savings are only short-term and are limited to the generic market share and generic substitutions.

Experts from Portugal highlight the following key issues:

- § The current rules regarding reference pricing are based on the highest generic price on the market. Since the generic drug's price is based on that reference price, the immediate consequence is the approval of generic drugs whose prices are very close to the maximum. [Nevertheless, this could be also contributing to the great increase of the generic's market share in Portugal over recent years.]
- § The industry substitutes active substances currently included on the reference price list with newer ones, often with the same results (efficacy and security) and therapeutic classification, but with no approved generic substitute available. For example, fixed combinations, salts, isomers and other derivatives of active substances.

It is a good experience and has helped to promote the generic market.

Romania

Budget impact is monitored quarterly.

Slovakia

Drug consumption is monitored and evaluated every three months. Insurance companies have direct access to available data.

Patient sometimes complain about the co-payment amounts.

One of the main difficulties cited by experts from Slovakia is the difficulty of adopt the EU Transparency Directive in the reimbursement system.

Slovenia

No formal monitoring is carried out in Slovenia. The Health Insurance makes quarterly reports to the Ministry of Health and annual reports to the National Parliament. Data are partly published on the Health institution website (<http://www.zzzs.si>). There are also therapeutic bulletins named "Recept" published quarterly and distributed to Health professionals and published in .PDF form on the above website.

The budgetary impact of reference pricing has been a savings of 3-5% of market value per year. The system has been well controlled and is growing moderately. Currently its impact is approximately 25% of the market value, on the MZZ+NPV list (mutually interchangeable medicines) there are currently approx. 1/6th of the total of approved medicines on the market

In the period prior to the system's introduction, patients were apprehensive about the shift toward generic substitution and the media were strongly involved. Since the system has been in place, no substantial claims regarding obstacles to access by patients or complaints from health professionals have been noted to date.

Concerning impact on reward, it has been found that the market shares of some originators have been reduced while market shares of pertinent generics have gone up. Even so, the share of innovative medicines is around 63% by value and slowly rising.

Sweden

In Sweden this practice was found to be of limited value because it generated a slow system that counteracted market forces and preserved pricing within the generic drugs. Still, it produced some impact on the cost of original drugs once generic products were introduced. It is believed that the system in use today, with reimbursement decisions based on cost-effectiveness and mandatory generic substitution, is superior.

Literature

Lopez-Casasnovas and Puig (2000) carried out an early literature review on RP focusing on its economic effects. They selected 45 studies covering the period 1998-1999 and distinguished three types of studies: a) those that are basically descriptive; b)

studies that include some form of modelling on which RP effects can be observed and tested; and c) empirical studies that describe the results following the introduction of a RP policy. The literature reviewed focused on the impact of RP on: 1) pharmaceutical expenditure, drug consumption and prices; 2) health and health-related effects; 3) physician choice; 4) dynamic efficiency; and 5) overall welfare effects.

The authors indicate that most of the studies were descriptive, which limits the possibility of any posterior application of the results. Only three papers provide a model of the pharmaceutical and health services market. Moreover, many countries apply a simple before-after approach, which is not very useful for obtaining valid conclusions on the effects of RP since it cannot be isolated from other simultaneous policies.

In conclusion, the authors do not seem to be able to derive from the literature identified any strong evidence of the impact on the target variables listed above.

One of the first serious studies to attempt an empirical assessment of RP was done by Danzon and Ketcham, 2003. The authors use IMS data from Germany, the Netherlands and New Zealand to validate a theoretical model's predictions and draw conclusions regarding the feasibility and interest in applying RP in the US context.

Some of the model's key predictions are:

- RP is expected to compress the range of reimbursement levels and manufacturer prices within each therapeutic class, with greater compression in countries with broad criteria for defining classes and where the RP price is based on the minimum manufacturer's price in the class
- RP is expected to reduce RP (subsidy) level for originator products
- RP (alone) is not expected to generate dynamic price competition leading to prices below the RP
- The kinked demand model predicts that demand will be highly elastic at prices above the RP and that manufacturers will drop prices to the RP if products in a class are good substitutes or if patients are unaware of any differences in efficacy or side effects

Some conclusions of the analysis are that:

- The effects of RP in any country will critically depend on the structure of pharmaceutical incentives to substitute cheaper products.
- The evidence from regression analysis that therapeutic referencing has not stimulated dynamic competition is further supported by the fact that all three countries found it necessary to adopt additional measures to control prices.

The authors state that the results are broadly consistent with predictions, although this claim is difficult to validate due to the commercial nature of the data, which makes them unaffordable for most independent researchers.

In a 2002 article Ioannides-Demos et al conclude that the evidence from countries that have implemented RP suggests that it has been successful at temporarily capping drug prices for the RP drugs and achieving short-term savings, but that the simultaneous occurrence of other factors makes it difficult to precisely quantify the impact of RP. The authors review the existing arguments for and against RP, but conclude that most claims – such as the potential to act as a disincentive to innovation or to increase overall costs - are speculative and unsupported by convincing data.

A recent systematic review of the Cochrane Collaboration on Pharmaceutical Policies (Aaserud et al, 2006) found only eleven studies that fulfilled the inclusion criteria. Although the scope of the review went beyond RP to include other types of economic policies, such as pricing and purchasing, ten out of the eleven studies selected refer to RP.

The report concludes that:

1. Use of reference drugs increases while the use of cost-share drugs decreased
2. The total use of drugs did not change much
3. RP appears to decrease drug expenditures form third party payers. This is the effect of a) shift in drug use from more expensive to less expensive drugs within the reference drug groups; b) patients or their private insurers paying a larger part of the expenditures; c) price reductions; and d) reduced total use of drugs within the reference drug groups.
4. No evidence found on the claim that RP does not reduce long term growth in drug expenditures
5. No evidence found of adverse effects on health
6. No clear evidence found of increased health care utilization
7. The potential effect of other factors on the results could not be assessed
8. Uncertainty regarding the transferability of the results to other settings and drug classes (most of the studies were for senior citizens in British Columbia)
9. No evidence found on the claim that RP could lead to disincentives in pharmaceutical innovation.

It is difficult to summarize the results of the review, because not all studies included the same indicators of impact. Compared with a “no RP” scenario, the utilization of drugs for which no extra payment was due rose between 60% and 249%, while that of cost-share drugs declined between –19% and –42%. Expenditure reductions went up to 50%¹, although in one case there was an increase of 5%. Net health care savings amounted to –3% to 18%.

It must be noted that the selection criteria used by the Cochrane Collaboration were much more restrictive regarding the validity of the methodologies employed than those applied in most literature reviews on the effects of pharmaceutical policies and, more generally, in the field of economics and other social sciences. This might reflect the clinical research tradition of the Cochrane Collaboration and the key role that controlled experiments play in clinical research as the gold standard for evidence.

Finally, it is worthwhile mentioning the report by Augurzky et al (2006) that used a large panel data set of nearly all German prescription drugs between October 1994 and July 2005, comprising almost 4 million observations, to assess the impact of RP on ex-

factory prices. The results indicate that a 1% change in RP leads to a 0.3% change in market prices; also, the first introduction of a RP reduces market prices of the affected products by approximately 14%.

IV. Discussion

Key messages

- RP can be considered a good practice to promote and reinforce generics policies.
- In principle there should not negatively impact innovation as long as patented drugs are not covered by the scheme.
- RP aims to reduce public expenditure in the groups under the scheme, though it is often claimed that it does not reduce overall drug expenditure, as utilisation might shift towards products not covered by the scheme (e.g. on-patent products) with higher prices and therefore expenditure might go up faster than otherwise. The assessment of RP in Germany suggests that this effect exists, but is not very large. However, even if this statement is true, RP might lead to a shift from funding marketing and advertising to funding R+D.
- Countries are usually aware of attaining savings with reference pricing (favourable budget impact), but they do not measure other impacts (on patients or innovation). there is usually no formal monitoring system

Risks

- By regulating/fixing one level of reimbursement for a category of medicines, the authority/payer might inadvertently prevent further price reductions that would be driven by the introduction of greater generic competition. The authority/payer therefore risks losing an opportunity for further savings.
- Where RP fixes a reimbursement-level, opportunities are limited for competition from new homogeneous medicines based on a lower price. The price-sensitivity of the consumer only plays above this reimbursed price-level.
- RP makes the co-payment cost higher for patients that need to or want to keep the medicine used. It is up to patients to decide whether they want to get a drug with no extra payment or prefer to pay for a given brand. Inconvenience and some risks, as well as additional health care costs (e.g. for adjusting the dosage), might arise in the case of chronic patients that have been taken a given brand (originator) for a long time and are faced with the choice of changing the brand or start paying for the drug they have been using

- RP with therapeutic equivalence might be detrimental to incremental innovation, which is supposed to be one of the most usual ways innovation takes place in the pharmaceutical sector. The assumed reason is that if new products similar to existing ones (me-toos) get the same price, there will be no incentive for investing in R+D that is expected to yield incremental (moderate) benefits over existing therapies. However, it might be argued that by decreasing the budget for drug classes where relatively cheap, off-patent alternatives are available, RP allows more resources to be directed to innovative areas, thus providing incentives to R+D.
- The price-sensitivity that drives the shift to cheaper products might be taken away if patients have a supplementary insurance for medicines.
- Reference pricing might lead to competition by means of discounts to pharmacists, which might receive the benefits that patients and insurers would receive in the case of competition by prices. This problem might be addressed by means of claw-back provisions.

Key success factors

- RP requires the existence of a third-party payer, as it is actually a mechanism for splitting the price of a drug between the consumer and the third-party payer.
- Additional insurers might need to be included in the agreement to keep the price-sensitivity of patients.
- RP is likely to have a larger impact in countries with no (or a weak) price control and high prices for innovators and a vibrant generics industry.
- To avoid negative impacts on incremental innovation, RP systems must include provisions that provide them with incentives, e.g., either on a certain premium over the reference price of similar products or by delaying for a certain period (e.g. one year) the inclusion in a RP group.

Payback

I. Introduction

Description

Payback is a financial mechanism that requires manufacturers (individually or collectively, e.g. via their industry association) to return a certain part of their revenue to a purchaser/Member State authority if sales exceed a previously determined or agreed target budget/maximum amount.

There are other mechanisms which look similar to payback and can erroneously be considered identical. They include:

- Rebates, which requires manufacturers to return a share of their overall revenue (without a specific target budget/maximum amount being passed). This return is normally based on a percentage of manufacturers' annual sales of reimbursed products (for example, in Germany, Ireland and in Spain's newly proposed system).
- Clawback, which refers to discounts on the dispensing fee of pharmacies that accrue to the third party payer (UK) or to discounts on pharmacy drug purchase costs (Netherlands).
- Price-volume agreements which usually apply to single new products where the negotiated price is conditioned by the expected number of units sold (France, Spain). A posterior increase in the number of units sold leads to higher expenditures on the product and, hence, to posterior price reductions or paybacks (Norway).

It is not within the scope of this study to explore all of these mechanisms in detail, but we will focus more specifically on payback, as defined above.

Purposes

Payback is used as a cost-containment measure to reduce deviations from a prospectively set budget. It offers a guarantee to the payer that real spending will be in line with budget estimates and reduces the payer's uncertainty regarding future levels of expenditure.

Theory/rationale

This mechanism ensures that pharmaceutical expenses will be controlled up to a previously agreed upon target budget level. Control is introduced through an a-posteriori correction when the budget has been exceeded.

This mechanism ensures that when the budget shows cost overruns, the financial risk is shared between manufacturers, other stakeholders and payers.

Expenditure is obtained by multiplying average price by volume. As price is normally set a-priori, the a-posteriori control of expenditure (and deviation of expenditure) relates mainly to volume. Drug expenditure and increases in drug expenditure are, thus, the result of manifold decisions - mainly by individual prescribers, who are often subject to pressures from patients and manufacturers to prescribe certain drugs. Payback is based on the implicit assumption that drug utilization (volume) and expenditure can, to a large extent, be influenced by manufacturers.

Modalities

The payback mechanism has different modalities according to:

1. Scope of the mechanism: global budget, expenditure by categories/therapeutic groups or by product
2. Target budget, a maximum amount of expenditure above which payback is demanded (trigger). This is usually related to a growth-rate
3. The amount due to be returned/paid back (full difference between target-budget and real spending or a portion thereof).
4. Allocation of amount due over different manufacturers or other stakeholders.

II. Application in Europe

Overview

Table 11: Payback systems in Europe

	Belgium	France	Hungary	Italy	Portugal
Year Started	2002	2002	2003	2002	1997
System working level	Pharmaceutical budget	Per group of (therapeutically related) products	Per product & pharmaceutical budget	Pharmaceutical budget	Pharmaceutical budget
Target	Estimation	Target voted by parliament	Fixed amount of money	13% budget healthcare	Nominal Growth of GDP
Amount due	72% extra spending	Around 50%		100%	69,60%
Contribution	Pharmaceutical industry (72%) & Insurance organisms (25%)	Pharmaceutical industry (according to spending and growth)	Pharmaceutical industry (according to market share in reimbursement)	60% industry & 40 % regions	Pharmaceutical industry (according to its market share & responsibility in NHS' expenditure growth)
Exemption		Innovation, Generics and Orphan drugs			

Source: Data from EASP's questionnaire

Individual replies provided by MS^{47,48}

Belgium

The payback system has been used in Belgium since 2002. It is based on a agreement reached at the end of the year 2000 between the Minister of Social Affairs and the pharmaceutical industry that was later written into health insurance legislation.

⁴⁷ Authors' note: The Austrian authorities who answered our questionnaire stated they used a payback system but, strictly speaking, and in accordance with terminology defined in an annex to the questionnaire, the Austrian practice, while containing an element of payback, does not comply with the definition of payback used in this study.

⁴⁸ Authors' note: The first draft of this study included that UK had payback system (defined as an element of the Pharmaceutical Price Regulation Scheme in which the Department of Health assesses profits in excess of the agreed profit target; companies are then required to repay the excess or reduce prices). As this is not a pure payback system, as defined in the study, it has been not included in the final version.

The amount to return is calculated on the turnover of all reimbursed medicines, without exception, and on the entire pharmaceutical budget. However, the government can decide to subdivide the payback per group of products (example: statins).

An “advance industry payment” took effect in 2006 and its functioning is explained in the footnote⁴⁹.

The pharmaceutical industry had to pay a part of the excess (72%). In 2007, the payback concept will be replaced by the concept of “provision of funds”, intended to fill any eventual budget deficit.

The following parties contribute to the payback:

- Pharmaceutical industry (72%)
- Insurance organisms (25% in case of deficit) [for this purpose, each insured Belgian must pay a specific contribution].

France

A payback system has been used in France since 2002 and it functions according to groups of therapeutically related products.

Target growth objectives are established by product groups. The selection is based on an evaluation of the needs of the different categories of drugs and the natural evolution of treatment (for example, there is almost no ceiling for cancer).

The global contribution is divided in three parts: 30% on turnover, 40% on growth and 30% on marketing (pharmaceutical sales representatives, ads etc.)

Initially, high value medicines and low-cost drugs/generics (innovative drugs, orphan drugs) are excluded for several years.

Once the general target for the pharmaceutical budget has been approved by a vote in parliament, a pricing committee assumes the responsibility of allocating funds across different drug groups (this includes negotiating with representatives of the pharmaceutical industry).

The global payback needs to be equal to the payback corresponding to the application of the legal rule (parliament vote) and not the conventional negotiation. The share is around 50%. Companies' contribution depends on their share of spending (65%) and their share of the growth (35%)

⁴⁹ Each year the target budget of year X is estimated, but the real expenditure of year X is calculated as year X+1. Firms pay an advance on the eventual payback during year X (a fixed percentage of the sales of year X-1). These advances are put in a special fund (the so-called “provision of funds”). During the year X+1 real expenditure is calculated and the difference between prior budget estimates and real expenditures is determined. In the event that real expenditures exceed budget estimates, each firm must pay a part of this overrun through a cash advance (“provision of funds”) and (if necessary) any remaining ? overruns (= the difference between the part of the exceeding and their advance).

Hungary

A payback system that has been used in Hungary since 2003 is based on a per product mechanism as well as mechanisms involving the global pharmaceutical budget. Payback is regulated by a contractual agreement between the government and the drug manufacturers. Part of the pharmaceutical budget's deficit must be paid back by drug companies; the amount paid back depends on the company's market share in the field of reimbursed products and its product portfolio (generic drug turnover is not included). Every product category with a reimbursement level higher than 0% is included.

Payback consists of a fixed amount that is paid back to the government every year since 2005 by the Contract (made in June 2004). The payback in 2005⁵⁰ was 20 billion HUF (80.000.000 € - 5.73% of the budget) and in 2006 was 22.5 billion HUF (90 000 000 € - 5,69% of the budget)

Up until the year 2006, in addition to payments based on the so-called reimbursement-volume agreements and debt coverage contributions, pharmaceutical companies were also required to expend a fixed payback amount.

Every company selling reimburseable drugs is required by law to contribute. The payback expended by companies is proportionate to their market share of reimbursable drugs. Each company must pay back 12% of its current drug subsidy, calculated at the ex-factory price.

Companies can be exempted from payback:

- A) if the price of the drug is less than – or at least equal to – 85% of the reference product's price in the relevant group
- B) in the group of specially reimbursed drugs
- C) if people who fall below certain living standards (socially disadvantaged groups) can receive full reimbursement.

Italy

Since 2002 public pharmaceutical expenditure cannot be higher than 13% of public health expenditure. If, at the year's end, that threshold is crossed (or if periodical monitoring during the year indicates it is likely to be surpassed), then the industry, wholesaler, pharmacists and regions have to refund the excess.

Regions refund 40% of the excess while the industry and distributors refund the remaining 60%. Payback applies to the entire pharmaceutical budget. The target is 13% of public health expenditure (16% if hospital expenditure is included).

⁵⁰ The total payback in 2005 was 23 billion HUF (92,000,000 € - 6,59% of the budget) – it also includes paybacks stemming from reimbursement-volume agreements and debts accumulated under the previous government's 2005 contract with manufacturers

Portugal

Four protocols covering the NHS's expenditure were agreed upon between the Ministry of Health and the Pharmaceutical Industry: 1997-1999, 2001-2003, 2004-2005 and 2006-2009. Prior to the year 2006, the payback was limited to a percentage of expenditure at the ambulatory level. Since 2006, it has included both the ambulatory and hospital level.

In the year 2006 the maximum growth target in public expenditure in the ambulatory market was set at 0% and an amount equal to the nominal growth of GDP for 2007 over the amount resulting from application of the annual gross rate of 0% in respect of 2006. For the hospital market, the goal for maximum growth is set at 4% over the 2005 sales volume.

The amount to paid is the 69,6% of the portion of the increase in the NHS's charges relating to reimbursement of ambulatory medicinal products exceeding the growth limits and has a limit of 35 millions €in 2006 and of 47 millions €in 2007.

Under the provisions of this protocol, the pharmaceutical companies, as signatories, agree to contribute to the payback system when the growth rate for NHS expenditure in any given year exceeds projected budget figures.

The breakdown contribution owed by the Pharmaceutical Industry by each marketing authorisation holder company shall be carried out in the following terms:

- a. In the first three quarters of each year during the protocol's validity, the companies shall pay a provisional contribution, which shall be calculated in accordance with the following formula:

$$V'/4 = (M' * C' * 75\%) + [M' * C' * 25\% * (1 + S')]$$

$V'/4$ = Value of each company's provisional contribution for the quarter;
 M' = Each company's market share, based on the latest available data;
 C' = Theoretical value of the pharmaceutical industry's contribution during the year in question, as stipulated under Clause 8 of the Protocol;
 S' = Each company's share of excess costs that were incurred by the NHS for medicinal products in the latest quarter available⁵¹;

⁵¹ Example

M'	Market share of Company Y	0.01%
C'	Value of the pharmaceutical industry's contribution during the year in question (1) – Maximum Value	35.000.000€
S'	S' = Share of Company Y's contribution to cover the NHS' cost overruns for medicinal products	0.0%

	NHS' charges related to medicinal products 2005	1.451.513.570€
	Growth Rate	3.5%
	NHS' charges related to medicinal products 2006	1.502.316.545€
	Increase in the NHS' charges	50.802.975€
	69.9% of the portion of the increase in the NHS' charges	35.000.000€

$V'/4$	Value of Company Y's provisional contribution for the quarter;	3.502€
--------	--	---------------

$V'/4 = [0,01\% \times 35.000.000\text{€} \times 75\%] + [0,01\% \times 35.000.000\text{€} \times 25\% \times (1 + 0,2\%)] = 3.502 \text{ €}$

The pharmaceutical industry's contribution shall in no event exceed thirty five million euros in 2006 and forty five million euros in 2007.

III. Impact

Experiences reported by countries

- § Savings reported: FR: 400mEUR ('05), 160mEUR ('06e); IT 800mEUR cut ('06e) – around 6,7% of the budget- ; PT: 10mEUR ('06);
- § Change in access: none, given that patients are not involved
- § Change in reward: no clear conclusion, except in FR: exemption for innovatives, PT: recoups go to R&D fund
- § Risks/success factors:
 - Good impact for MS with low GDP, where price-reductions are hard to get
 - Difficult to reallocate recoups in a decentralised health system

Individual replies by countries

Belgium

In Belgium, the budgetary impact is evaluated once a year⁵².

The percentage of the budget's overrun in terms of total sales for 2004 was calculated. The percentage obtained is then applied to each firm. The difference between this value

(1) If in 2006 and 2007 the increase in expenditure on reimbursement for ambulatory medicinal products exceeds the growth rates of:

- a) In 2006, the annual growth rate shall correspond to the application of a 0% rate to expenditure on medicinal products in 2005;
- b) In 2007, the annual growth rate shall correspond to application of the nominal growth in the Gross Domestic Product foreseen for 2007 over the amount resulting from application of the annual growth rate of 0% in respect of 2006 for the purposes of this Protocol.

The Pharmaceutical Industry shall pay a Contribution to the State in an amount equal to 69.6% of the portion of the increase in the NHS' charges relating to reimbursement of ambulatory services.

⁵² For example, in 2004:

Expenditure 2004	+/-3.100.000.000
2004 Target Goal	+/-2.700.000.000
Overrun	+/- 400.000.000
65% of Overrun (firms' share)	+/- 260.000.000

and the advance cash payment (a fixed percentage of sales in 2003) is calculated and must be paid.

The main drawback of this method lies in the difficulty of obtaining payments in time, but timely payments can be guaranteed by clearer descriptions of obligations and penalties. The experience is recommended.

France

France evaluates the budgetary impact on its health insurance budget and on each individual company.

According to the annual report of the Economic Committee for Price of Health Products (CEPS in its French initials), the budgetary impact was approximately 400M€ in 2005; in 2006, a year of slower growth, it was approximately 130M€. It is the amount paid at the year's end by practically all the companies under contract.

There is no expected impact on innovation because innovative drugs are exempted for a certain period of time

In practice it has been found that a ceiling exists for payback that can be requested from drug companies. Therefore, in comparison with price control mechanisms, use of rebate methods should be more limited (by class, by products etc.).

The experience has been a good one and lends an element of predictability to the health insurance budget without placing too much of a strain on very innovative products.

Hungary

If the budget exceeds the planned limit, drug manufacturers have to contribute to financing the overrun. The payback system operates as follows:

1) If the overrun is under 9%, then:

Budget overrun (in percentage)	Government's share (in percentage)	Manufacturers' share (in percentage)
0-5%	50	50
5.01-6%	40	60
6.01-7%	30	70
7.01-8%	20	80
8.01-9%	10	90

2) If the amount of budget overrun exceeds 9%, then everything above that amount must be paid by the manufacturers.

20.74 billion HUF (82,960,000 €) were paid back by drug manufacturers in 2006.

Because of the parallel trade phenomenon and international price referencing, the industry cannot decrease prices of pharmaceuticals below certain limits. Therefore, the payback system is a useful and EU-compliant tool to control expenditure.

Italy

In Italy expenditure is monitored periodically. On October 1st 2006 a predictable increase in expenditure above the established 13% threshold limit led to an intervention that reduced expenditure by an estimated 800 million euros.

There is no impact on access for patients because these reductions target the industry and distributors and, to a lesser extent, the regions.

For this kind of mechanism to be effective, a very good system for monitoring drug use and expenditure must be in place.

The 40% to be paid by the regions is currently deducted from their next year's budget. New systems to improve and increase regional responsibility are under consideration. It appears very difficult to further reduce prices and in Italy is moving to a "real" pay back mechanism.

Portugal

The current protocol valid in Portugal is subject to quarterly evaluations of the expenditure's growth rate. Protocols in effect prior to the year 2006 contributed more than 10.1 million € to the NHS budget.

The pharmaceutical industry's contributions revert into a fund created to support health research and to finance strong, technologically innovative projects developed by pharmaceutical companies.

This method helps to control the growth of expenditure and share risks.

Literature

No articles on the topic were found, probably due to the relatively recent introduction of this mechanism.

Only some grey literature, of questionable validity, addresses the issue of payback, particularly through private research institutions such as the IMS. In most of the cases these cover only economic aspects.

IV. Discussion

Key messages

- Payback is relatively new and not a well-established practice; therefore evidence on its impact is scarce or lacking
- A payback system is an alternative to price regulation as an unsophisticated, easy-to-apply cost-containment tool
- There is no direct impact on patients as this concerns an a-posteriori mechanism between industry and payors, without involvement of patients. Though regulations/exemptions for innovative medicines may affect availability of these medicines for patients.
- Payback (as well as discounts to final providers and third-party payers) might lead the way towards a reduction in the actual price (increase) of drugs in a low-price country in a way that avoids the raise or exacerbation of parallel trade, as published prices remain high

Risks

- Payback might discourage the introduction of innovations, if the additional expected revenue is going to be partly of fully paid back. In order to avoid this effect, the payback system must differentiate unwanted expenditure increases from those to be encouraged (e.g. from new effective and cost-effective treatments) or take account for those elements like e.g., R&D investment.
- If a payback system applies a progressive rate, it discourages business mergers and is relatively more burdensome for larger companies.
- In countries where the payback is paid when the growth target for aggregated pharmaceutical expenditure has been exceeded, the entire industry is jointly liable to pay the discount, whereas the benefits of marketing a new and truly innovative product accrue to a single company. It is thus in that company's interest to promote and heavily advertise the breakthrough product, as the payback payment is partly socialized.
- A payback system reduces market transparency, as it makes the observation of actual market prices in other Member States difficult, and therefore makes cross-border price-comparisons hard to apply. The published prices in a given country do no longer reflect the actual transaction prices as these are adjusted for payback. Consequently, the feasibility of making valid and reliable price comparisons and constructing valid price indexes is undermined

- Payback might initiate a shift towards the utilization of product-categories uncontrolled by payback. This could lead to a final increase in overall expenditure, despite the limited budget in the product-categories controlled by payback.
- Local industry, often less innovative and with lower sales growth, might be relatively favoured by the payback clauses, at the expense of foreign companies.
- The experience of some countries suggests that it might be sometimes difficult to make companies return the amounts due.

Key success factors

- In the payback system it is in principle easy to avoid a negative impact on innovation, by simply excluding innovative drugs

Incentives for good prescribing practices

I. Introduction

Description

Incentives can be defined as any factor that affects a decision-maker's behaviour. Incentives to prescribers might be explicitly set by an employer or regulator, but in many cases they are established with no explicit purpose (implicit incentives); nonetheless, they still might affect prescribers' behaviour.

Many actors are involved in the prescribing process: physicians that prescribe, pharmacists that dispense (and sometimes also prescribe, as in the UK, or can choose to provide a generic substitute), patients that pay or co-pay, and third-party payers that also pay or co-pay. However, physicians are the main actors in determining the utilization of treatments, in general, and so-called prescription or ethical drugs, in particular.

Physicians are supposed to assess the benefits and risks involved in the use of a certain treatment by an individual patient. Despite this, many prescribers' approaches don't always respond appropriately to the situation, since they must confront a series of factors (patients' increased information, pressure from the industry...) that influence their prescription habits. As a result, medicines are not always prescribed effectively (some drugs may be prescribed unnecessarily and lower-cost alternatives are not always taken into consideration).

The traditional context decision of prescribers has become more complex due to several factors.

1. The rising cost of medical treatments and pharmaceutical expenditure.
2. The increasing role of third party payers, which may mean that a patient does not pay for the treatment, or pays only a part of it. Prescribers might not have any incentives to consider the financial impact of their decisions on patients.
3. The high rate of innovation in medical treatments, which requires a constant effort to stay on top of new information regarding the characteristics of available treatments.
4. Increasing pressures from different parties – technology providers, third party payers, patients, etc.- to influence prescribers' behaviour

In this section we will focus on the measures taken by third party payers (public or private health insurers) and regulators to improve the performance of prescribers.

Modalities

Financial incentives

- § Coercive
 - Type of remuneration for doctors
 - Global or individual budget (Germany)
- § Non-Coercive
 - Indicative budget (North Ireland)

Non-financial incentives

- § Information
- § Education/Training
- § Cost-effectiveness guidelines
- § Clinical/therapeutic guidelines

Mixed incentives

- § Coersive
 - Guidelines with financial incentives (France: *Références Médicales Opposables*)
- § Non-coercive
 - Indicative Drug Targets (Ireland)

Purposes

The objectives of incentives designed to promote good prescribing practices tend to vary depending on the different aims and priorities of those who establish them. In general terms it can be assumed that incentives are mainly aimed at maximising effectiveness and minimising risk and cost. However, some incentives might simply have the purpose of reducing public pharmaceutical expenditure while others only aim to rationalize prescriptions from a clinical perspective.

Sometimes the purpose of setting an objective is explicitly stated, but occasionally policy-makers and managers are unwilling to disclose the real purposes of an incentive, often because they might not be politically convenient or popular.

Theory/Rationale

Doctors are motivated by an array of factors, both external and internal, that determine their prescription activity. Factors such as moral hazards or the theory of imperfect agency relationship can also affect to their prescription activities.

Incentives provide a way to counteract such factors and encourage prescribers to incorporate habits that will lead to compliance with consensuated instruments (prescription guidelines, for example).

In order to analyse and predict the likely effects of an incentive, it is essential to have a model or theory that explains the agent's behaviour. Earlier economic models of prescribing behaviour have assumed that physicians behave as profit-maximising firms. However, this assumption has been progressively replaced by more complex models based on the concept of agency relationship. In a perfect agency relationship the physician would behave as if the patient were making his decision based on the same knowledge and information available to the physician; in economic terms, the objective of the physician would be to maximise the utility function or the well-being of the patient. If we accept, however, that the agency relationship is imperfect, we will see that a physician will mix his own objectives – maximising income, minimising working time, etc – with the assumed objectives or interests of the patient. In addition, he will have to take into account those of the third party payer or insurer that employs or contracts him.

Third party payers or insurers might assume that physicians' and patients' objectives conflict with their own objectives, which are assumed to represent the collective or public health interest, because doctors do not bear the (full) economic responsibility of their consumption decisions. They might also assume that physicians and patients do not have the appropriate information or are influenced by prestige or by external economic incentives. This kind of an assessment can provide the rationale needed to design incentives for good prescribing practices.

II. Application in Europe

Overview

Table 12: Incentives for good prescribing in Europe

	Physicians						
	Clinical practices /prescriptions Guidelines	Educational and information	Monitoring of prescribing patterns	Prescription quotas	Pharmaceutical budgets	Financial incentives	Other
AT	ü	ü	ü			ü	
BE	ü	ü	ü	ü		ü	
CY							
DE	ü	ü	ü	ü		ü	
DK	ü	ü	ü				
EE	ü	ü					ü
EL			ü				
ES	ü	ü	ü	ü	ü	ü	
FI	ü	ü	ü				
FR	ü	ü	ü				
HU	ü		ü				
IE		ü	ü			¼	
IT	ü	ü	ü				
LT	ü			¼		¼	
LV	ü	¼	ü	ü	ü		
MT	ü	¼	¼				
NL	ü	ü	ü			ü	
NO	ü	ü	ü	ü			
PL		ü					
PT	ü	ü	ü				ü
RO		ü	ü		ü		
SE	ü	ü	ü		ü	ü	
SK	ü	ü	ü	¼	¼		
SI	ü	ü	ü				
UK	ü	ü	ü		ü	ü	

ü Currently applied

¼ Once applied but discontinued

Source: Data from EASP's questionnaire

Individual replies by countries

Austria

In 2004, the Austrian Federation of Social Health Insurance Institutions (FASt) published its *Economic Guidelines for Prescribing Pharmaceuticals and Medical Products* (RöV, www.avsv.at). These guidelines encourage doctors to prescribe the most economical pharmaceutical out of several therapeutically similar alternatives. The new positive list - the reimbursement code (Erstattungskodex – EKO, formerly

Heilmittelverzeichnis)- has been in place since 2005. Under the guidelines established by the reimbursement code (EKO) doctors are encouraged to give preference to pharmaceuticals listed in the green box of the reimbursement code (EKO), which contains three of the cheapest generic options available.

The health funds generally monitor the prescription patterns of doctors and specialists who are under contract with them to assess their compliance with the established guidelines (RöV, www.avsv.at). The most common monitoring tool is to benchmark the prescription volume of a given doctor in a given region.

Generally speaking, doctors do not get regular feedback on their prescription behaviour, except in cases of non-adherence. In such cases, a doctor will first be informed about his/her over-prescribing then an individual meeting is set up to discuss possible solutions. When serious discrepancies occur, doctors must report to the head physician of the contracting health funds. As a final measure, they may be required to repay the difference between the price of the prescribed pharmaceutical and the average prescription price. However, the latter case is very rare and most critical cases can be solved through discussions with the arbitration board.

There have only been a few county-specific pilot projects to introduce financial incentives for economically responsible prescribing (e.g. in Upper Austria). However, in those cases it is not the doctors under contract who receive a financial incentive, but rather their regional medical association, which receives a specific amount of the savings as an earmarked sum for the training and education doctors.

There are no explicit “positive” incentives, but there are “negative” ones. For instance, in the event of non-adherence to the guidelines doctors will be admonished, and the consequences in a “worst case scenario,” could be the rescission of their contract with the social insurance fund (although, so far, this has only happened in the case of overspending).

In addition to encouraging doctors to prescribe in accordance with the criteria in contained in the guidelines, they must also conform to criteria reflected in the reimbursement (EKO) code. The health fund provides information leaflets and newsletters to doctors (e.g. *Arznei und Vernunft*⁵³).

Belgium

Belgium sets prescription targets through consensus conferences (organised twice a year). A report on the good practices agreed upon in these conferences is made available on the website (www.inami.be), and a summary of that report is sent by post to all practising physicians and pharmacists.

In addition to these conferences other initiatives exist that focus on good prescribing practices. The Belgian Centre for Pharmacotherapeutic Information publishes a yearly drug formulary that not only contains a list of all the medicines available in Belgium, but also comments on the rational use of these drugs. Updates on this drug formulary

⁵³ www.sozialversicherung.at/esvapps/page/page.jsp?p_pageid=110&p_menuid=2988&p_id=3

are sent monthly (bulletin) to all physicians and pharmacists in the “*Folia Pharmacotherapeutica*” which also contains summaries of recently published articles focusing on rational drug use. Another of this centre’s activities, which is jointly financed by the Department of Health and RIZIV, is the publication of what are denominated “transparency brochures.” These publications focus on objective evidence and other pharmaco-economic aspects of drug treatments available for specific diseases.

Another important initiative in Belgium is the publication of “*Guidelines for Rational Antibiotic Use in Ambulatory Practices and in Hospitals*,” by the Belgian Antibiotic Policy Coordination Committee.

Doctors are expected to prescribe a certain amount of “cheap drugs” (premium system) and their prescribing behaviour is followed-up or monitored. “Cheap drugs” are generic drugs and original medicines included in the reference reimbursement system with a price not exceeding the reimbursement basis. The National Council for the Promotion of Quality of Care, a part of RIZIV, organises periodical feedback reports to physicians that display their prescription patterns and compare them with the prescription patterns of other physicians with the same speciality and within the same region. Feedback has been sent to these professionals on antibiotics, antihypertensive drugs and, more recently, quinolones. General practitioners receive individual data on their antibiotic and NSAID (non-steroidal anti-inflammatory drugs) prescription habits. Physicians who work in hospitals can obtain data about drug use in their hospitals on the Internet (<https://tct.fgov.be>).

There are no financial incentives for medical doctors aimed at improving good prescribing practices. However, medical doctors who participate in “local consultation group” meetings are allowed to charge a higher fee. In these groups they discuss Good Publication Practices (GPP), among other topics of interest.

The information and support that doctors receive in order to improve prescribing practices include:

- § Brochures by post (on reference pricing - price comparison tables – and general information on reimbursement)],
- § Consensus conference reports (by post /on a website),
- § Website RIZIV INAMI (<http://www.riziv.fgov.be>), and
- § Infodesk (central mailbox for questions on medicines).

Cyprus

Doctors in the private sector are free to prescribe medicines of their choice and all cost is paid out-of-pocket by the patient. In the public sector, physicians can only prescribe from a list of approved products. Doctors are not monitored.

Denmark

The Institute for Rational Pharmacotherapy (IRF) produces non-binding recommendations to medical doctors and other healthcare providers. This is often done

in close co-operation with regional medical consultants. The IRF issues general recommendations/folders to be used by doctors and laymen. More information about the latest recommendations can be found on IRF's homepage⁵⁴. In addition to written material, IRF also organizes conferences, training sessions, and other events, e.g. at educational institutions, to inform and educate about rational use.

The counties/regions follow-up on doctors' prescription practices on the basis of statistics reported from individual pharmacies.

Prescription feedback is also a county/regional responsibility. The systems differ from one county or region to another. The IRF has a purely advisory role. However, the Danish Pharmaceutical Agency does pass on the data it obtains regarding regional prescription patterns. If the level of pharmaceuticals prescribed by a specific doctor is found to significantly exceed the county or region's average level, official actions will be taken by the third party payer that runs the reimbursement system. This rarely occurs in practice, however. According to the agreement with the Organisation of General Practitioners doctors are expected to follow rational and financially responsible criteria when filling out their prescriptions.

Estonia

In Estonia, General Practitioners get feedback once a year. There are no financial or non-financial incentives. Clinical guidelines and drug information bulletin are made available to them from the State Agency of Medicines.

Finland

The prescription register at Kela (Social Insurance Institution of Finland) includes information on the prescribing doctor (health insurance code => speciality). Based on that register, Kela publishes annual statistics on pharmaceutical costs according to doctors' prescriptions (by speciality), medicine costs and their reimbursement classified by hospital district. Data are also made available annually in the publication, "Finnish Statistics on Medicines" and on Kela's website⁵⁵.

Kela sends a personal summary of prescriptions dispensed from the pharmacies once a year to each physician who has written at least 200 prescriptions for reimbursable medicines. The summary compares information on the prescription habits of all doctors within the same speciality as the recipient. Furthermore, the letter includes information on current medicinal topics: in 2004 the topic was sleeping medicines, in 2005 diabetes type 2, and in 2006, statins.

The Centre for Pharmacotherapy Development (ROHTO)⁵⁶ was established in 2003 to rationalise prescription practices. ROHTO evaluates, summarizes and disseminates information on evidence-based, cost-effective pharmacotherapy, implements knowledge

⁵⁴ <http://www.irf.dk>

⁵⁵ <http://www.kela.fi/research> – Reimbursement of medicine costs – Statistics

⁵⁶ http://www.rohto.fi/index_en.php

to promote more rational pharmacotherapy, monitors, describes and studies prescription practices and conveys benchmarking data to prescribers. It also reinforces the development of electronic decision making support systems.

Seventy-one current care recommendations are available at the moment. Articles concerning the costs and consumption of medicines are regularly published in trade magazines and other publications.

Reimbursement decisions made by the Pharmaceutical Benefits Board (PBB) can also influence doctors' prescribing behaviour.

France

France has not established individual targets for prescription practices but rather relies on national "contracts" between institutions representing the doctors and the health insurance system to establish "priorities". An acceptable degree of compliance with these priorities is a condition for any re-evaluation of the doctors' remuneration.

Doctors receive feedback from the health insurance system on how prescription patterns compare to those of colleagues. They are visited several times a year by delegates from the health insurance system.

Individual financial incentives do not exist. Raises in doctors' salaries are linked in a variety of ways to prescribing objectives for the profession as a whole.

Apart from providing statistics, the health insurance system organizes meetings and "peer group" exchanges. Occasionally, representatives from the system may also contact a specific doctor for advice, etc.

Germany

In Germany, targets for medical prescription are agreed upon annually between regional doctors' associations and health insurance funds.

There are two types of targets:

- a) Target for global prescription costs (no real budget) and
- b) Detailed Saving Targets
 - Targets for DDD-Cost for groups of pharmaceuticals: Bonus-Malus for individual prescribers (all details to be negotiated) are expected to start by January 2007
 - Maximum prescription cost per doctor and per patient: doctors may have to repay excess costs to the health funds (only for drugs not affected by DDD-cost targets)
 - Other saving targets (to be negotiated)

Every single prescription is reported electronically when invoiced to the health funds. Doctors regularly receive a detailed summary of their prescription costs from the health fund (details are subject to regional agreements between health funds and doctors' associations).

Concerning financial incentives in relation to DDD-Cost, bonuses may be paid to doctors who prescribe economically. Doctors are obliged to pay back excess prescription costs (starting in 2007). Maximum prescription cost per doctor and per patient has also been established, and doctors may have to pay back excess costs to the health funds (only for drugs without targets for DDD-cost).

All doctors receive individual support from another doctor (medical inspector) on the basis of their individual prescription data. They can also participate in quality groups to improve prescribing habits.

Greece

Up until now only some Greek insurance funds have monitored doctors. By June 2007 it is expected that all insurance funds will have set up prescription control mechanisms (doctors will have a unique ID number and this number will be correlated with bar-coded drug packages and prescription forms to produce data on prescription habits).

Currently doctors only receive feedback from funds where pilot projects are running, with some additional information from the National Medicines Organisation (e.g. National Formulary).

Hungary

Pharmacies report all single sale details to the Insurance Fund: doctor's code, patients' insurance number, drug's name and amount, etc.

Therapeutic protocols are created by the Chamber of Physicians.

Physicians are obliged to prescribe reference medicines. If patients ask them to prescribe other medicines not included on the reference list, the price differences have to be covered by the patients.

Ireland

In Ireland, GPs contracted to provide services for fully eligible patients may take part in the Indicative Drug Target Savings Scheme (IDTSS), which was intended to promote more rational prescribing. The scheme is currently under review by the Health Services Executive.

Concerning feedback, information on prescribing patterns and costs has been provided to doctors to enable them to keep within their budgets and improve their performance

The IDTSS provides for national savings to be available for draw down for practice investment.

The National Medicines Information Centre provides independent information and advice to healthcare professionals in primary and secondary care, particularly doctors and community pharmacists, on all aspects related to the therapeutic use of medicines, along with global prescribing analyses from the National Centre for Pharmacoeconomic Evaluation and through the Indicative Drug Target Savings Scheme.

Italy

Responsibility for setting prescription objectives lies in the hands of regional authorities. They may use a variety of systems that can vary in their effectiveness and efficiency. Due to this situation, it is quite difficult to describe any “national” pattern.

Most Local Health Authorities and regions monitor prescription behaviour. The most common system is based on dispensing data obtained from the pharmacies. Some areas have very sophisticated systems, capable of cross-controlling the expenditure of patients, doctors and pharmacies. Some trials have been performed to monitor behaviour by collecting data from doctors who use e-prescribing methods.

Many Local Health Authorities provide GPs with some kind of feedback on their prescription patterns. In several areas facilitator pharmacists visit doctors or meet with them on a regular basis to discuss prescribing patterns and increase appropriateness. In some areas doctors are assigned a certain budget and receive a financial incentive if they stay within their budget.

At a national level AIFA (Italian Medicines Agency) produces several relevant tools aimed at all health professionals. These include an Italian translation of the British National Formulary, the Italian *Prontuario Farmaceutico Nazionale*; other sources of advice are oriented toward the care of children, a periodical *Bollettino di informazione sui Farmaci*, and so on. All these publications are sent by mail to all registered health professionals (doctors, pharmacists and nurses) in the country.

Latvia

In Latvia, the prescription of medicines is targeted by Rational Pharmacotherapy Guidelines worked out by the Medicines Pricing and Reimbursement Agency (MPRA). Doctors are, occasionally, monitored based on an analysis of prescription data.

Doctors may be penalized if they go over their annual budget without a justification. One existing non-financial incentive includes the possibility of receiving an invitation to become an external expert for the Pharmaceutical Pricing and Reimbursement Agency (professional recognition).

Doctors receive independent information on drugs, as well as advice and support, in the form of Rational Pharmacotherapy Guidelines.

Lithuania

Doctors here receive treatment protocols and recommendations regarding objectives or targets for prescribing medicines,

Every three months doctors are informed about the amount of reimbursed medicines prescribed. Doctors improve prescribing practices through professional courses about innovations and new treatment algorithms.

Malta

Goals are not set for doctors to prescribe medicines, however, criteria/guidelines do exist that restrict prescriptions. Doctors do not receive feedback on any regular basis, but rather on an *ad hoc* basis.

Guidelines consist of prescription protocols that are established based on evidence and financial considerations.

Netherlands

There are no objectives for prescription of medicines by individual doctors. However, physicians usually adhere to reimbursement restrictions in their prescription behaviour. Some insurance funds have started offering financial incentives to GPs based on the efficient prescription of statins and PPIs; a new policy (“preference policy”) enables insurance companies to reimburse the lowest-priced generic when a generic is prescribed.

Regional pharmacotherapeutic platforms, indirectly subsidized by the authorities and made up of physicians and pharmacists, exist to improve prescribing practices and enable professionals to discuss the efficient and protocolised use of pharmaceuticals.

Norway

Many guidelines exist, but few are enforced by law. Doctors’ prescription behaviour is monitored, but not systematically. No feedback mechanisms exist.

For some therapeutically equivalent medicines it has been established a first choice (a preferred product) for the prescribers. This means that the prescriber has to prescribe the first choice product unless there are medical reasons for not doing so. For statins, for instance, the first choice is simvastatin. This is done as an alternative to therapeutic reference pricing.

The complete reimbursement system will be made accessible in the prescription systems for the doctors.

Portugal

The Portuguese health system has five regional health administrations called ARS', which are responsible for following-up/monitoring doctor's prescriptions. Some ARS inform doctors on their prescription behaviour.

Doctors have access to information on medicines, reimbursement levels and prices. A national hospital formulary exists that is designed to guide prescription habits in hospital settings. In the ambulatory sector, a handbook is available with information on the reimbursement level category for each product (non-statutory). Generics guides and reference price guides are also available and distributed to physicians. These publications are available on INFARMED's web site.

Romania

In Romania family practitioners and specialist are monitored get feedback of their prescription behaviour

Slovakia

Insurance companies evaluate the prescription behaviour of physicians according to their specialities (e.g. clinical oncologists, cardiologists, diabetologists, etc.). Prescription protocols (when they exist) are produced by insurance companies, which also control drug consumption and the indications for which drugs are prescribed.

Doctors receive feedback on their prescription behaviour by insurance companies on an irregular basis, perhaps once or twice a year. In order to improve their prescription behaviour, they receive guidelines for the prescription of certain drugs – protocols – which are controlled by the insurance companies.

Slovenia

Prescription targets are set by the Health Insurance Institution. A periodical assessment is performed on individual prescribers who occupy the high quartile of frequency distribution and outliers (physicians that prescribe too much) may be reviewed by supervisors, who also penalize them for excessive prescribing (The health insurance laws foresee the financial penalties but are done rarely)

Physicians are monitored by analysing the number of prescriptions; this information is obtained from physician code numbers and data supplied by pharmacies where the prescriptions are filled.

A national bulletin on prescribing behavior, as well as incentives to improve prescription practises (for example, improving the equipment and other access to the education programmes, participation in professional meetings governed by the institutional management where the physicians are employed), is also available.

Spain

Prescription objectives and targets for Spanish doctors are defined by each autonomous region.

Doctors' prescription behaviour is followed-up or monitored by relevant authorities in each autonomous region. Doctors receive feedback on their prescription behaviour but the type of information available may vary from one region to another. Despite some regional differences, however, all prescribers receive feedback on their prescription practices.

Some autonomous regions issue drug information bulletins to doctors. Furthermore, periodic meetings at the health area level with the doctors to inform them about new medicines and clinical guidelines.

Sweden

The responsibility for the Swedish health care budget (including medicines) is decentralized to the county councils. In general, the county councils allocate resources to the sites (a hospital, a clinical department, etc). Hence, each site's drug costs are included in the budget for the health care produced.

Recommendations concerning quality and costs are often made when the county council allocates resources to specific sites. Some examples of the types of recommendations made follow: "of all statins prescribed the share of simvastatin should be 80%"; or "the percentage ARB of the total ARB+ACE should be 20%"; or "omeprazol should constitute 60% of all PPIs prescribed"; and "each site may set up their own targets."

Each doctor has a personal code that enables his/her closest superior to oversee prescription patterns. Also, each site is assigned a code number which the community/region/health care (budget) provider can use to follow a particular site's prescription behaviour.

Doctors can request feedback on his/her prescription behaviour from the pharmacy, which then prepares the information based on the doctor's personal code.

There are no financial incentives on a personal level.

United Kingdom

The Department of Health has occasionally published targets or benchmarking indicators to guide and incentivise local NHS activity on GP prescribing. For example, for some years the Department used the publication of a national indicator on generic prescribing (i.e. prescribing a drug by its generic, chemical name rather than by any associated brand name) as a tool to promote more cost-effective prescribing behaviour. It is likely that other indicators will be developed, either for general aspects of prescribing behaviour (e.g. prescribing by generic name) or on other specific classes of drugs.

Primary Care Trusts (PCTs) commonly define local formularies or lists of recommended drugs which they consider sufficient to meet the clinical needs of their resident populations in as cost-effectively as possible. GPs are under no legal obligation to follow these formularies, but they could be asked to justify prescribing outside the recommendations.

Prescribing advisers, mainly pharmacists, are employed at various levels within the NHS (Strategic Health Authority –SHA- and Primary Care Trust - PCT)), with the common aim to encourage and secure rational and cost-effective prescribing. There are now more than 1,200 advisers, many of whom undertake face-to-face reviews with General Practitioners (GPs) and carry out reviews of repeat prescribing activity. The Prescribing Support Unit at the Information Centre for Health and Social Care (Special Health Authority) has produced a number of analytical tools to aid advisers in their tasks.

The Prescription Pricing Division of the NHS Business Services Authority collates a large amount of prescribing data and makes it available to prescribers, prescribing advisors etc. via various electronic systems.

Prescribers who are prescribing on behalf of a GP practice can obtain their prescribing data through “Electronic Prescribing and Financial Information for Practices” (ePFIP). If prescribing costs are met directly by the Primary Care Trust (PCT), prescribers can obtain their prescribing data through their PCT via ePACT.net. Hospital ePACT.net is a service offered to Trusts whereby they can receive electronic information about their prescriptions which are dispensed in the Community.

Concerning financial incentives, the Quality and Outcomes Framework (QOF) is a part of the General Medical Services (GMS) contract that resources and rewards GPs for how well they care for patients rather than simply how many they treat. It is a voluntary part of a GP’s contractual arrangements designed to incentivise delivery of evidence based high quality care. The framework comprises a list of indicators in four domains: clinical; organisational; patient experience; and additional services. Payments are due annually. Some PCTs run prescribing incentive schemes, whose basic objective is to incentivise cost effective, clinically appropriate prescribing. They get modest payments for achieving targets.

Non-financial incentives might differ for each prescriber. Some may be motivated by peer group pressure or by getting their work published in journals. Primary Care Trusts do publish practice by practice prescribing data. This type of information sharing among practitioners does motivate some individuals to amend their prescribing behaviour.

All the information detailed above is available to doctors to help them to improve their prescribing practices. Many doctors receive support and supervision from other prescribers and there is also a wealth of information and advice available from other sources.

Prescribers should be familiar with current guidance published in the British National Formulary (BNF) and the BNF for Children (BNFC), including the use, side effects and contraindications of the medicines that are being prescribed. They should also be aware

of the guidance on the clinical and cost-effectiveness effects of interventions, published by the National Institute for Health and Clinical Excellence (NICE), a special health authority.

The National Prescribing Centre (NPC) is funded by the Department of Health and the National Institute for Health and Clinical Excellence. Its aim is to promote and support high quality, cost-effective prescribing and medicines management across the NHS, to help improve patient care and service delivery.

III. Impact

Overall experience reported by countries

- § Normally difficult to evaluate because so many different practices exist (guidelines, education, financial incentives...).
- § Some countries have objectives (700mEUR in FR), not only on pharmaceuticals but also on sanitary transports, sick days, etc.
- § Success factors: information on rational use of medicine should be generated in a neutral and scientific way, while taking national health systems into consideration (DK).

Individual replies by countries

Austria

In Austria budgetary impact is not monitored at the central level, however regional health funds do have individual monitoring tools.

Since implementing the new reimbursement code (EKO), based on a packaging system distinguished by the color of its boxes, it is easier for doctors to prescribe pharmaceuticals included in green packages (mainly generics). Doctors can freely prescribe pharmaceuticals that are dispensed in green packages. However, pharmaceuticals packaged in red (mainly expensive, innovative pharmaceuticals) require more administrative paperwork, which could be unfavourable for patients.

Since the new reimbursement code (EKO) was only implemented in 2005, no evaluations have yet been carried out. In early phases's of implementation doctors complained of difficulties in using EKO's packaging system .

Belgium

In Belgium no formal monitoring system exists to evaluate budget impacts.

There are no formal barriers to patients' access. Medical doctor still have the therapeutic freedom to prescribe whatever medicines they want. However, tools for good prescribing practices should encourage medical doctors to implement them and, in the process, slow down patient demand, if deemed inappropriate. Some might considered this as a measure that limits access to certain medications.

The many initiatives underway to promote good prescribing practices are not expected to have a negative impact on the uptake of innovative medicines (no feedback on this is currently available). Uptake of innovative medicines depends more on pharmaceutical companies' strategic decisions and on reimbursement conditions than on any other factor.

The main difficulty with implementing good prescribing practices from the government's point of view is getting the message across. Medical doctors need to be made aware of the fact that GPP –good publication practice- guidelines, even when issued by the government, are an aid and not another impediment to their therapeutic (clinical) freedom.

Although it is very difficult to evaluate the effects of GPP guidelines on prescribing patterns due to numerous external influences, it is considered think that GPP guidelines have a beneficial effect. It is recommended to other countries.

Denmark

In Denmark no formal monitoring system is in place for evaluating budget impact. However, two recent research projects have been carried out at the county level by the Institute for Rational Pharmacotherapy- IRF - to assess the impact of information related to good prescribing practices (e.g. as recommended by IRF) on real prescribing practices. The research was done in a controlled environment. Although results show some positive links between information and prescribing practices, further studies are required.

Experts from Denmark recommend that information on the rational use of medicine be done in a neutral and scientific way, taking national health systems into consideration.

Finland

The prescription register at Kela (Social Insurance Institution of Finland) includes information on prescribed medicines and prescribing doctors. Based on this register the *budgetary impact* and the changes in prescribing behaviour can be studied. For example, the reimbursement of atorvastatin and rosuvastatin was restricted in early October of 2006. Through use of the Kela register, information can be obtained regarding which products are prescribed and, more specifically, which statins are being used to treat new patients.

Pharmaceutical companies claim that the *patient* does not receive the best possible treatment (e.g. statins) when restrictions are applied to drug reimbursements.

Currently there is no independent determination on the degree of *innovation*. Experts estimate that 95 % of new medicines fall into the category of the so-called ‘me-too’ drugs.

Pharmaceutical companies can make use of extensive budgets to launch and market new products, and their assets are manifold when compared to the resources of authorities. Independent information on new medicines and their therapeutic value is lacking. Education and information, in the absence of mandatory actions, are slow in changing doctors’ prescribing behaviour. Physicians are free to decide on an individual basis what medication to prescribe to their patients since current care guidelines only serve as recommendations. More resources are needed to provide independent information on medicines.

France

In accordance with a goal laid out under French legislation to finance health insurance, a budget impact evaluation is done at least once a year. The objectives were around 700M€ in 2006 (not only on pharmaceuticals but also sanitary transports, sick days etc.)

Experts state that it is very difficult to measure the objectives’ real impact and also very hard to negotiate them.

It has been pointed out that these instruments are one of the most powerful ways to regulate demand. It has been recommended to other countries, but preferably on a doctor by doctor basis.

Germany

In Germany budget impact is evaluated by regional doctors’ associations and by health insurance funds. They report on request to their regional health ministry and to the Federal Ministry of Health. Results vary significantly from region to region.

Concerning impact on patients’ access to drugs, no severe problems have been reported.

The regions cannot restrict access to innovative medicines and do not attempt to do so.

Although targets for medical prescription began functioning in 2003, it has not yet met expectations and for that reason more regulations are being developed. A cost system (Targets for DDD-Cost for groups of pharmaceuticals: Bonus-Malus for individual prescribers) is planned for the year 2007 and, under newly proposed draft legislation, regulations for maximum prescription cost per doctor and per patient will be reformed.

Regulations to limit excessive prescribing of high-cost medicines are very complicated and have to be developed in conjunction with doctors.

Ireland

In Ireland, budgetary impact is currently under evaluation.

Certain innovative or expensive drugs are budget neutral (ie disregarded) for the purposes of the scheme.

The main difficulties that experts from Ireland reported are lack of governance, accountability, and specific measurable objectives; as a recommendation, the use of pre-empt evaluations.

Latvia

In Latvia, budget impact is monitored occasionally. The main budgetary impact can be considered the situation that the annual budget for drug reimbursement is not overspent and prescribing in general lines is based on the recommendations

The success factors for this system are:

- 1) Rational prescribing. Guidelines should conform with the principles of evidence-based medicine and data on pharmaceuticals' cost-effectiveness;
- 2) Involvement of professionals in preparing the guidelines.

Prescription guidelines can be an efficient means to influence prescribing behaviour and contain costs.

Malta

In Malta there is no formal budget impact monitoring

Access to drugs is restricted for patients who do not fall within the criteria of established guidelines (patients complain; doctors; industry).

The established guidelines restrict prescriptions to areas where they can be most cost-effective (best utilisation of resources).

It is recommended when operating within a restrictive budget.

Slovakia

Insurance companies control the budget. Guidelines for prescription– protocols –can have influence on the contract of the physician or their health organisation for the next year

Slovenia

In Slovenia budget impact is evaluated within a system used to monitor national drug expenditures.

Budgetary impact cannot be stated directly but is reflected in a relatively moderate annual growth rate for medicinal products (currently below 6%). Current rate of prescribing is 7 prescriptions per capita per annum. Maximum quantity prescribable per prescription is a 3 month's-worth supply.

Access is generally good. Of approximately 3000 authorized products, 1200 are on the positive list and an additional 400 are included on the intermediate list. The lists are updated semi-annually.

There is no claimed impact on reward for innovation; however, for the same reasons stated above, there is an inherent impact on innovation because of the functioning reimbursement system.

One difficulty that should be mentioned is the lack of transparency in direct marketing practices employed by the pharmaceutical industry via direct contact with medical professionals

One recommendation would be to review and upgrade prescription guidelines.

Spain

Impact evaluations are performed by the autonomous regional governments.

Sweden

County councils monitor budget performance monthly, quarterly and annually.

A risk associated with a decentralised health care budget in which costs for pharmaceuticals form an integral part of the budget is that drug costs are kept low favouring other parts of the budget. However, on a local level it has been noticed that with prescription recommendations issued resources are redistributed from drugs for which patent has expired and instead used to pay for new drugs.

Concerning reward for innovation, discussions on this topic are ongoing and the use of certain drugs is monitored.

An additional potential risk would be inequities in access to medicines throughout the country.

Evaluation remains to be performed

UK

It is almost impossible to isolate any single incentive for good prescribing practice and identify if it was successful or not. This is because we have no control group with which to compare the results.

Literature review

Best evidence studies

Studies on changes in doctors' prescribing behaviour

Gill *et al* (1999) made a systematic review that contains studies from a database maintained up until May 1996 by the Cochrane Collaboration on Effective Professional Practice - including randomised controlled trials and non-equivalent group designs with pre- and post-intervention measures. Its aim was to identify interventions that change doctors' prescribing behaviour and to derive conclusions for practice and further research.

Outcome measures were those used by the study authors. For each study they determined whether these were positive, negative or inconclusive. Positive studies (+) were those that demonstrated a statistically significant change in the majority of outcomes measured at level of $p < \text{or} = 0.05$ between the intervention and control groups. Negative studies (-) showed a significant change in the opposite direction and inconclusive studies (approximately) showed no significant change compared to control or no overall positive findings.

They identified 79 eligible studies which described 96 separate interventions to change prescribing behaviour. Of these interventions, 49 (51%, 41%-61%) showed a positive significant change compared to the control group, but interpretation of specific interventions is limited due to wide and overlapping confidence intervals

Table 12: Types of interventions aimed at changing doctors' prescribing behaviour

Intervention		Number of interventions	Positive findings	% Positive interventions	95% CI
	Distribution and educational materials	7	3	43	13-78
	Audit and feedback	33	17	52	24-66
	Outreach	4	2	50	10-90
	Patient mediated	8	5	63	30-90
	Conferences	1	1	100	-
	Marketing	0	0	0	-
	Multifaceted*	43	21	49	20-80
	Overall	96	49	51	41-61

*two or more of the above interventions

Source: Article "Gill PS et al. Changing doctor prescribing behaviour. Pharm World Sci 1999; 21(4):158-167.

Soumerai *et al* (1989) made a review of 44 empirical studies indicating that different strategies to improve the prescription practices of primary care physicians have proved effective to varying degrees. As a result, administrative reminders and feedback systems appear to be suitable for group practices, while one-on-one educational interventions may work well in less-structured office settings. One of the conclusions was that better-controlled trials and quasi-experimental designs, together with cost-benefit analyses, are still needed to enhance the efficacy and efficiency of prescribing practices

Information

Related to periodic letters, Dormuth *et al* (2004) uses a pair, cluster randomized community design to assess the effect of periodic letters on evidence-based drug therapy on prescribing behaviour. The effect of regular and expected printed educational materials on physician prescribing behaviour had not been studied and for this reason they sought to measure the impact of a series of evidence-based drug therapy letters mailed to physicians in British Columbia on prescribing to newly treated patients. Previous studies found that although changes in prescribing behaviour attributable to the reception of printed materials tended to be small, printed materials do have the potential to be a cost-effective method of education.

As a result, it was found that the probability of prescribing a drug recommended in the Therapeutics Letter rather than another drug in the same class increased by 30% in the 3 months after the mailing of the letter, relative to the preceding 3 months, adjusted for any before-after changes in the control group (relative risk 1.30; 95% confidence interval 1.13-1.52). No letter achieved statistical significance on its own. However, 11 of the 12 letters produced prescribing changes in the predicted direction. It was also observed that it is easier to persuade physicians to prescribe than to persuade them to stop prescribing. They concluded that printed letters distributed as an ongoing series from a credible and trusted source can have a clinically significant impact on

prescribing to newly treated patients. It was also pointed out that further work needs to be done to determine the components of the message and the characteristics of the physicians that lead to changes in prescribing.

Prescription guidelines (2 studies)

Lagerlov *et al* (2000) used a randomized control trial to study the effect on the quality of prescribing by a combined intervention of providing individual feedback and deriving quality criteria using guideline recommendations in peer review groups. The educational intervention used in the study improved the prescribing behaviour of doctors in accordance with guideline recommendations, and is thus an aid in significantly improving the quality of patient care. The study detected a significant change in behaviour despite extrinsic factors that could mask these observations (promotional activities, for example). As a conclusion it was found that doctors were able to derive quality-based criteria to orient their prescription behaviour and receive credible information to assess whether or not their treatment of individual patients was acceptable, through discussions on guideline recommendations. When presented with feedback on their own prescribing habits, doctors were able to assess what they did right and what they did wrong. This provided a foundation for improvement and resulted in doctors improving the quality of care provided to their patients.

Martens *et al* (2006) made a quasi-experimental pre/post study with a concurrent control group and a random sample of GPs within the intervention group to assess the effects of a dissemination strategy of multidisciplinary guidelines on the volume of drug prescribing. The study included two designs, a quasi-experimental pre/post study with concurrent control group and a random sample of GPs within the intervention group. The intervention area with 53 GPs was compared with a control group of 54 randomly selected GPs in the south and centre of the Netherlands. Additionally, a randomisation was executed in the intervention group to create two branches with 27 GPs who were more intensively involved in the development of the guideline and 26 GPs in the control group. A multidisciplinary committee developed prescription guidelines. Subsequently these guidelines were disseminated to all GPs in the intervention region. Additional effects were studied in the subgroup trial in which GPs were invited to be more intensively involved in the guideline development procedure.

As results, significant short-term improvements were seen for one recommendation: *mupirocin*. Long-term changes were found for cholesterol drug prescriptions. No additional changes were seen for the randomised controlled study in the subgroup. GPs did not take up the invitation for involvement. In their conclusions the authors stated that disseminating multidisciplinary guidelines developed within a region had no clear effect on prescribing behaviour in that region, even though GPs and specialists were involved more intensively in their development. Apparently, more effort is needed to bring about change.

Computerized system (2 studies)

Through an observational design, Anton *et al* (2004) analysed the effects of a computerized rule-based prescription system on changes in prescription behaviour. The authors set out to test the hypothesis that doctors' prescribing behaviour would improve after having experience with a computerised rule-based prescribing system. They designed a prospective observational study of changes in prescribing habits resulting from the use of a computerised prescribing system in (1) a cohort of experienced users compared with a new cohort, and (2) a single cohort at the beginning and after 3 weeks of computer-aided prescribing.

The conclusions are that doctors were influenced by the experience of using a computerised prescribing system. When judged by the number of warning messages generated per prescription, their prescribing habits and numbers of prescriptions extended improves with time. Consultants and registrars are more likely to use their clinical judgement to override warning messages regarding prescribed drugs. The key messages of the study are that computerised prescribing systems can help doctors to modify their prescribing to reduce errors, the number of warning messages generated by prescriber decreases as experience with the system increases, and changes in prescribing behaviour occur within weeks.

McMullin *et al* (2004) used a retrospective cohort designed study to evaluate the impact on prescription costs of a computerized support system that provides evidence-based recommendations to clinicians during the electronic prescribing process. Results showed that clinicians who received evidence-based messages had significantly lower prescription costs than those in the control group. In their conclusions the authors stated that providing electronic, evidence-based decision support during the prescribing process can shift prescribing decisions toward more evidence-based care and significantly decrease primary care prescription costs.

Financial incentives

A systematic review of the literature (English or French, January 1993 to May 1999) carried out Chaix-Couturier *et al* (2000) identified financial incentives and, when possible, to assess the results of these incentives on costs, process or outcomes of care.

The main results found concerning financial incentives were, in general:

- § Financial incentives concerned the modalities of physician payment and financing of the health care system.
- § Confounding factors included: doctor's age, training, speciality, place and type of medical practice, previous sanctions for over-prescribing, type and severity of disease, type of insurance.
- § The risks of financial incentives were limited access to certain types of care, lack of continuity of care, conflict of interests between the physician and the patient.
- § Any form of fund-holding or capitation decreased the total volume of prescriptions by 0-24%, and hospital days by up to 80% compared with fee-for-service.
- § Annual caps on doctors' incomes resulted in referrals to colleagues when target income is reached.

And concerning incentives and prescription, the main issues were:

- § Physicians who were informed on the threshold that would trigger sanctions (volume of prescriptions, for example), and on the actual financial risk to themselves, were more likely to respond. (When the threshold is known, physicians tend to reduce their prescriptions – randomised trial)
- § Concerning fund-holding (capitated payment for each patient registered) in UK, positive results have been found, include a 0-24% reduction in prescription costs (the null hypothesis is not excluded). When a financial incentive is close to that of their fund-holding colleagues, non-fund-holders reduced prescriptions by 1-3% and shifted to generic drugs. The major limitations of these studies were the poor level of evidence and the short duration of the follow-up
- § From the results of the studies currently available, it is not obvious that the effects of an incentive were magnified by the managed care environment, in part because physicians adapted their prescriptions to the level of reimbursement to the patient and cross-subsidized patients with poor medical coverage.

As a conclusion the authors state that financial incentives can be used to reduce the use of health care resources, improve compliance with practice guidelines or achieve a general health target. It may be effective to use incentives in combination, depending on the target set for a given health care programme.

Other information from less evidence studies

General studies

In Gómez Martínez et al (1999) there is a summary table that compared degrees of effectiveness with different types of instruments used to improve prescription behaviour.

Table 13: Effectiveness of certain instruments on the improvement of prescription habits

Instrument	Effectiveness
Education	
Dissemination of written material	-
Lessons	-
Education to small groups	+
Education face to face	+
Performance Control	
Feedback	+
Reminders	+
Partners' guidance	
Protocols	+
Formularies	+
Financial Incentives	?
Coercive measures	?

Notes: + studies have been published in which the intervention group improves in comparison to a control group

- publications exist with evidence on the inefficacy of an isolated measure
- ? Nothing published on the effectiveness of the measure

Other results were found in Davis *et al* (1995), who stated that “Effective change strategies included reminders, patient-mediated interventions, outreach visits, opinion leaders, and multifaceted activities. Audit with feedback and educational materials were less effective, and formal CME - continuing medical education- conferences or activities, without enabling or practice-reinforcing strategies, had relatively little impact”.

Concerning the **relation between industry and physicians**, and their relations with prescribing issues, several articles were found. Some general observations included: “Physicians are affected by their interactions with the pharmaceutical industry. Further research needs to be done in most cases to determine whether such interactions lead to more or less appropriate prescribing practices”; “If physician-industry interactions are shown to lead to inappropriate prescribing behaviour, then the issue becomes whether guidelines are a sufficient solution to the problem. If they are not, other measures will be necessary” (Lexchin, 1993). One conclusion from Galan *et al*, 2004 was that: “Results confirm both the starting hypotheses: a) the nature of relationships between PCDs –Primary Care family doctors- and the PI –Pharmaceutical industry- and its representatives affects prescribing behaviour, and b) there are differences between what doctors think they should do and what they really do in their dealings with the PF”, and another Windmeijer, 2006, “We conclude that GP drug price sensitivity is small, but adversely affected by promotion” .

Clinical Practices/Prescription Guidelines/Educational and Information

Different opinions have been found concerning these instruments. The main one is that these “passive” instruments do not improve prescribing practices. With can find opinions in Anderson, 1996 (“The dissemination of printed material alone does not lead to improved prescribing practice, but specific education and feedback strategies can”; “mailed educational material alone may change knowledge but has little or no detectable effects on actual prescribing practice”; “research on provider behaviour has suggested that interventions that combine education and feedback are more successful than interventions that rely on a single strategy”); Gray, 2006: (“Printing materials and practice guidelines have not been shown to change prescribing behaviour. Evidence-based educational approaches that do have an impact on provider behaviour include: teaching aimed at identified learning needs; interactive educational activities; sequenced and multifaceted interventions; enabling tools such as patient education programs, flow charts, and reminders; educational outreach or academic detailing; and audit and feedback to prescribers”); and Laing, 2001 (“Several simplistic approaches have proven ineffective, such as disseminating prescribing information or clinical guidelines in written form only”).

Monitoring prescribing patterns

New instruments, such as those available for monitoring prescribing patterns, are highly recommended as is evidenced in the following statements:

“Better prescribing decision monitoring and support through policy development and educational intervention is needed to reduce prescribing uncertainty” and “The absence of monitoring mechanisms of prescribing decisions, coupled with under utilization of the community pharmacist, resulted in uncertain prescribing outcomes” (Carthy et al, 2000); “This systematic review provides evidence to support the use of computer assistance in determining drug dosage” (Walton et al, 2001); and “Prescription monitoring as a method for following-up drug usage may be instrumental in evaluating the effect of drug educational efforts” (Wessling et al, 1990).

Financial incentives

Financial incentives are also well recommended by different studies and experts:

“Our results link incentive payments with prescribing change. Larger rewards were associated with PCO – Primary Care Organization- prescribing underspends in the second year”; “The association of larger rewards with improved budgetary control over time implies that larger rewards may have contributed to this issue” (Ashworth et al, 2004); “Our findings suggest that an incentive scheme can be an important component of a prescribing strategy”; and “The incentive scheme did not seem to reduce the quality of prescribing” (Bateman et al, 1996).

Nonetheless, more research is needed: *“Larger prescribing incentive scheme payments may have contributed to prescribing cost control but their effect on prescribing quality is uncertain” and “Whether financial incentives influence prescribing quality improvements can only be determined by additional research.” (Ashworth et al, 2004).*

Visits by Clinical Pharmacists

“A US study showed that visits by a clinical pharmacist to physicians reduced prescription drug costs for patients treated in a general medicine outpatient clinic, compared with costs for patients treated by a control group of physicians that did not receive any information on costs or by a group that received weekly feedback on their overall prescription drug costs and those of their peers” (Anderson et al, 1996).

IV. Discussion

Key messages

- § Education and information without any mandatory actions or incentives are likely to be a slow way to change doctors' prescribing behaviour.
- § Financial incentives are not well implemented, but recommended by literature (studies)

Risks

- Too much pressure on cost saving might lead to inadequate service for patients
- If good performance for financial incentives is defined in terms of changes on historical trends, doctors that were having a good performance before implementing the system are likely to be unfairly treated, as their prescription patterns might not be not so easily improved as those of inefficient/irrational prescribers
- Inadequate measurements of good performance and incentives systems for efficiency might have perverse effects, e.g. physicians prescribing less drugs and referring patients to specialists and hospitals

Key success factors

- Availability of adequate information systems to provide independent information on medicines. New information technologies (computerised prescribing system) can play a very important role.
- Adequate behaviour should be defined according to an objectively agreed upon profile reflecting either an accepted standard or the average behaviour of prescribers under similar conditions.
- But appropriate information and education, might need to be backed monitoring and follow-up, as well as by financial incentives, in order to attain behavioural changes in prescribing habits
- The information that the doctors receive should be independent and up-to-date
- The activities should be reiterated (including reminders)
- Professionals should be involved in designing and implementing their incentive systems

Generics Policies

I. Introduction

Description

“Generics policies” is a broad term comprising a heterogeneous set of specific practices. There is no internationally agreed upon definition of what a generic medicine is.

In countries with a long and well established tradition of product patents for medicines, generics define products that are marketed with an International Non-Proprietary Name (INN), once the patent protection and other exclusive marketing rights of an originator expires. Generics do not have to meet the same safety and efficacy tests required of the originator in order to receive marketing authorisation, however they must show interchangeability / bioequivalence with a reference drug, usually the originator.

In the USA, the most paradigmatic country in that respect, generics policies were established as a mean to balance the temporary monopolies provided by patents. Generic policy was aimed at promoting a strong and aggressive national generics industry.

However, the situation is different in countries that recently introduced strong (product) patent regimes for pharmaceuticals. In those countries branded and unbranded versions of the originator products have existed for a long time, and the industry is basically divided into two segments: foreign industry, formed by big companies with strong innovative capacity, and domestic industry, producing mainly branded or unbranded generics or licensed under multinational corporations.

Modalities

Since they are a combination of several components, the modalities of generic policies can be characterised both by how precisely they apply combined components and by the way each single component is applied. Potential components of a generics policy include several types of push, pull and other measures, such as:

1. Fast track registration: generics might undergo an abbreviated and less costly registration procedure;
2. Encouraged or mandatory prescribing by API –Active Pharmaceutical Ingredient- (generic name);
3. Generic substitution by pharmacists;
4. Information and incentives for generic utilization to prescribers, pharmacists and consumers;

5. Selective financing of generics in positive lists, reference price systems, procurement by tendering, IPR policies;
6. Pricing policies: prices of generics might be free, under the assumption that price control is not necessary, as generics generate competition. However, many countries set a maximum price for generics as a certain percentage of the price of the original reference drug.

Some of the components of a generics policy are not specific, i.e. they can be also applied in the absence of an explicit generics policy.

Purposes

The main purpose of generic policies everywhere is to increase competition and, as a consequence, to improve access and to contain/reduce pharmaceutical expenditure (to consumers, third party payers or both). Provided the quality and therapeutic equivalence of generics is granted by pharmaceutical policy, the former objectives can be attained at a standard quality, i.e. without compromising the quality and health objectives.

In the first set of countries, generic policy is supposed to provide a balance to the social cost that exclusivity-based incentives provide to innovators, whereas in the second group, it is more of a policy to control expenditure and to protect the national industry.

Theory/Rationale

From an economic perspective, generics bring price competition into pharmaceutical markets, which are characterised by situations of market exclusivity and product differentiation, often linked to the former. Economic theory predicts that under (perfect) price competition, prices will be lower and quantities larger than under either monopoly, oligopoly or product differentiation. (Market exclusivity essentially leads to higher prices via extraordinary profits, whereas product differentiation leads to price increases due to the costs of marketing and promotion of a proprietary brand. Marketing and promotion has a limited interest for producers of unbranded products as without a brand they are less likely to attain consumer loyalty for a company's product.)

Of course, a generic policy in itself does not directly address the objective of promoting innovation, although by reducing the cost of old products to society such a policy might allow it to increase funding (and prices) for new, innovative drugs.

II. Application in Europe

Overview

1. Declared policy and/or target objectives set: France, Hungary, Italy, Norway, Portugal, Spain, Sweden and UK.

2. Fast-track registration and/or lower registration fees: Austria, Finland, France Hungary, Italy, The Netherlands, Portugal, Slovakia, and Sweden.
3. Doctors are encouraged (UK, The Netherlands) or obliged (Portugal, Romania) to prescribe generics, by INN or the cheapest alternative
4. Price control of generics (Austria, Cyprus, Finland, France, Hungary, Ireland, Ireland, Italy, Portugal, Slovenia)
5. Financial incentives for physician (Italy, in some cases)
6. Mandatory generic substitution by the pharmacist, including substitution by lowest priced equivalent (Cyprus, Denmark, Italy, Sweden), or by the cheapest or close to the cheapest equivalent (Finland).
7. Voluntary generic substitution (France, Hungary, Malta, Romania Slovakia, Slovenia)
8. Financial incentives for pharmacists (France, The Netherlands)

Individual Country Replies

Austria

In Austria, there is no explicit generic drug policy. However, there are rules of procedure published by the Austrian Federation of Social Health Insurance Institutions (FASI) including specific rules on the pricing of generics. These rules are based on the Austrian Social Insurance Law (ASVG)

Favourable administrative procedures exist for generics, such as fast track registration and lower registration fees.

There are also separate pricing rules for generics, meaning that the economic efficiency of the first generic is given when the price is less than 48% (2006) of the original product's price. The economic efficiency of the second and each other following generics is thus given when a sufficiently large price difference is given. The originator's price has to be reduced by at least 30% within 3 months of the first generic's inclusion into the green box to ensure economic efficiency of the originator.

Doctors are obliged to prescribe the cheapest therapeutic alternatives to medicines that are equally effective, according to the *Economic Guidelines for Prescribing Pharmaceuticals and Medical Products* (RöV, www.avsv.at). Doctors also have to prescribe according to the reimbursement code (EKO).

Doctors receive information material from the health funds. In general, however, there are no incentives for patients, doctors or pharmacists to ask for, prescribe, or dispense generics.

There is no generic substitution in Austria. Doctors are not even allowed to prescribe by INN; they must always use the brand name or the generic product name.

There have only been a handful of pilot projects to evaluate generics policies in some regions of Austria (e.g. Burgenland). Nevertheless, these projects have been quite difficult to implement since they require support from the health funds, the doctors' associations, and hospitals.

Belgium

In the reference reimbursement system if a (cheaper) generic medicine is available which contains the same active component (or components), the original medicine enters the reference reimbursement system. This means that its reimbursement basis is diminished by 30% (ex-factory level), although its applied price remains the same. In accordance with this principle, a generic medicine must be at least 30% cheaper than the original medicine at the moment it is admitted to the list of reimbursed pharmaceutical specialities.

Special procedures are in place to authorize the introduction of generics into the market. For example, compared to other medicines, generics do not need to demonstrate their therapeutic value.

The applied price of generic medicines is fixed according to the price applied for the corresponding reference speciality.

When the reference speciality enters the reference reimbursement system, its reimbursement basis is lowered to the level of the generic alternative, while its applied price remains unchanged. From that moment on, the applied price of the generic medicine must always be lower than (or at the most equal to) the reimbursement basis of the reference speciality.

Doctors are encouraged to prescribe generics because prescription percentages for "cheap drugs"⁵⁷ are set (premium system).

Concerning information, brochures (cost comparison of pharmaceuticals by the reference reimbursement system - original and generic drugs), destined to health care professionals are edited by official instances; comparable brochures, targeted toward the public at large, are edited by health assurance institutions. Official websites offer search engines to compare the cost of pharmaceuticals (aimed at health care professionals, but also accessible to the public).

⁵⁷ Definition of "cheap drugs": generic drugs; original medicines included in the reference reimbursement system with an applied price equal to the reimbursement basis

While pharmacists are not allowed to make substitutions, doctors can prescribe by INN, in which case the pharmacists must dispense a “cheap drug”.

Generic medicines have the same absolute margin as the corresponding original medicine.

Cyprus

There is no generic policy in the private sector. In the public sector the government buys by generic name, so when a generic is available it is bought and only that generic is available at government pharmacies and hospitals.

Procedures are the same for all products and generics cannot exceed 80% of the originator’s price. Generic substitution is applied at all times.

Denmark

There is no specific generics policy, but rules on generic substitution do exist. In Denmark substitution (replacement) means that the pharmacy might dispense a different and cheaper medicinal product than the one the doctor has prescribed. The product dispensed must contain the same active substance in the same amount and the same form. The assumption is that the product will have the same effect, even though it might look different and be sold under a different name. The pharmacy can - instead of the medicinal product prescribed - dispense either a medicinal product which is produced by another pharmaceutical company under another name or a medicinal product which is manufactured by the same firm and possibly has another name (parallel imported medicinal product). Using the search page at www.medicinpriser.dk, medicinal products which can substitute (replace) the prescribed product can be found. The Danish Pharmaceutical Agency scientifically evaluates all these medicinal products. The pharmacy must dispense a cheaper medicinal product, unless the doctor has decided against substitution by writing "ej S" (not Substitution) on the prescription. The patient can, however, also decide for him/herself if he/she does not want a cheaper medicinal product. If neither the patient nor the doctors decide not to choose substitution, the patient will receive the cheapest medicinal product available. However, if the price difference between the cheapest and the prescribed medicinal product is within certain limits - DKK 5 to 20, depending on the medicinal product’s price – the pharmacy is not obliged to substitute to the cheapest product.

There is no fast-track approval system for generic applications.

Doctors are not encouraged to prescribe generic medicines; it is up to the individual doctor to prescribe according to the rational use principle.

Finland

In Finland, generic substitution has been in use since April 2003. The rules for substitution are enacted in law. Substitution places the dispensing pharmacy under an

obligation to substitute a medicinal product, prescribed by a physician or dentist, with the cheapest, or close to the cheapest, interchangeable product. However, the prescriber or the customer may reject the substitution should they wish to do so. The reimbursement payment will be based on the price of the dispensed preparation, whether the product has been substituted or not.

The lowest price and the price only marginally different from the lowest price for substitutable medicinal products (the difference between these two prices constituting the price corridor) are determined on the basis of the prices reported by pharmaceutical companies to Kela (Social Insurance Institution). The lowest price of interchangeable medicinal products is defined as the retail price (incl. VAT) of the product with the lowest price as of the first day of each quarter. A medicinal product is only marginally different from the lowest price if the difference in price to the least expensive substitutable product is

- § less than 2 euros, if the least expensive product costs less than 40 euros, or
- § less than 3 euros, if the least expensive product costs 40 euros or more.

When generic substitution was implemented in 2003 large information campaigns were carried out by the Ministry of Social Affairs and Health, the National Agency for Medicines and Kela. A “Medicinal Products Database” is freely available on Kela’s website⁵⁸. Website users can look up information about the price and reimbursability of medicines, clinical nutrients and emollients marketed in Finland, and find out which generic equivalents are available for each product.

Generic prescribing was introduced in Finland in 1996. However, prescribing based on active substances is very rare.

The registration procedure for generics is the same as for original products, although the documentation required differs. The registration/application fee for generics is lower than for original products.

Reimbursement and price approval procedures are, in principle, the same for generics as for original products. If the proposed wholesale price for the first generic product is 40 % lower than the original product’s price and for the subsequent generic products not higher than for the other generics, the General Secretary of the Pharmaceuticals Pricing Board can decide the reimbursement rate and a reasonable wholesale price. In such cases, the procedure is faster than the basic procedure when the decision is made by the Board.

France

In France, there is a general agreement with the industry with some targets savings. When the spending target for the whole public health insurance system is build, these targets are taken into account.

⁵⁸ http://kelaapp.kela.fi/laakekys_app/LaakekysApplication?kieli=en

In order to guarantee a lower price for generics than for originator products, one specific supply-side mechanism used is to set the generic's price at half the originator's price.

Pharmacists have a financial incentive for generic substitution as equal margin with originator plus specific discounts are authorized.

Another mechanism to promote the use of generics is the establishment of target substitution objectives. There is price alignment of originator and generic if substitution does not pick up (strong incentive to pharmacists as margins are much higher in generics). Generic substitution is voluntary and patient consent is required.

Germany

In Germany there is no explicit generic drug policy, but there are DDD-cost-regulations and limits on prescription costs.

There are no specific supply-side mechanisms that guarantee a lower price for generics than for originator products, but price transparency within the reference-price system provides incentives for doctors to prescribe generics, if they achieve savings by doing so.

All regional prescription targets agreed upon between doctors' associations doctors and health funds include a share of generic prescriptions as a percentage of the total prescription volume. This data is regularly published.

Generics with prices at least 30 % under reference prices are totally free from co-payment. Since November 2005, 80% of all reference price group drugs have been available without co-payment. Since then, generic prices have dropped on an average of 22%. By June 2006, generics with prices at least 30 % lower than the reference price had gained a 45 % share of total sales volume for generics (Source: IMS Health).

Voluntary generic substitution is possible without consent of prescriber and patient, but pharmacists don't do this often.

There are no other mechanisms or practices aimed at promoting generics, but generics are grouped with drugs under patent in the reference pricing system.

Greece

Greece has no explicit policy on generics, but does use a specific supply-side mechanism to guarantee a lower price for generics than for originator products: the price of generic medicinal products is set at 80% of the original product's price.

Hungary

Hungary does have an explicit generics policy. Currently its main goals include facilitating the marketing of generics by offering fast-track registration and reimbursement procedures, reducing administrative fees, broadening the RP system and excluding generics' turnover from pay-back. The decision process for reimbursing a generic drug is shorter and simpler than the one involving innovative drugs, and the application fee for reimbursement is also lower: 300,000 HUF (1,200 €) for generics, 1,500,000 HUF (6,000€) for innovative drugs. The first generic's price must be lower than or equal to 70% of the original drug's price. If a reference price group exists (which means that there are at least two brands with the same active ingredients on the market), a new generic drug's daily treatment cost (DTC) cannot be higher than the reference group's DTC.

In 2006, the number of reimbursed generics was 2,596 - 10% higher than the number of original drugs (2,367)-. The annual turnover of generics in 2006 was 17% higher than that of originators (30.3 million packages, while that of original products were 25.7 packages)

Physicians are required to prescribe reference drugs – which are mainly generics. If patients ask them to prescribe other medicines, the price difference has to be covered by the patient.

Pharmacists can substitute generics on a voluntary basis, but there are no financial incentives for either physicians or pharmacists.

Ireland

In Ireland, there is no explicit generics policy within community (out-patient) provision. Under an agreement with the industry, prices are cut by 35% in two steps when a patent expires, with generic prices being similarly affected. It is estimated that this will reduce the growth in the State's drugs bill by approx €320 m over the next four years, a significantly greater figure than would be realised in primary care by generic prescribing and dispensing mechanisms, such as generic substitution and reference pricing.

Individual hospitals have their own generics policies – it is possible that in the future a generics policy for hospital prescribing will be developed and formalised under the Health Service Executive. Generic prescribing is a feature of current medical education.

There are no specific reimbursement application or approval procedures for generic products. Registration is a responsibility of the Irish Medicines Board

Under the new industry pricing and supply agreement, the reimbursable price for a generic must reflect the reduced price for a patent-expired proprietary product.

There is an incentive scheme (IDTSS) to promote rational prescribing by state-contracted GPs, but there is no specific generic component in the scheme. It is the Department's view that the provision of incentives to prescribe and dispense generics is, in the longer term, counter-productive, particularly in light of the recently agreed 35% price cuts for end-of-patent items. Generic and INN prescribing is seen as a component of prescribers' training by means of initial and ongoing educational programs.

There is no generic substitution by pharmacists. State-contracted pharmacists, except in exceptional circumstances, must dispense as per the prescription. If a drug is prescribed generically the pharmacist chooses which product to dispense and will be reimbursed for the cost of that particular brand.

Italy

The generic market in Italy is considered to have begun formally in 2001. Targets are not set by law; they are defined by the Italian Medicines Agency.

Administrative procedures used to favour the use of generics include fast track approval and lower registration fees.

Under the law, the price of a generic being introduced in the market must be 20% lower than the originator's price. In fact, for some products the reduction is much larger.

Doctors have only a limited incentive to prescribe generics as a tool to stay within their budget (where it exists).

Patients are encouraged to request (the lowest price) generics or else pay the difference between the lowest price and that of other generics or the originator.

By law pharmacists are obliged to inform patients of the possibility of generic substitution. If the doctors indicate in the script "*substitution not allowed*" or if the patient does not accept it, he/she has to pay the price difference. Generics are exempted from the mandatory discount of pharmacies to NHS.

Latvia

In Latvia there is no explicit generics policy, but there are special administrative procedures to favour generics, such as a faster inclusion in the reimbursement system.

There are no specific supply-side mechanisms to guarantee a lower price for generics, but in practice the system works on a competitive basis and a relatively high proportion of generics exist on the market.

Due to budget constraints, doctors are encouraged to prescribe cheaper therapeutical options within the reimbursement system. They can not justify overspending their budgets if they have not prescribed the cheapest medicines.

Occasionally promotion and education programs are available.

It is mandatory for a pharmacist to inform the patient about the possibility of substitution. However, consent from prescribers or patients is required.

Regressive margins for generics act as financial incentives for substitution by pharmacists.

Lithuania

In Lithuania there is no formal generics policy. Since October 2005 the price of the first generic product reimbursed was not allowed to be greater than 70% of the originator price.

The reimbursed price for generics which entered the reimbursed medicinal products list prior to October 2005 is left as ordinary products and the price is determined according to the cheapest product in the group.

Doctors and pharmacists are both encouraged by a Health Ministry Decree (Decree 112, March 8, 2002) to inform patients about other available products with the same INN, as well as on the prices and co-payments of those products.

Patients choose the specific medicinal product. Pharmacists are encouraged to have available the cheapest medicinal product of every INN.

Malta

Within the NHS, prescribing is done by INN and pharmacists do automatically substitute the medicine which is being procured, either branded or generic. For the private sector there can be voluntary substitution by the pharmacist.

Voluntary substitution by pharmacists is permitted unless doctors specifically request the use of a particular branded product.

A disincentive exists in private practices, as the margin is %, because the higher the price the bigger the profit.

Some companies give free samples to pharmacists to promote generics.

The Netherlands

Under a contract between the industry, pharmacists and the government, an agreement was reached to reduce the total cost of generics (and relevant off-patent brands) by 40%. A project is under study to formalise the new regular reimbursement system.

A special administrative mechanism that favours the use of generics is a fast track reimbursement procedure.

Doctors are asked to prescribe by active ingredient and pharmacists are then expected to dispense generics; discounts accrued by pharmacists are subject to a claw-back.

Doctors should inform patients about the value of generics.

There is voluntary generic substitution: prescribers can block substitution by prescribing by brand name rather than by active ingredient.

There are discounts as financial incentives to pharmacists

Norway

A formal policy and specific regulations exist for generics. A special administrative procedure (lower registrations fee) also exists to promote generics.

Generic prices cannot exceed the maximum market price of the original branded product. A price model called the stepped price model (Trinnprismodellen) took effect on January 2005. Under the new scheme, a maximum reimbursement price is set for affected drugs (both branded and generics). The maximum price level is automatically reduced in stages (steps) following a patent expiration. The percentage cut depends on annual sales:

- § With sales over NoK 100 million, the maximum reimbursement price is cut by 30% upon patent expiration and generic competition by 50% after six months, and by 70% after one year.
- § With sales below NoK 100 million, the respective percentage decreases are 30%, 40% and 50%.

Following an evaluation, the stepped price system was “tightened” after January 2007. The 3 steps were reduced to 2 and the final cut is now reached after 6 months. The maximum cut rose from 50% to 55% and from 70 to 75 %. In the case of simvastatin the maximum cut rose from 70 % to 85 %.

The stepped-price system does not include regulations on the pharmacies’ mark up. Pharmacists, therefore, have a financial incentive to carry out generic substitution and dispense the cheapest available product (generally, there are higher margins for generics).

Generic substitution has been mandatory since 2001

Poland

In Poland, there is a generics substitution policy. According to Polish law, the pharmacy is obliged to inform the patient about the possibility of purchasing a drug, other than the prescribed one, having the same international name, pharmaceutical form and therapeutic application and not exceeding the price limit. The above provisions are not applicable if the prescription form indicates that the drug cannot be substituted.

Portugal

Portugal has made an effort to promote the use of generics, a key feature of its drug policy. The National Health Plan, in place since 2005, set a goal to achieve a generics market share of 15-20% by 2010.

Several measures have been taken and legislation has been issued to implement it:

- § Pricing of generics: the public price of generics introduced in the national market must be at least 35% lower than the public price of the reference medicine with an equivalent dosage and pharmaceutical form. The reference medicine is the original sold in the Portuguese market. The respective public price of a generic medicine introduced in the market for which an “homogeneous group” (GH) already exists, will be equal or inferior to the reference price of this group.
- § In 2000, generics had an extra 10% reimbursement level. This feature was removed after 2005.
- § In 2003, the reference pricing system based on generics available in the market was established.
- § In 2003, the status of some medicines (copies) was changed to generic.

As a special administrative procedure for generics, reimbursement applications are evaluated faster than other medicines.

Doctors are obliged to prescribe by INN (only for medicines with an authorized generic available).

Pharmacists can substitute generics unless doctors indicate otherwise.

Concerning education and promotion, Infarmed publishes generics and reference price guides every three months and these are distributed to doctors. This information is also available on Infarmed's web site. Campaigns on TV and radio promoting the use of generics are also organized.

Romania

In Romania, doctors are required to prescribe by INN, not by the commercial names of medicines.

Pharmacists may suggest generic substitution to the patients.

Slovakia

There is no formal generics policy in Slovakia, but there is a special administrative procedure for fast track reimbursement: three months after application, a generic drug is placed on the reimbursement list (not the six months that would usually apply), (run-

on sentence; where does this go?) when the price for DDD is lower than 10 % of the existing drugs in the reimbursement list.

In many cases the co-payment of generic drugs is lower than that of the original drug. This encourages patients to ask the doctor to prescribe a generic drug with no or lower co-payment than the original⁵⁹

Special legislation allows physicians to offer patients a generic substitute. Patients are likely to request generic substitutions mainly because of their lower co-payment. Physicians can prohibit generic substitution by indicating this on a prescription. Pharmacists in community pharmacies can offer the patient generic substitution, but if they do, the pharmacists have to inform the physician about the substitution.

Slovenia

Under Slovenian legislation there is no explicit generics policy, however, an agreement made within a coalition of political parties does mention a policy on generics.

There are no specific supply-side mechanisms to guarantee lower prices for generics than for originator products. However, pricing rules calculate the average price of the cheapest generics available in EU MS to compare and set the maximum price level at 95% of that average. Since originators can choose a lower-than-maximum price level, nominally and under exceptional circumstances, they are cheaper than the generic versions⁶⁰.

Formal possibilities exist to encourage "generic" prescribing (INN prescribing), however, they are not used by physicians.

Concerning education, there was a country-wide promotional campaign for physicians and pharmacists prior to the MZZ+NPV system's introduction in 2003.

Pharmacists can voluntarily provide substitutes. They are allowed to substitute expensive drugs for cheaper products if the patient is unwilling to co-pay the difference between the maximum attributed value (NPV) and the product's price. Currently, the pharmacist can not substitute in the opposite direction, although this is likely to be allowed in the near future. This rule holds for products officially listed on the mutually interchangeable products list.

The pricing system allows price bidding every six months.

⁵⁹ e.g. Amlodipin –Ratiopharm 5 mg tbl. 30 x 5 mg no co-payment, Norvasc 30 x 5 mg 70 % co-payment by patient– 261.5 SK, Simvastatin- Ratiopharm 10 mg tbl, 30 x 10 mg no copayment, Zocor 28 x 10 mg 93 % co-payment by patient – 1155.5 SK

⁶⁰ From January 2007, the ceiling for the price of generics is 85% of 85% of the mean of the cheapest and most expensive generic on the comparative countries.

Spain

In Spain there is a generic drug policy, defined in the Strategic Pharmaceutical Plan (November 2004). More specific objectives are defined by the Autonomous Governments.

There are specific administrative procedures to encourage the use of generics, such as:

- § The Spanish Medicines Agency systematically identifies which patents will expire in order to plan the authorisation process of generics and speed up availability
- § Fast-track mechanism for setting generic prices.

For medicines under the reference price system, pharmacists should provide the lowest-priced product. Consent from prescribers or patients are not required.

Sweden

There is a formal generic policy, with no specific objectives

There is a “fast track” procedure for generics, with simplified applications and speedy decisions. After an application has been registered, reimbursement is granted at the earliest possible meeting of the Pharmaceutical Benefits Board (which occurs monthly), providing the requested price is lower than, or similar to, the most expensive pharmaceutical in their group of substitution (maximum price). Price changes, and hence competition, is facilitated as generics may be priced freely below the maximum price. Applications must be sent in to the Pharmaceutical Benefits Board (LFN) six weeks before the new price should be set and decisions on price changes are made at the end of every month.

There is mandatory generic substitution at the pharmacy level. Whenever generics are available, prescribed patented drugs are to be substituted for the cheapest substitutable product available. (Unless the patient is willing to pay the difference between the reimbursement price of the patented drug and the gross pharmacy retail price of the cheapest available generic, in which case no substitution occurs.)

In principle, generic substitution (for which the pharmacies are responsible) replaces generic prescription. However, doctors are encouraged to prescribe less expensive treatment alternatives when available, for instance simvastatin instead of Lipitor.

As generic substitution functions very well, there is a very low level of generic promotion/education/information. However, Formulary Committees within the County Councils do encourage doctors to prescribe generic alternatives.

Generic substitution is mandatory. No substitution occurs should a patient be willing to pay the difference between the reimbursement price of the patented drug and the gross pharmacy retail price of the cheapest available generic. Also, prescribers can object to generic substitution for medical reasons. This rarely happens, however (>5% of prescriptions).

UK.

In the UK doctors are encouraged, whenever possible, to prescribe drugs by their generic name, for reasons of good professional practice (because it provides the pharmacist with the widest range of options to meet prescriptions) and because it represents best value for money (branded medicines generally being more expensive than their generic counterparts). For some years the Department of Health used the publication of a national indicator on generic prescribing (i.e. prescribing a drug by its generic, chemical name rather than by any associated brand name) as a tool to promote more cost-effective prescribing behaviour. The share of prescription items written generically increased from 79% in 2004 to 80% in 2005. This rate is higher than anywhere else in Europe. A wide range of organisations and individuals work to promote and encourage generic prescribing.

The National Prescribing Centre (funded by the Department of Health and the National Institute for Health and Clinical Excellence (NICE)) provide a wide range of documentation, workshops etc. to promote generic prescribing for all prescribers. The NHS employs nearly 1,200 local prescribing advisers whose function is to work closely with practices to improve all aspects of performance. They draw on information and tools provided by the Prescription Pricing Division of the NHS Business Services Authority and the Prescribing Support Unit at the NHS Health and Social Care Information Centre.

The Department has an agreement with the manufacturers of generic medicines to supply price and volume data quarterly. The category M reimbursement prices reflect the actual market prices charged by manufacturers. The scheme provides that new generic products introduced following the granting of a marketing authorisation may be sold at a price decided at the discretion of the supplier upon entering the market, provided that the price is no more than that of the equivalent branded medicine at the date of its patent expiration. In practice this means that some generic medicines are reimbursed at levels higher than the brand originator because category M has an intrinsic multiplier of the market price. These cases are rare in terms of value. The majority of high volume products attract several manufacturers into the market and there is effective price competition.

Pharmacists in England cannot carry out generic substitution. If a branded medicine is prescribed, that is what the pharmacist must dispense.

III. Impact of Generics policies

Overall experiences reported by countries

1. Several countries claim to have done budget impact evaluations of generics (Austria, Denmark, Finland, France, The Netherlands, Portugal, Sweden), but some of them do not provide a summary of the methodology used, the results obtained or a reference document.

2. Impact evaluation is limited to utilization and expenditure, but does not address health outcomes.
3. Most respondents assume no negative impacts on innovation.
4. It is noted that the impact of generic policies cannot be evaluated independently from other related policies, such as reference pricing.

Individual replies by countries

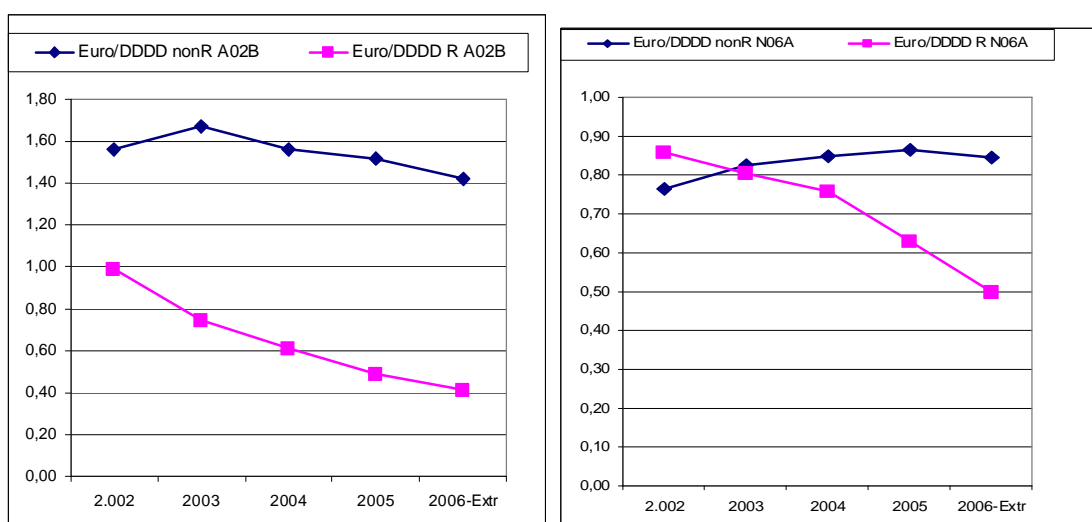
Austria

There have been only a few pilot projects on the evaluation of the budgetary impact of generics.

Belgium

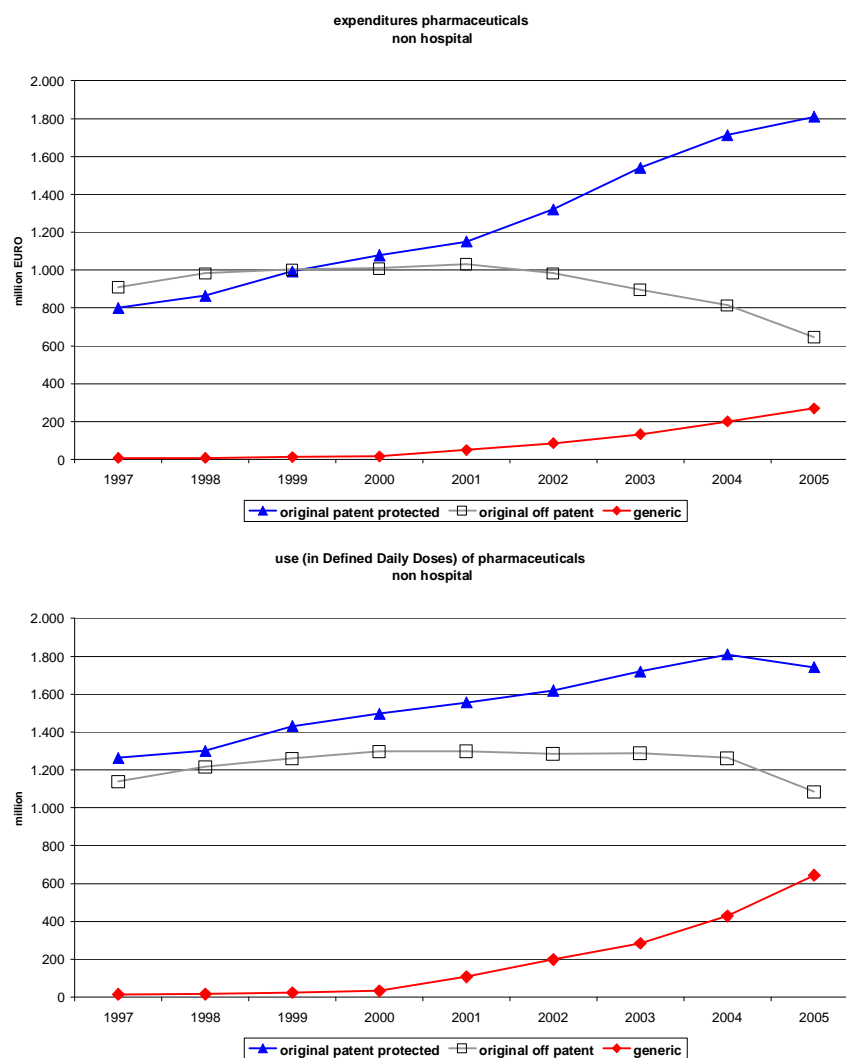
Budgetary impact is evaluated in Belgium. Evaluation is based on FARMANET data (data on sold and reimbursed drugs). Evaluation is executed as a result of (1) the six-monthly review of the reference reimbursement system and (2) the admission of a generic drug on the list of reimbursed pharmaceuticals.

Graph 5: Evolution over time of price per DDD for 2 ATC-4 classes



Source: Belgium. Health Ministry

Graph 6: Evolution of expenditures and use (DDD) of generics



Concerning impact for access to patients, if the reference reimbursement system is applied when only one generic alternative is available, provision problems are possible.

Cyprus

Concerning budgetary impact, since there are no incentives or levers to promote generics the price of branded products is not usually affected after patent expiration, unless it comes through the reference pricing system.

In the public sector, where it is used, it is estimated that this practice brings substantial savings. However, patients and physicians sometimes view generics as ineffective or low quality medicines.

Experts from Cyprus recommend educating doctors, pharmacists and patients regarding generics and providing incentives for generic prescribing.

Denmark

There is no formal monitoring system, but the Danish Medicines Agency delivers information on an ad hoc basis for the purpose of evaluating.

As stated under the impact assessment of “reference prices”, public reimbursement is around DKK 100 million less per year when compared with the previous reference price system’s level. This figure includes effects from the Danish substitution policy. This estimate is based on a comparison of the total annual reimbursement under the previously applicable reference price system (based on the latest available sales data for one year) and a calculation of what the total annual reimbursement would have been for the same period of time if the rules of the new system where the reimbursement price is the cheapest product in each substitution group had been applied.

The Danish government has, in general, had a good experience with the substitution system. Communication with stakeholders about the system is a key success factor. Information to the patients about the effect and quality of generics is important.

Finland

Kela (Social Insurance Institution) does quarterly evaluations on the budgetary impact of generic substitution. The information available on Kela’s website⁶¹ provides data on generic substitution and the savings made, with reference to both the patient and drug reimbursement payments. The savings made through actual substitution are calculated by comparing the cost of prescribed medicinal products to the cost of products actually dispensed to the patient.

Before the introduction of generic substitution, the estimated annual savings to be gained were in total EUR 45.4 million (EUR 18.5 million for patients and EUR 26.9 million for drug reimbursement system). The estimation did not include the savings generated through price competition.

The average saving per substitution of medicinal products was EUR 15.80 in 2005. The total savings of the actual substitution were EUR 25.7 million, of which EUR 12.0 million were for the patient and EUR 13.8 million for drug reimbursement payments.

Combined savings made through substitution and drug price reductions brought on by price competition were calculated for only the first year of the new practice, by comparing the costs of the dispensed substitutable products with the corresponding costs at March 2003 prices. During the first 12 months the total cost savings in reimbursable medicines were EUR 88.3 million; EUR 39.2 million were for patients and EUR 49.1 million for drug reimbursement payments. Two thirds of the savings were attributable to price reductions and one third to the actual substitution of medicinal products.

⁶¹ <http://www.kela.fi/research> – Reimbursement of medicine costs – Generic substitution

After introducing generic substitution, patients' cost awareness increased and they requested cheaper medicines when visiting their doctor. The electronic systems made available to doctors reinforces their decision-making processes by providing the prices of medicines and also the cheapest alternatives. According to first year's study on generic substitution, it was very rare for prescribing physicians to forbid substitution. If the patient has been prescribed a medicinal product that was outside the limits of the preset price corridor, in two cases out of five the purchasing individual will reject substitution. The consumers have a positive attitude towards the possibility of substituting their medicines. The customer's wish to save money in medicine purchases is the main reason for accepting substitution at a pharmacy.

The price corridor has shown to be effective in reimbursement categories where patient's share of the cost is bigger. In the higher special reimbursement category, where a patient only pays a fixed co-payment of EUR 3 per purchase of medicinal product, the price corridor does not seem to work. In this case the patient has no financial interest in substitution. A 2–3€ price difference can also have a budgetary impact for both patients and social insurance funds when affecting widely-used medicines. Based on such information, it would be reasonable to assume that even further savings could be obtained by introducing a reference price system. A working group was set up in June 2006 to evaluate the suitability of a reference price system in Finland. The working group was scheduled to report its recommendations by February 2007.

The Pharmaceuticals Pricing Board (PPB) confirms the maximum wholesale price for reimbursable medicines. In the beginning of a quarter, when the price corridors are determined, the pharmaceutical companies can decrease the prices momentarily and later increase them to the price corridor's upper limit provided that the price does not exceed the price confirmed by PPB. This can lead to a situation where no medicine with the corridor's floor price is available.

Pharmacies have claimed that when a new quarter begins the cheapest products might be momentarily out of stock, or that supplies of the cheapest products may cover only a few weeks of demand. Increasing stockpiles in pharmacies have also proven to be problematic.

Launching new procedures requires good co-operation among all partners. Generic substitution has been found to be effective in reducing the costs of medicines. However, the system does not affect the costs of non-substitutable drugs or the so called "me-too" medicines.

France

Budgetary impact is evaluated regularly and the Health Ministry calculates distribution data.

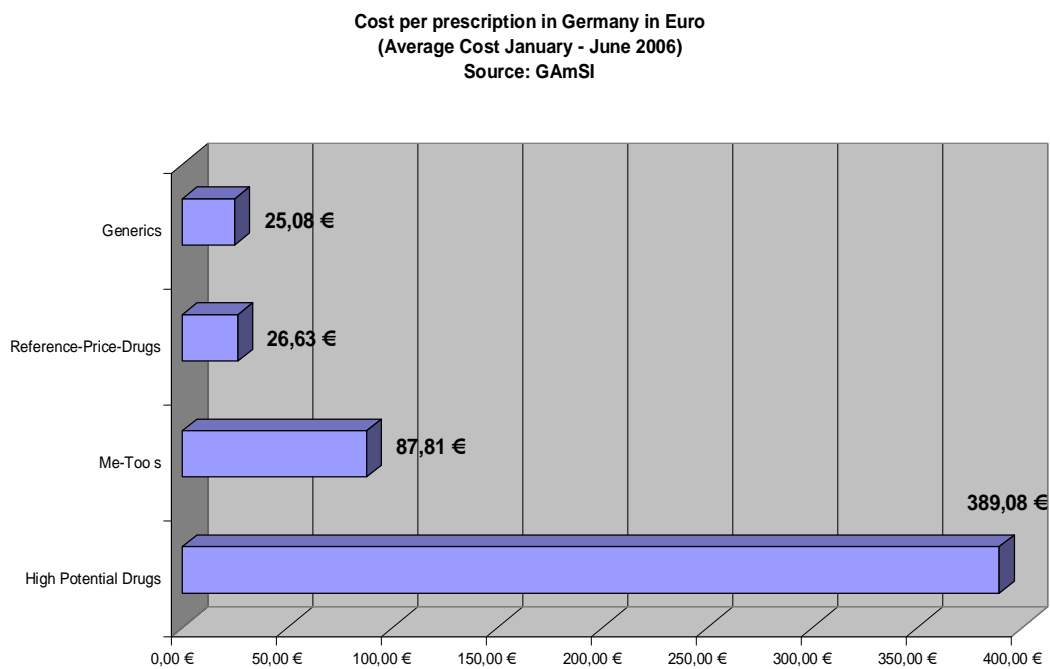
Generic penetration is around 65%. Price discount of generics is 50% (ex-factory price). Budgetary impact is approximately 500M€

French experts suggest making recommendations aimed convincing patients without forcing them (in France, patients do not pay for pharmaceuticals); doctors are not interested and financial incentives might work faster. It is reported as a positive experience.

Germany

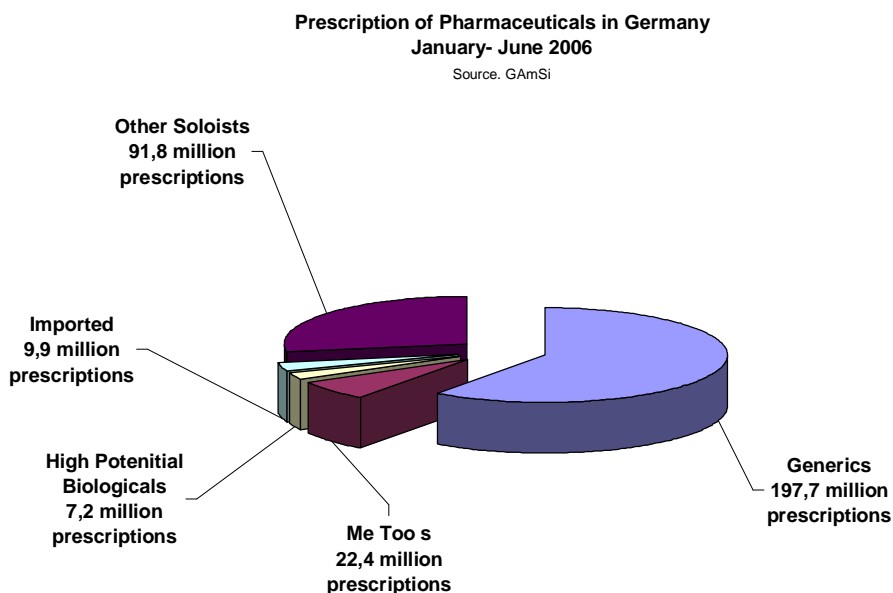
Cost-development for generics and patented drugs are regularly reported

Graph 7: Cost per prescription in Germany (Euro)



Source. Germany . Health Ministry (EASP's questionnaire)

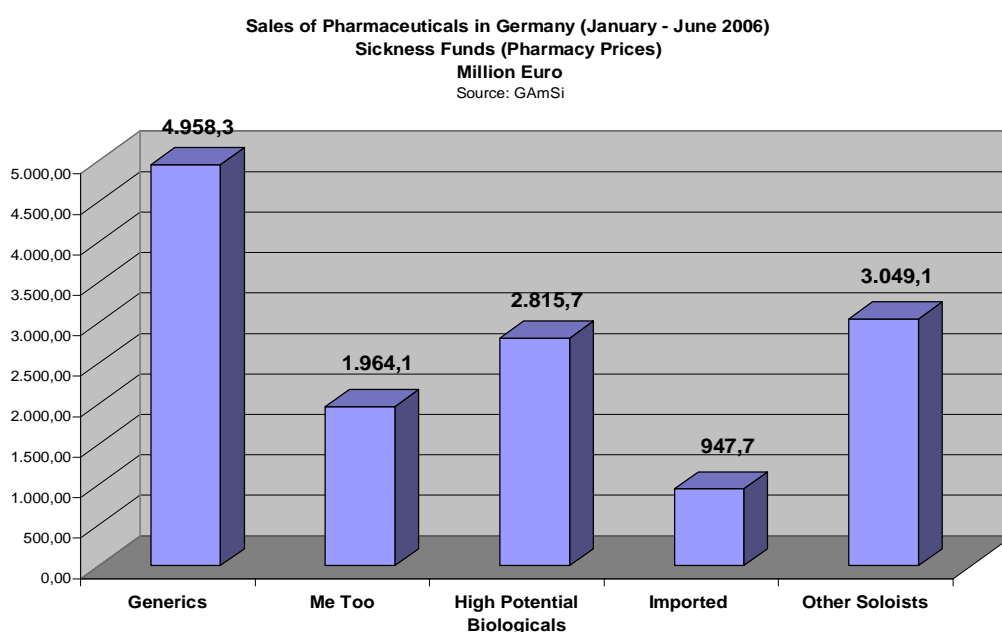
Graph 8: Prescription of Pharmaceuticals in Germany



Source: Germany. Health Ministry (EASP’s questionnaire)

The main difficulties have been that doctors and patients have to get used to generic substitution. Experts conclude that more savings can be achieved if products for generic substitution are tendered by the health fund. This practice is foreseen under new draft legislation.

Graph 9: Sales of Pharmaceuticals in Germany



Source: Germany. Health Ministry (EASP’s questionnaire)

Greece

Budgetary impact analysis mechanisms are expected to be applied in early 2007.

Ireland

The new system will be evaluated in due course.

Italy

The impact of generics is included in OsMed's (Drug Monitoring Centre) activities, but Italy is analysing specific indicators for more exact monitoring and a yearly report.

Existing legislation provides for a 20% reduction and it may move to more substantial reductions. The penetration rate of "pure" generics is relatively low for several reasons, including the reduction in price of the originator compound (i.e. after a generic's introduction, the originator's price is lowered to that of the generic).

The generic market in Italy is in development and needs further relevant modifications. A complementary protection law exists that contemplates a lengthy period for harmonising Italian protection mechanisms to EU levels (a reduction of 1 year every two years; this means that to move from the present 20+18 to 20 years, an average of 36 years will be required). One other relevant obstacle is the absence of transparency and available information on the date of patent expiration. Moreover, the country does not have a strong generic industry, as in Germany, and there is stiff competition among originators. Last but not least, a shift from non-patented products to more expensive patented products has been observed. For instance, enalapril had a relevant reduction of utilisation, around and after its generic introduction, while the same ingredient had a relevant increase in utilisation in Germany after its generic introduction.

Latvia

Budget impact is evaluated annually. The share of generics on the market and within the reimbursement system in Latvia is one of the highest in the EU.

Generic substitution is recommended because it reinforces the rational use of drugs, helping allocate existing resources more cost-effectively and producing savings for new medications.

Malta

In Malta, there is no formal monitoring system for the private market.

Concerning impact on access to patients, when changes result from awarding tenders through competitive bidding processes, patients find themselves having to change their medication from one brand/generic to another and it doesn't like them.

In Malta it was proposed that the NHS purchase alternatives at the same price as the product winning the tender, thus increasing market access to medicinal products while at the same time increasing patients' access to medicines – without obliging them to change product brands.

Netherlands

In the Netherlands budget impact is continuously evaluated.

The main difficulties are: achieving maximum cost containment (through generics) without blocking market access of generics by affecting profitability; to establish a system that has flexibility in each sub-market (e.g. diseases); and achieving optimal reductions in the prices of generics based on the dynamics of each sub-market.

Norway

Norway carried out one evaluation that showed that the system works well⁶².

Poland

Poland evaluates budget impact each time a new decree is prepared to include a new generic on the list. Financial impacts on the National Health Fund are estimated.

Portugal.

Infarmed carries out monthly evaluations on the growth of the generics market. This information is available on Infarmed's site.

It was estimated that if generic medicines did not exist, there would be annual increase of approximately 31 million euros on NHS expenditure and nearly 14 million euros for patients. No formal report on estimates is available, however the following conditions were assumed to reach the above-mentioned figures on impact:

- the current behaviour of the market would be maintained;
- the consumption volume of generic and non-generic medicines (total number of packages sold would not change);
- Packages of generic medicines would be sold at the same price as the non-generics.

⁶² Author's Note: Since the evaluation was in Norwegian, the authors could not review it.

The main difficulties associated with a generics policy center on concerns regarding credibility, quality, efficacy and safety. The main advantage in using generics is that they result in lower prices.

Portugal's experience has been a positive one. Its generic market went up from a total market share (in volume/value) of 0.10%/0.13% in the year 2000 to 9%/14.9% in July 2006.

Slovakia

Consumption is evaluated every three months.

Concerning impact on access, when patients do not want to change from a brand name drug to a generic brand with a lower co-payment, complaints sometimes arise about high co-payments for original drugs.

Slovenia

Health insurers do not carry out any formal monitoring or annual evaluations. The savings of MZZ+NPV (a system of mutually interchangeable medicinal products with maximum attributed value) are estimated at 3-5% of the market value⁶³.

No impact on patients' access has been found. Indirectly, savings can be used for other medicinal products and other health programmes.

The main difficulties center on how to convince patients, doctors and the media that generic products are interchangeable with respect to originators.

Spain

Currently, the market value share of generics in Spain is close to 8% expenditure and 15% in volume; impact has been positive and the tendency will be for that share to increase.

Experts state that the main threat to generic market growth could come from problems derived from sacrificing quality to competitive pricing. Another aspect of concern is the possible confusion that generics sometimes generate, particularly among elderly patients, who have trouble getting used to the the idea of different shapes and colors in generics containing the same active substance.

This practice is considered successful in reaching cost containment goals and is recommended to other countries.

Sweden

⁶³ From January 2007, additional 5 % savings of the market value after implementation of the new pricing law

There is no formal yearly evaluation of the budgetary impact, but the system has been evaluated by independent researchers (article by Engström, Jacob and Lundin)⁶⁴. Also, a description of the price level for pharmaceuticals is included in the annual report of the Pharmaceutical Benefits Board.

Pharmaceutical prices in Sweden have decreased by about 15 percent since generic substitution was introduced, that is from October 2002 to December 2005. This means that patients and taxpayers get access to the same amount of pharmaceuticals today for a price 15 percent lower on average than three years ago. This drop in prices is due entirely to the decrease in prices for off-patent drugs. Market prices for generic drugs have fallen by approximately 40 percent. The accumulated savings in the pharmaceutical budget during the period above have been almost 7 billion SEK (approximately €760 million).

Literature review

Andersson et al (2005) analysed if the implementation of generic substitution was associated with changes in patients' expenses and reimbursed cost for prescribed pharmaceuticals included in the Swedish Pharmaceutical Benefits Scheme (PBS)⁶⁵. The study period ranged between 1 January 2000 and 31 December 2004.

⁶⁴ Summary: Pharmaceutical prices in Sweden have decreased by about 15 percent since generic substitution was introduced, that is from October 2002 to December 2005. This means that patients and taxpayers get access to the same amount of pharmaceuticals today for a price 15 percent lower on average than three years ago. This drop in prices is due entirely to the decrease in prices for off-patent drugs. Market prices for generic drugs have fallen by approximately 40 percent. The accumulated savings in the pharmaceutical budget during the period above have been almost 7 billion SKr (approximately €760 million).

For some groups of pharmaceuticals the price decreases have had a substantial effect on the cost of treatment. The biggest fall in prices has been for statins used for treating high cholesterol. For these the average price has fallen by 71 percent. The price today, for treating a patient with statins, is thus less than a third of what it was three years ago.

The average price for antidepressants (SSRI) fell by about 66 percent. For pharmaceuticals against ulcer and heartburn (proton pump inhibitors) it fell by 41 percent and for calcium antagonists (used in treating hypertension) the price fell by 35 percent.

The main cause for the lower average prices for these groups of pharmaceuticals is that one or more of the drugs in the therapeutic area in question has lost its patent and prices have fallen, as was the case for the statin Zocor (simvastatin) and the proton pump inhibitor Losec/Prilosec (omeprazole).

Another reason is that the use of other more expensive, and still patented drugs, decreases in favour of the drug which has lost its patent. We estimate that the average price for proton pump inhibitors would have decreased by only 28 percent rather than 41 percent, if the still patented Lanzo (lanzaprazole) had not lost market share to generic omeprazole.

The effects of generic substitution are thus not limited to the generics market, they also affect the competitive situation in an entire therapeutic area.

For generic substitution to work efficiently it requires an efficient market where companies can quickly change their prices and react to their competitors. The Pharmaceutical Benefits Board (LFN) has developed such a marketplace to stimulate price competition between generic drugs. In total, more than 20,000 price change decisions have been made for these drugs, of which 80 percent have been price decreases.

⁶⁵ In Sweden pharmacy personnel are obliged to offer the patient the cheapest available medically equivalent drug according to the Medical Products Agency's list of substitutable products, unless substitution is restricted. This applies for all prescriptions issued after 1 October 2002 within the PBS. Prescribers can restrict substitution by marking "substitution not allowed" on the prescription. In certain situations the pharmacist can also restrict substitution. This can be done when there are differences in

The results showed that the introduction of generic substitution was associated with a shift in trend from an increase into a decrease both for patients' and society's expenditures, indicating that the reform has had an impact on the growth of pharmaceutical expenditure.

A more recent study by Engström et al (2006) analyses how generic substitution at patent expiration in Sweden (since its introduction in October 2002, until December 2005) has reduced pharmaceutical prices by about 15%. For groups more affected by substitution the effects have been much larger. The biggest fall has been for statins, 71%, bringing the average price of a treatment to about one third of what it was three years ago. The price of antidepressants (SSRI) fell by about 66%, 41% for proton pump inhibitors and 35 % for calcium antagonists. The authors recognise that the reduction cannot be exclusively accounted to generic substitution policies, as the prices would probably have come down to some extent as a result of patent expirations. This study illustrates quite well the recurrent problem of observational studies: the need to construct a counterfactual (in this case, the evolution of prices without a substitution policy) in order to validly attribute an effect to each causal factor.

In Taiwan, the government has been introducing many strategies to control the pharmaceutical expenditure (PE) the National Health Insurance (NHI) programme's inception, including price adjustment based on the prices of international products or existing products (inter-brands comparison), or market price and volume survey; delegation of financial responsibility to regional bureaux; co-payment for outpatient drugs; generic grouping (the reference pricing scheme based on chemical equivalence); a global budget payment system for clinics and hospitals; and reduction in the flat daily payment rate of drugs for clinics. A study by Lee et al. (2006) tried to evaluate the impact of these cost containment strategies on the PE of the NHI programme from 1996 to 2003.

The study's hypotheses were that: (a) generic grouping, but not international and inter-brand price comparison, would have had a significant impact on PE (H1); (b) without other direct financial incentives, global budgeting alone would not have controlled PE (H2); (c) outpatient drug co-payments would not have had a significant impact on PE (H3); and (d) reduction of flat payment rates for pharmaceutical costs of the clinics and delegation of financial responsibility would have had a significant impact on PE (H4).

This study applied a "quasi-experimental design" and used the time-series intervention methodology of Box and Tiao to examine the impacts of all cost containment strategies on the monthly PE. Box-Tiao's method determines the nature and magnitude of the changes due to certain policy interventions by comparing the change of a measure before and after that intervention. The study confirmed the hypotheses that generic grouping (the reference price scheme based on chemical equivalence) and the reduction of the flat (fixed) payment rate for drugs were associated with a significant reduction in PE. Delegation of financial responsibility to regional bureaux also had a significant impact on PE in the inpatient sector. Brand-specific price-cuts, based either on

taste or if the dosage is comprised of divided doses, such as divided tablets. If the physician or the pharmacist restricts substitution, the total cost of the prescribed drug will be added to the patient's accumulated drug purchase costs within the PBS. The patient can oppose substitution if he or she pays the price difference between the prescribed and cheapest product. In this case the cost of the cheapest product is added to the patient's accumulated cost of drugs purchased within the PBS.

international prices, existing prices or on market price, all failed to control PE. They also found that providers in different sectors, i.e. clinics versus hospitals, responded differently to a global budget payment system.

A study by Christian-Herman et al⁶⁶ used pharmacy claims to show that an involuntary switch from brand name to generic-only coverage led to increased out-of-pocket drug costs for patients and to decreased use of important medications (e.g., angiotensin-converting enzyme inhibitors for heart failure). This study adds to that evidence using data from patient surveys (1) to adjust for patient characteristics (e.g., income and health status) and to describe which seniors may be most affected by brand name coverage discontinuation, (2) to ask about financial burden, (3) to describe whether seniors adopted other cost-cutting strategies besides decreasing medication use (e.g., switching drugs and using samples), and (4) to evaluate how discontinuation of brand name coverage affected medication use for a broader range of treatment classes (e.g., non-sedating antihistamines and antihypertensives).

This study found that discontinuation of brand name coverage among Medicare beneficiaries increased their rates of switching medications, decreased their medication use, and led to greater financial burden. Because generic equivalents were often unavailable and not all therapeutic classes had generics, health providers and policy makers must examine how to help patients make use of generic-only benefits to maximize their health and to ensure access to necessary medications.

With drug spending rising rapidly for working-aged adults, many employers and health insurance providers have changed benefits packages to encourage use of fewer or less expensive drugs. It is unknown how these initiatives affect drug costs.

In this study, Joyce *et al* (2002) use data for a wide array of employers and benefit designs to assess how multitier formularies, increased co-payments, and MGS requirements affect spending for generic and brand drugs and patients' out-of-pocket costs. The study found that many of the tools used to influence pharmaceutical use were effective in reducing drug expenditures for working-age enrollees with employer-provided drug coverage. Adding an additional level of co-payment, increasing existing co-payments or coinsurance rates, and requiring MGS (mandatory generic substitution) all reduced health insurance plan payments significantly. Doubling patient co-payments lowered average drug spending by as much as one third, reducing both the likelihood of having a claim and the level of spending conditional upon use. The reduction in drug spending largely benefited employers, as the fraction of drug costs borne by patients increased significantly.

⁶⁶ The study assessed the associations between the switch to a generic-only pharmacy benefit and outcomes among members of a large Medicare HMO. Administrative data used for the study included enrolment information, facility claims, professional service claims, and outpatient prescription drug claims for more than 550,000 Medicare HMO members in California who were enrolled in 2001 or 2002, or both. Analyses included both a case group (changed to generic-only benefit) and a control group (continued brand-name and generic benefit). In 2001 the groups had similar prescription coverage for both brand-name and generic drugs. In 2002 the case group, which represented a mix of metropolitan and non-metropolitan counties in California, switched to a generic-only prescription benefit with no coverage of brand-name drugs. The control group, which included two large metropolitan counties, continued with a benefit that covered a range of brand-name and generic drugs. We evaluated the effect of the benefit design change by comparing the change in endpoints for the groups from 2001 to 2002.

McManus et al. (2001) describe the effects of introducing minimum pricing and generic substitution policies on the dispensing of PBS prescriptions both at the aggregate level and, for two examples (fluoxetine and ranitidine, that received generic competition, and subsequently a brand premium, in the years 1996 and 1997 respectively), at an individual patient level.

From zero base in 1990 when the Minimum Pricing Policy was introduced, the relative proportion of premium and benchmark prescriptions was examined four years later, in 1994, at a time immediately prior to generic (brand) substitution by pharmacists being permitted. These proportions were examined again five years later, in 1999. These data were obtained from PBS claims processed by the Health Insurance Commission (HIC) and available to the Department of Health and Aged Care.

The introduction in 1990 of the Minimum Pricing Policy without allowing generic substitution had a relatively small impact on the selections of medicines within the Pharmaceutical Benefits Scheme (In 1994, four years after, the percentage of the eligible PBS items dispensed at the benchmark level was only 17%). However, the effect of generic substitution at the pharmacist level, which was introduced in December 1994, resulted in a marked increase in the percentage of eligible PBS items dispensed at benchmark. In 1999, five years after the introduction of generic substitution, the percentage of eligible PBS items dispensed at benchmark rose from 17 to 45%. Case studies showed a larger premium resulted in a greater shift of patients from drugs with a brand premium to the benchmark alternative.

IV. Discussion

Key messages

- § A generics policy is an available strategy to reduce costs while maintaining a standard quality of the service.
- § As the case of the USA, the UK and other countries show, an adequately designed generics policy is compatible with a strong innovative industry.
- § There are no specific needs associated to generics regarding quality control, as it equally applies to originators, branded and unbranded generics. In order to guaranty therapeutic equivalence, countries should have the technical capacity to carry out bioequivalence or other types of tests required, e.g. bioavailability.
- § Generic policies face in many countries strong obstacles and opposition derived from lack of information, prejudices (both justified and unjustified) and vested interests from all parties involved: patients, prescribers and pharmacists, as well as from the innovative multinationals corporation and domestic branded generics producers.

Risks

- § Some of the risks associated with generics policies is that trying to protect the local non-innovative industry, governments do not fully enforce the quality control of generic manufacturing, or they may fail to provide the level of IPR protection that the most innovative (or potentially innovative) domestic industry requires.
- § Factors limiting the availability of generic drugs:
 - the pharmaceutical industry prefers to market products with a brand name than products under a generic name
 - intellectual property rights impede or delay the approval of generic products
 - small market size
 - lack of incentives for the supply chain (production, distribution, prescription, and dispensing)
 - non-bioequivalent pharmaceutical alternatives are available in the market
 - bioequivalence is not required (or was not required in the past) for drug approval by the regulatory agency
 - regulatory barriers
 - slow approval process: an abbreviate approval process is not available
 - high cost of drug approval and registration
 - problems with market competition in production, importation, distribution, or health care provision
 - barriers to drug imports
 - public regulation and policy do not support the use of generic drugs
- § Factors limiting the utilization of available generics:
 - lack of incentives for the use of generic drug by the supply chain
 - economic incentives in the supply chain for use of branded instead of generic products
 - the supply chain and the consumers prefer branded drugs because there is not a quality assurance system established in the country
 - generic drugs are believed to be lower quality products
 - third party payers pay for branded products when generic products are available
 - legal prohibition of generic substitution
 - generic drug prices are not profitable for generic manufacturers
 - negative marketing and public campaigns against the use of generic drugs are promoted).

Key success factors

Ideally an overall strategy is designed to promote generic use that addresses all potential barriers, including several measures:

- Authorities could ensure that generics attain the same standards of quality than other drugs (originators) and to educate and inform patients, prescribers and pharmacists on the safety, efficacy and economic advantages of generics. A successful policy also requires competition on the supply side: if producers can agree on a common price or price policy, RP would not attain the desired results.

- Parties on the demand side should have no reason to object against generics, and ideally one of the parties drives the use of generics through some specific incentive, e.g.
 - Patients' financial incentives for using generics (RP system or co-insurance)
 - Pharmacists' financial incentives for generic substitution (mark-ups, claw back systems)
 - Physicians' financial incentives for generic prescription linked to target budgets, generic prescription targets, etc.

D. Global perspective on pricing and reimbursement policies

I. Similarities and dissimilarities in EU MS pharmaceutical policies

(regarding the six selected policy practices)

EU MS differ greatly in their priorities regarding pharmaceutical policy: providing incentives for innovation, supporting domestic (generics or innovative) industry and employment, ensuring and improving access to drugs, limiting public expenditure on drugs, etc. Although concerns about limiting public expenditure are rather common and growing in most countries, differences in priorities persist.

Differences are obviously related to the different characteristics and levels of development of the pharmaceutical sector, to general level of income, and to the characteristics of health policy and the health system, among other factors. As these differences are likely to continue, one should not necessarily expect pharmaceutical policies in the EU to converge in any spontaneous way.

Direct product price regulation is losing its traditional role in Europe, probably less as a result of an intended policy than because of its decreasing effectiveness in the new context of the Single European Market. Innovator companies are now interested in having similar prices all over the EU – in order to avoid or minimise parallel trade – and are more able than in the past to resist pressures of national regulators to reduce the price of new drugs, because the EU's upwards harmonization of Intellectual Property Rights implies that no agreement in price negotiation might imply, especially for relatively small countries, a delayed access to innovations and to the associated health benefits.

Cost-plus approaches to price control seem to be abandoned in favour of those based on international price-comparisons. A few countries have started to use economic

evaluation and cost-effectiveness criteria for determining the administrative or reimbursement price of new drugs financed by the public health system.

Cost-sharing has been maintained in most countries, but new sophisticated approaches are being developed – especially in the Nordic countries – that try to minimise the negative effects on access and equity.

RP is rapidly spreading across Europe. Most countries define the equivalent groups/clusters in a narrow sense (active ingredient), but a few countries (Netherlands, Germany) have shifted to groups based on therapeutic equivalence. There are also broad differences in the way the reimbursement price is set and how exceptions are made.

Payback is one of the most recent additions to pharmaceutical policies, but it is apparently applied in an “ad hoc” way, resulting from specific negotiations. These two characteristics contribute to not much being known about how this practice is applied or about its impact.

Regarding incentives for prescribing, most countries provide guidelines, information and education, but only a limited number goes beyond “low-intensity” approaches to monitoring and providing feedback and personal advice to prescribers. Financial and other incentives are very rarely applied.

Great variations are also found in generics policies, which have often been developed in conjunction with RP systems. Generic policies have made limited progress in countries that have developed a strong non-innovative industry producing branded generics with prices relatively close to the originators. There are also substantial differences in the leading element of the generic policy: selective/priority financing, prescription by generic name, reference pricing, substitution by pharmacist, etc.

II. Evidence of impact

Evidence of impact will always imply a certain level of subjectivity, both at the time of setting the criteria and at the time of applying them to specific studies or analyses. Moreover, we have not attempted to assess the validity of the manifold studies, analyses and opinions found in the literature search and in the responses to the questionnaire with a single set of criteria. We are, rather, confronted with a heterogeneous set of reviews—each one using different criteria, with analyses based on varying combinations of empirical evidence, logical reasoning, technical and value judgements, and so on.

Probably no two studies have used exactly the same methodology and literature reviews use different criteria to include studies in the review and to assess validity. Most studies are impossible to reproduce; therefore we must rule out the possibility of bias due to vested interests or technical errors and trust the author’s capacity and honesty. Accepting the former constraints and assumptions – and others not mentioned here – we can formulate a few statements on the evidence of impact of the practices selected in our study.

Price control

Direct product price control of pharmaceuticals is criticised by most authors, and especially by individuals close to the interests of the manufacturers, because it is said to be difficult to implement in a fair and efficient way. When it is effectively applied to lower the prices of innovative products beyond a certain level, some claim the incentives for innovation are removed. Such effects are, however, are not convincingly documented. Pricing based on a set of international prices in countries with similar characteristics looks quite reasonable for a small country that has no capacity to impose its own criteria and preferences. Finally, pricing based on economic evaluation and profit control makes a lot of economic sense but is, again, not convincingly assessed. Probably the main difficulties in assessing price control practices is the relative vagueness of its formulation, the fact that they have been applied for a long time and without radical changes in most countries.

Due to the assumed difficulties of assessing the impact of price control, no questions were included in the questionnaire on that issue.

Cost-sharing

Cost-sharing is an old practice, as well, which has been frequently assessed: it seems reasonable to assume that cost-sharing is likely to disproportionately affect the most vulnerable individuals and households - low income and high need/use of expensive services. These negative effects can be overcome if the payment has the appropriate safeguards: criteria for excluding diseases and individuals, expenditure caps, etc.

According questionnaire responses, there has been a limited monitoring and follow-up of the effects of this practice in most countries, beyond the calculation of aggregate volume of payments by the patients: 13% in SL, 14% in AT, 20% in SE; £422m in UK (04-05).

However, in order to manage their individually defined cost-sharing systems DK, FI, and SE have set up a patient-level reporting system that allows the impact of cost-sharing to be analysed in terms of equity, accessibility and other microeconomic impact variables; this later serves as the basis for a system that progressively decreases cost-sharing by patients (DK, SE) or patient's annual ceiling for co-payments (FI).

No assessments were reported on cost-sharing's impact on expenditure and utilisation/access.

Reference Pricing

Reference pricing has been relatively well studied, but only in some of its modalities – especially generic RP – and research has been concentrated in a few settings: Canada (British Columbia), Germany, etc. It is often difficult to separate the effects of RP and generics policies, two policies which are often implemented together. There have been claims from big pharma that therapeutic RP reduces the incentives for incremental innovation, which is assumed to play a key role and be the main form of attaining – step

by step – major innovations in a cumulative way. Some studies and experts have also concluded that RP does not actually promote competition, therefore prices do fall below the RP.

Savings were reported in the questionnaire by some countries: HU: -5% in 6 months; IT: basis for price cut in 2004 with 500-600 M EUR saving; LV: 0.6 M EUR in 6 months; DK: 100 M DKK

Changes in access are assumed to be, in general, limited, except for some reported increases in out-of-pocket payments and the possibility of discontinuation in the availability of products.

Payback

Payback is a very new a practice and the evidence on its impact is therefore close to nil.

Some countries reported their estimated savings: FR: 400 M EUR ('05), 160 M EUR ('06e); IT 800 M EUR cut ('06e); PT: 10 M EUR ('06); UK: ~15m£/y ('92-'99)

Payback is not assumed to change access, given that patients are not involved. Opinions regarding its possible impact on incentives for innovation differ. Moreover, in FR innovative products are exempted; and in PT recoups go to a R&D fund. The practice is deemed appropriate for MS with low GDP, where price-reductions are hard to get (HU).

Incentives for good prescription practices

Incentives for more efficient prescribing are not a single practice, but a large set of heterogeneous practices, sometimes excluding each other and sometimes reciprocally reinforcing each other; for instance, convenient unbiased information on the characteristics of medicines, guidelines for rational use, and financial incentives linked to some prescription targets might be implemented simultaneously in order to obtain a larger impact. Some of the existing incentives for more efficient prescribing – especially, financial incentives - have a documented effectiveness, but many countries are reluctant to incorporate performance incentives into the retribution system for health personnel.

Some countries have explicit objectives for these types of policies, e.g. 700 M EUR in FR, although the target savings refer not only to pharmaceuticals but also to patient transportation, sick leave, etc.

Generics policies

As in the case of prescribing incentives, a generics policy is usually the result of a large combination of both demand and supply side practices. There are in the literature a substantial number of studies showing the impact of specific generics policy practices, such as generic substitution by the pharmacist. Generic policies haven been applied for a long time, supported by selective reimbursement, differential cost-sharing, patient and

prescriber information and education. In recent times, generics policies have been complemented by RP and stronger financial incentives to pharmacists and prescribers.

Several countries claim that they have carried out budget impact evaluations of generic policies, though few provide data. Assessments seem to focus on utilisation and pharmaceutical expenditure, while overall health expenditure and health outcomes are usually not covered. FI reported 49 M EUR in public savings and 39 M EUR in savings for patients one year after mandatory generic substitution had been introduced, and SE claims to have attained ~760 M EUR accumulated savings between Oct'02 and Dec'05.

Most respondents assume no negative impact on innovation. It has also been noted that the impact of generics policies cannot be evaluated standalone from different related practices, in particular reference pricing.

In summary:

Throughout the EU it seems that direct product price control based on cost-plus approaches is being progressively abandoned. It is either being substituted by alternative pricing criteria – international prices, pharmacoeconomic criteria, etc. – or replaced by reimbursement policies, including more complex cost-sharing schemes that contemplate annual expenditure caps and decreasing co-payments, together with RP. RP and generics policies both face a challenge which limits their effectiveness: lack of incentives for efficiency on the demand side that would lead to the choice of value for money and allow consumers and insurers to take full advantage of generic competition. For innovative drugs, competition is legally excluded through patent protection and other exclusivity rights. The most rational approach to pricing innovative products, which constitute a real monopoly, is to control the prices in accordance with certain cost-effectiveness threshold criteria, a measure that could provide the right incentives for private R&D and innovation.

III. Interactions/interdependence between practices

This report basically analyses pharmaceutical policies on a practice-by-practice basis. In fact, pharmaceutical policies consist of a set of practices that can reinforce or counteract each other and should, therefore, be chosen and designed by taking these interactions into account, taking advantage of synergies and reducing contrary or conflicting effects. These effects should also be taken into account when assessing the impact of a given practice.

The following interactions should, for instance, be expected among the six policy practices analyses in this report:

Price control, if effective, reduces the impact on access of some forms of cost-sharing, such as co-insurance, but not the impact of a fixed co-payment. RP should be expected

to have a larger impact in terms of price reductions in systems where prices are high; if prices are already lowered by an effective price control policy, the additional effects of introducing RP cannot be expected to be as large as it otherwise would be. The same can be assumed for incentives aimed at efficient prescribing or for generic policies: the potential gains of these practices are larger when prices are higher, which is often the case when price controls are absent.

Cost-sharing and RP have a similar effect: they shift part of the drug cost burden onto the consumer. The difference is that under a cost-sharing scheme the patient can not avoid paying, while under a reference pricing system payments can be avoided if the consumer chooses drugs priced at/under the RP. However, when the consumer is not able or willing to shift to a low price product, the two effects will be compounded. RP can be seen as a selective form of cost-sharing that discriminates against price-insensitive consumers. Cost-sharing can act as an incentive for demand, as long as prescribers act as perfect agents and show concern for the financial impacts of their decisions on patients. The impact of cost-sharing will be reduced by an effective generics policy that succeeds in lowering the price of the drugs consumed.

The main role of RP is to replace/substitute the lack of incentives for cost-conscious behaviour on the demand side in an insured market. If the demand for drugs worked under perfect information and were price-sensitive, RP would be unnecessary. Some authors indicate that RP does not generate competition below the RP, but this is exactly what one should theoretically expect, because RP is not supposed to change prescribers' and consumers' goals and values, but to make consumers financially accountable for the prescribing decisions. Since there is no reward for choosing products priced below the RP, it is logical that no one be surprised over the lack of competition in this situation.

RP is closely related to generics policies. Many RP systems restrict RP groups to drugs that have at least one generic version on the market. Competition among generics is the factor expected to lower generics prices and, hence, the RP over time, dragging down originators' prices or else reducing their market share. Generic manufacturers have, however, no incentives to lower prices below the RP, as this is not likely to result in an increase of sales or market share.

Incentives for efficient, cost-conscious prescribing are essential if generic policies are to be successful, especially if the latter are not accompanied by a RP system. In fact, they can be considered an essential demand-side component of a global generics policy.

Pay-back is basically aimed at shifting/sharing the risks of unexpected increases in drug expenditure between the payer/insurer and the suppliers (industry and distribution sector). Pay-back is quite independent from the rest of practices mentioned so far. In fact, its recent introduction is an implicit recognition that the other traditional approaches often do not work. Cost-control systems that rely on international price-comparisons with countries applying a payback system, might be working in a less accurate way.

IV. Conditions for application

The effects of any policy practice depend on a broad set of factors, including the health system's characteristics and global pharmaceutical policies, but also on other more general cultural, social and economic factors that vary from country to country, and sometimes within a given country as well. Therefore, it cannot simply be assumed that effects found in one or several settings, even when they are based on well-designed, valid studies, will hold if applied in different times and settings. Even in the cases when good evidence on the effects of a given policy exists, decision-makers will have to apply technical judgements and assumptions that might not be backed up by any previous empirical evidence.

In the present section we will try to list the main factors to consider when assessing whether policy practices with proven effectiveness in previous applications are likely to work as well in different settings.

One common success factor for all practices is the strength and credibility of the insurer and regulator. Countries with a single insurer covering all or a high percentage of the population and their health care costs (monopsony) are in a good position to either regulate and enforce regulation, negotiate successfully with other parties, appropriately educate and inform key stakeholders (physicians, pharmacists), etc. If the public sector is large enough to impose certain price and reimbursement conditions, these are likely to spread and benefit, to some extent, the private sector as well.

Price control

Direct price control is, in principle, relatively simple to apply but in practice it is quite difficult to apply effectively and makes it harder to avoid unintended effects (e.g. update prices to account for inflation or for changing market conditions).

For off-patent products that have been in the international market for a long time it is relatively easy to find a set of international prices that can be used as a reference for initial pricing in a country where they are being newly introduced.

If the administrative price is determined by a cost-plus approach, the regulator should be able to obtain reliable economic and financial information, particularly on the production costs, including the cost of active ingredients that might be imported from the originator's country, which might require audits on the headquarters' costs. Brazil seems to have used the information of public manufacturers to obtain acceptable estimates on production costs that it uses in price negotiations.

The need to have access to economic and financial information is also a requisite of a profit control mechanism, such as the one in the UK. PPRS is usually assumed to work fairly well, but experts claim that it would be difficult to apply in most settings, not only due to the technical capacity and information management required, but to a more subtle set of factors related to an assumed culture of fair-play in the negotiations between public regulators and industry.

Cost effectiveness-based pricing (based on economic evaluations of new drugs) requires technical capacities and a management culture that might take a few years to develop in countries that do not yet have it.

Direct price control by national regulators in the EU is becoming less effective due to the single market's logic: removal of barriers leads to parallel trade that hurts profits in high price countries if companies allow the same products to be priced lower in other EU countries. Consequently, one should expect cost-containment policies to progressively shift from direct product price control to other policy practices.

Cost-sharing

This can only be a potential tool if the insurer covers a large share of the related expenditure (i.e. pharmaceuticals). It requires a more elaborately organized and administered health system, as well as a strong commitment from its personnel to ensure rigorous enforcement.

Cost-sharing schemes that link the amount paid to individual conditions in order to avoid negative impact on access and equity require a complex information system that records individual data and can produce individual expenditure data and profiles. Introducing or extending cost-sharing might additionally require a strong and legitimated government, and even a multi-party agreement, given the usual opposition from citizens and the political costs that accompany such a measure.

Reference pricing

As in the previous case, a reimbursement-based practice requires and is likely to play a key role in the market if the third-party-payers cover a large share of the pharmaceutical expenditure. Reference pricing also requires a dynamic generics sector that provides the competition required to lower prices – and, as a consequence, the RP - when exclusivity rights expire.

Pay-back

This practice seems quite simple to apply in technical terms, as it only requires the capacity to collect information on sales at either the global or company level.

Incentives for efficient prescribing

This is probably the most difficult practice to implement effectively. Prescribers have traditionally not been held economically responsible for their prescribing decisions. Rather, they are subject to intensive marketing pressure and industry incentives to prescribe - usually newer and increasingly expensive products which often are no safer or more effective than the earlier, less expensive ones. Moreover, the medical profession is quite successful in resisting pressures from their employers to accept rules and guidelines that restrict their freedom to prescribe whatever is supposed more

appropriate for the patients regardless of cost or cost-effectiveness considerations, or to accept remuneration and rewards systems linked to prescribing performance.

Generics policies

Generics policies are considered by many to be a valuable option to ensure adequate accessibility since they lower pharmaceutical prices and contain costs while maintaining a standard quality.

In developing countries generic policies have been identified with weak IPR protection systems but, in fact, generic policies have increasingly become a more sophisticated and essential part of pharmaceutical policy in countries with a strong IPR system and innovative industry, such as the US, UK and Germany.

In countries where IPR are well-established, generics' manufacturers have broad opportunities to develop by taking advantage of existing high-priced products that, at some point in time, will lose their market exclusivity. In that sense, the existence of strong IPR and an innovative pharmaceutical market sets the conditions for generics to develop, in spite of the conflicts often arising between innovators and generics' manufacturers.

In countries with no domestic innovative industry some aspects of generic policies – use and prescription by active ingredient or INN – are opposed both by foreign and local companies alike, since all have grown accustomed to brand marketing-oriented business.

Promoting the use of generics is easy in integrated health systems where patients receive drugs free at the health centres and drug procurement is centralised through competitive tenders. However, in more complex decentralised health systems, and this would include the most developed countries and (increasingly) developing countries as well, increasing the use of generics requires clear and sustained support from the public sector in the form of a global policy that addresses the varying and often conflicting interests of manifold stakeholders throughout the product's whole life cycle: from development, to registration, information and education of consumers, pharmacists and physicians, as well as appropriate economic and financing mechanisms that promote generic use.

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Supply side		
Drug Price	Initial	Negotiated Price
		Price Caps
		Cost-Plus
		Price Comparison (International)
		Price Comparison (Interchangeable medicines)
	Recurrent	Cuts
		Freezes
		Reductions
Total expenditure	Claw Back / Pay Back	
	Price-Volume Agreement	
	Public tendering	
Return on Investment	Economic Evaluation (HTA - Health Technology Assessment)	
Other	Profit control for companies	
	Tax benefits	
	Number of items by prescription	
	Penalties for inadequate professional practices	
Demand Side		
Doctors/Physicians	Educate	Clinical Practices Guidelines/Prescription Guidelines
		Educational Methods (e.g. academic prescribing advisor, computerized decision support, ...)
		Measures backing up rationalization of prescribing
	Steer	Monitoring of prescribing patterns
	Incentivize	Prescription quota
		Financial Incentives
		Maximal pharmaceutical budgets
Pharmacists	Educate	Information Campaigns
	Steer	Generic Substitution (voluntary or mandatory)
		Promotion of parallel trade
	Incentivize	Reductions of margins (also for wholesalers)
		Financial Incentives
		Control Profit Margins
Patients	Educate	Public Health Educational Campaigns
		Information Campaigns
	Steer	Conditional reimbursement
	Incentivize	Copayment (cost-sharing)
		*Co-insurance (%)
		*Flat rate payment (fixed fee)
		*Deductible
Reimbursement	Initial	Reference Pricing (different interchangeability level)
		Positive Lists
		Negative Lists
	Recurrent	Reclassification Rx to OTC
		Reclassification on list

QUESTIONNAIRE ON THE IMPACT ASSESSMENT OF PHARMACEUTICAL POLICY PRACTICES

Informant's data

Country	
Name of informant	
Organisation / Ministry	
Unit	
Function	
Phone	
Email	

Part 1: Pharmaceutical policy practices applied in EU Member States.

Country:

Pharmaceutical Policy	Practice	Within your Member State this practice is (a) currently applied, (b) once applied but discontinued or (c) never applied	Do you have any evidence of the impact which you can share? (Yes/No)	Comments
Supply side				
Product Price Regulation	Initial price decision based on clinical performance			
	Initial price decision based on economic evaluation			
	Initial price decision based on cost of existing treatments			
	Initial price decision based on cost-plus calculations			
	Initial price decision based on international prices			
	Controlled price updates			
	Other (indicate)			
Control of expenditure	Use of discounts/rebates			
	Payback			
	Price-volume agreements			
	Use of price-freezes and cuts			
	Other (indicate)			
Industry regulation	Profit Control			
	Tax benefits			
	Other (indicate)			

Product Reimbursement	Reference Price System			
	Positive Lists			
	Negative Lists			
	Based on economic evaluation			
	Other (indicate)			
Demand side				
Physicians	Clinical Practices Guidelines/ Prescription Guidelines			
	Educational and Information			
	Monitoring of prescribing patterns			
	Prescription quotas			
	Pharmaceutical budgets			
	Financial incentives			
	Other (Indicate)			
Patients	Information education campaigns			
	Cost-sharing			
	Other (Indicate)			
Pharmacists	Generic substitution			
	Financial incentives			
	Claw-Back			
	Other (Indicate)			

Part 2: Impact assessment of selected policy practices

REFERENCE PRICING

Set-up

1. Over which period has reference pricing been used in your country?
2. How do you group the drugs in the RP system?
 - a. Drugs that have the same active ingredient(s) and form(s)
 - b. Drugs that have the same active ingredient(s)
 - c. Medicines chemically slightly different but related
 - d. All medicines treating similar condition
 - e. Others (please explain)
3. Do you use a standard classification (like ATC¹, etc) to group the drugs? (If so, indicate the level of aggregation - ATC1, ATC2...)
4. How do you set the reimbursement level?
 - a. The lowest drug price in the group
 - b. The weighted average price of the group
 - c. The weighted average generic price in the group
 - d. Others (explain)
5. Is reference pricing applied on all medicines or only on some groups of medicines? If only on some groups, can you explain how these are selected?
6. Are there product categories which are excluded from reference pricing? (e.g. on-patent products, highly valued medicines, ...)?
7. What experience did you use to set-up this practice (literature, experts, experience of other countries, ...)?
8. Other comments or particularities that should be known?

Impact

9. Do you evaluate the budgetary impact of this practice? If so, is there a formal monitoring system or evaluation exercise? At which time-interval does this evaluation take place? Please describe briefly
10. What is the budgetary impact of this practice? Can you give some recent data and explanations?
11. Is there any (claimed) impact on access for the patients to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)

¹ PPRI: ATC (Anatomic Therapeutic Chemical Classification System): In this classification system **pharmaceuticals** are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties.

12. Is there any (claimed) impact on reward for innovation to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
13. What are, in your experience the main difficulties to set this system up? Are there key success factors or risks you would recommend other Member States to look at?
14. In general, what is your experience with the success of this practice? Would you do it again? Would you recommend it to other countries?

PAYBACK

Set-up

1. Over which period has payback been used in your country?
2. On which level is the payback system working?
 - a. Per product
 - b. Per group of (therapeutically related) products
 - c. On the sales of a company
 - d. On the entire pharmaceutical budget
 - e. Others. Please explain
3. Is reference pricing applied on all medicines or only on some groups of medicines? If only on some groups, can you explain how these are selected?
4. Are there product categories which are excluded from reference pricing? (e.g. on-patent products, highly valued medicines, ...)?
5. How is the target budget defined (expenditure above which payback is demanded) e.g. in function of last-years budget, growth of GDP, ... ? Please explain
6. Is the entire expenditure above the target budget to be paid back, or only partly? Are there specific rules/calculations for this? Please explain.
7. Which parties need to contribute to the payback? How is the amount to be paid back distributed over these parties? Please explain.
8. Other comments or particularities that should be known?

Impact

9. Do you evaluate the budgetary impact of this practice? If so, is there a formal monitoring system or evaluation exercise? At which time-interval does this evaluation take place? Please describe briefly
10. What is the budgetary impact of this practice? Can you give some recent data and explanations?
11. Is there any (claimed) impact on access for the patients to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
12. Is there any (claimed) impact on reward for innovation to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
13. What are, in your experience the main difficulties to set this system up? Are there key success factors or risks you would recommend other Member States to look at?
14. In general, what is your experience with the success of this practice? Would you do it again? Would you recommend it to other countries?

COST-SHARING

Set-up

1. Do you have any of type of cost sharing in your country? Please explain
2. Are there any criteria of exclusion for some categories of users (for example, pensioners, people with low incomes, etc) or products? Are there *Out-of-pocket maximums*²? Please explain
3. Other comments or particularities that should be known?

Impact

4. Do you evaluate the budgetary impact of this practice? If so, is there a formal monitoring system or evaluation exercise? At which time-interval does this evaluation take place? Please describe briefly
5. What is the budgetary impact of this practice? Can you give some recent data and explanations?
6. Is there any (claimed) impact on access for the patients to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
7. Is there any (claimed) impact on reward for innovation to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
8. What are, in your experience the main difficulties to set this system up? Are there key success factors or risks you would recommend other Member States to look at?
9. In general, what is your experience with the success of this practice? Would you do it again? Would you recommend it to other countries?

² PPRI: Out-of-pocket Maximum: The maximum amount (e.g. a certain percentage of income) that an insured person has to pay for all covered healthcare services for a defined period (often a year),

INCENTIVES FOR GOOD PRESCRIBING PRACTICES

(aimed at maximising effectiveness and minimising risk and cost)

Set-up

1. Do medical doctors get objectives/targets for prescription of medicines? How are these defined? Please explain
2. Are doctors followed-up/monitored on their prescription behaviour? Can you explain how?
3. Do doctors get feedback of their prescription behaviour? How and how regularly?
4. What kind of financial incentives do medical doctors have? (for example, rewards or penalties)?
5. What kind of non-financial incentives do they have (for example, professional recognition, etc)?
6. Can you indicate which type of information, advice, support or supervision doctors get in order to improve prescribing practices
7. Other comments or particularities that should be known?

Impact

8. Do you evaluate the budgetary impact of this practice? If so, is there a formal monitoring system or evaluation exercise? At which time-interval does this evaluation take place? Please describe briefly
9. What is the budgetary impact of this practice? Can you give some recent data and explanations?
10. Is there any (claimed) impact on access for the patients to the medicines covered by this practice? If so, can you list these (mentioning who claims this impact if needed)
11. Is there any (claimed) impact on reward for innovation to the medicines covered by this practice? E.g., is there any evidence of uptake of valuable innovative medicines, ... ?
12. What are, in your experience the main difficulties to set this system up? Are there key success factors or risks you would recommend other Member States to look at?
13. In general, what is your experience with the success of this practice? Would you do it again? Would you recommend it to other countries?

PRICE CONTROL (at manufacturer or import level)

Set-up

1. Are price decisions taken together or independently from reimbursement decisions?
2. Is the price of pharmaceutical products regulated in your country?
 - a. Yes, for all products
 - b. Only for reimbursable products
 - c. Only for locally manufactured products
 - d. There is no (direct) product price regulation
 - e. Others (Please explain)

International Prices

3. Can you list the countries that you use as a reference?
4. What price are you comparing (ex-factory, post-wholesale, retail/pharmacy)
5. Which criteria/formula do you use for setting the price in your country?
 - a. Average price of selected countries
 - b. Minimum price of selected countries
 - c. Maximum price of selected countries
 - d. Others (Please explain)

Cost-Plus

1. Does this apply for all products or only for locally manufactured ones?
2. Which cost do you take into account for your price-calculation?
3. Which `plus` do you add to the cost?
4. Which sources of information are used to define this cost-plus price?

Others

1. Do you use other elements to define prices than clinical performance, economic evaluations, cost of existing treatments, cost-plus or international price comparisons? If so, can you briefly explain?

GENERICS POLICIES

Set-up

1. Do you have a formal (explicit) generic drug policy? Are there specific objectives set (% volume in generics, savings target, ...)? Are these defined within your legislation?
2. Do your administrative procedures are favourable for generics? (e.g. Fast-track registration, lower registration fees, etc)?
3. Do you have specific supply-side mechanisms/rules which guarantee a lower price for generics than for originator products? Can you explain?
4. Are doctors encouraged to prescribe generic medicines? Can you explain how?
5. Are there in your country generic promotion/education/information programs for users, doctors, pharmacists, etc ? Are patients encouraged to request generic medicines? Can you explain how?
6. Do you have generic substitution for pharmacists in your country? Is this mandatory or voluntary? Is a consent from prescribers or patients required?
7. Do pharmacists have a financial incentive for generic substitution? Can you explain how this incentive works (e.g., progressive or regressive margins, fixed fee, ...)
8. Are there any other mechanisms and practices aimed at promoting generics. Please explain

Impact

9. Do you evaluate the budgetary impact of this policy? If so, is there a formal monitoring system or evaluation exercise? At which time-interval does this evaluation take place? Please describe briefly
10. What is the budgetary impact of this policy? Can you give some recent data and explanations? For instance, (a) what is the level of average price discount from branded product 2 years following patent expiry, or (b) what is the average rate of generic penetration 2 years following patent expiry?
11. Is there any (claimed) impact on access for the patients to the medicines covered by this policy? If so, can you list these (mentioning who claims this impact if needed)
12. Is there any (claimed) impact on reward for innovation to the medicines covered by this policy? If so, can you list these (mentioning who claims this impact if needed)
13. What are, in your experience the main difficulties to set this system up? Are there key success factors or risks you would recommend other Member States to look at?

14. In general, what is your experience with the success of this practice? Would you do it again? Would you recommend it to other countries?

“Analysis of differences and commonalities in pricing and reimbursement systems in Europe”

A study funded by DG Enterprise and Industry
of the European Commission

Annex III - Literature Review

June 2007



Escuela Andaluza de Salud Pública
CONSEJERÍA DE SALUD



SPECIFIC STRUCTURED REVIEWS

Index

1	GENERAL TOPICS.....	3
1.1	OBJECTIVE	3
1.1	METHODOLOGICAL TOPICS.....	3
1.2	IDENTIFICATION OF RESEARCH	4
1.1.1	<i>Aim of the search for studies</i>	4
1.1.2	<i>Data sources (Databases and Journals)</i>	4
1.1.3	<i>Search strategy</i>	5
1.3	SELECTION OF STUDIES	5
1.4	STUDY QUALITY ASSESSMENT	5
1.5	DATA EXTRACTION AND ANALYSIS	6
1.6	DATA SYNTHESIS	6
2	SUMMARY OF SEARCH RESULTS.....	7
3	PRICE CONTROL. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW	8
3.1	SEARCH STRATEGY	8
3.2	SEARCH RESULTS	8
3.2.1	<i>Articles selection (Reference List)</i>	8
4	COST-SHARING. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW.....	10
4.1	SEARCH STRATEGY	10
4.2	SEARCH RESULTS.....	10
4.3	ARTICLES SELECTION (REFERENCE LIST).....	11
5	REFERENCE PRICING. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW	13
5.1	SEARCH STRATEGY	13
5.2	SEARCH RESULTS.....	13
5.3	ARTICLES SELECTION (REFERENCE LIST)	13
6	PAYBACK. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW	16
6.1	SEARCH RESULTS.....	16
7	INCENTIVES FOR GOOD PRESCRIBING PRACTICES. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW.	17
7.1	SEARCH STRATEGY	17
7.2	SEARCH RESULTS	17
7.2.1	<i>Articles selection (Reference List)</i>	17
8	GENERIC POLICIES. METHODOLOGY FOR THE SPECIFIC STRUCTURED REVIEW	20
8.1	SEARCH STRATEGY	20
8.2	SEARCH RESULTS.....	20
8.2.1	<i>Articles selection (Reference List)</i>	21

1 General topics

1.1 Objective

The objective of these specific reviews is to assess the impact of the six policy practices selected, according with the three main goals: 1) cost-containment, 2) reward for innovation and 3) access to patients.

The six pharmaceutical practices selected have been:

1. Price control
2. Cost-sharing
3. Reference pricing
4. Payback
5. Incentives for good prescribing practices
6. Generic policies

The purpose of this document is the description of the search methodology used for each of them.

1.1. Methodological topics

For the characteristics of the studied topics, in this case it was not possible to apply with accuracy the methodology established for systematic reviews^a.

In this case a structured review was carried out, because the publications related to the selected practices have different levels of evidence, depending on the degree of implementation and development in different health systems. Some practices are more novel or have a recent implementation with which investigation exists less published (in quality and in quantity) with regard to others that can be more studied. For this reason, there were applied more strict criteria of incorporation / exclusion or more flexes depending on the finds on having applied a strategy of general search for each of 6 practices.

Nevertheless, the main procedures were use to get structured reviews that allow us to obtain reliable conclusions.

The 6 structured reviews were made according to the procedures established by the Centre for Reviews and Dissemination (University of York)^b and the Cochrane Collaboration^c

^a In systematic and structured review a research question is answered across identifying, evaluating and interpreting scientific existing evidence. The structured reviews are not a conventional literature review though they are less strict than the systematic reviews. The structured reviews follow steps that allow reproducing it for other authors though they do not have the aim to derive in a quantitative meta-analysis. They are adapted to explore of a concrete topic with studies published of diverse levels the scientific evidence.

^b Centre for Reviews and Dissemination. Review Methods and Resources. Available from: <http://www.york.ac.uk/inst/crd/crdreview.htm>

^c Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions Available from: <http://www3.interscience.wiley.com/homepages/106568753/handbook.pdf>

According to the CDR stage about conducting the review, the following steps were realized:

1. Identification of research
2. Selection of studies
3. Study quality assessment
4. Data extraction and analysis
5. Data synthesis

The common aspects of the methodology used for the 6 structured reviews are described below.

1.2. Identification of research

1.1.1 Aim of the search for studies

To assess the impact of 6 selected practices (price control, cost-sharing, reference pricing, payback, generic policies and incentives for good prescribing practices) taking into account three main goals: cost-containment, reward for innovation and access to patients.

1.1.2 Data sources (Databases and Journals)

A search for published articles on the price control, cost-sharing, reference pricing, payback, generic policies and incentives for good prescribing practices, such as pricing and reimbursement system and cost containment practice, was carried out.

The consulted databases were:

- § Medline [online via Pubmed]
(<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed>)
- § Web of Knowledge (<http://www.accesowok.fecyt.es/login/>)
- § Ovid (<http://gateway.ovid.com/>)

Also a specific search in specialized journals was done:

- § The European Journal of Health Economics
([http://www.springerlink.com/\(1sspb0jtxlsyx0ylx14bvp45\)/app/home/journal.asp?ref=error=parent&backto=linkingpublicationresults,1:110376,1](http://www.springerlink.com/(1sspb0jtxlsyx0ylx14bvp45)/app/home/journal.asp?ref=error=parent&backto=linkingpublicationresults,1:110376,1))
- § Journal of Health Economics
(<http://www.sciencedirect.com/science/journal/01676296>)
- § Health Policy
(<http://www.sciencedirect.com/science/journal/01688510>)
- § Health Economics
(<http://www3.interscience.wiley.com/cgi-bin/jhome/5749?CRETRY=1&SRETRY=0>)

1.1.3 Search strategy

The search terms, called descriptors^d, were used in order to make a suitable strategy search. Some of these descriptors are available as MeSH terms^e in the dictionary of health terminology (Medical Subject Headings of National Library of Medicine). The key words that were directly related to pharmaceutical policies and that were not MeSH terms were determined.

The descriptors for the 6 search strategies have been determined between the MeSH terms and between accepted key words.

The search strategy was carried out combining all the descriptors using boolean operators within them. Additionally, reviews in the "related articles" links were consulted when they expressly mention evaluation of pharmaceutical policies in Europe.

This step was done according to the search terms adapted for each of the 6 selected practices.

1.3. Selection of studies

The selection was carried out independently by 3 researchers and the differences were solved through consensus.

The first step was to select, after the first search, articles according with the relation between the topic and the title. Once the title fits into the topic, all the abstracts were read.

After that, the selection of the studies was according to:

- § Effects and impact on pharmaceutical policies
- § Methodology, where experimental design, temporal series and cross-sections were foreground.

Due to the time limitation of the study, it has not been a review of all the studies selected. It has been taking into account previous reviews and the main studies have been read

It has been selected, at least, the five more relevant studies (with the best methodology and with more significant results) in most of the practices.

1.4. Study quality assessment

The quality criteria used to assess the studies that fulfilled the inclusion criteria were those established by the researchers as follows:

- § Are the objectives well-defined?

^d A descriptor is an index term used to identify a record in a database.

^e MeSH is the U.S. National Library of Medicine's controlled vocabulary used for indexing articles for MEDLINE/PubMed. MeSH terminology provides a consistent way to retrieve information that may use different terminology for the same concepts.

- § Is the methodology appropriate to the searched objectives?
- § Are the data appropriate to evaluate the impact and the analysed policies?
- § Are the conclusions and recommendations derived logically from the results?

1.5. Data extraction and analysis

The analysis was focused on the following aspects:

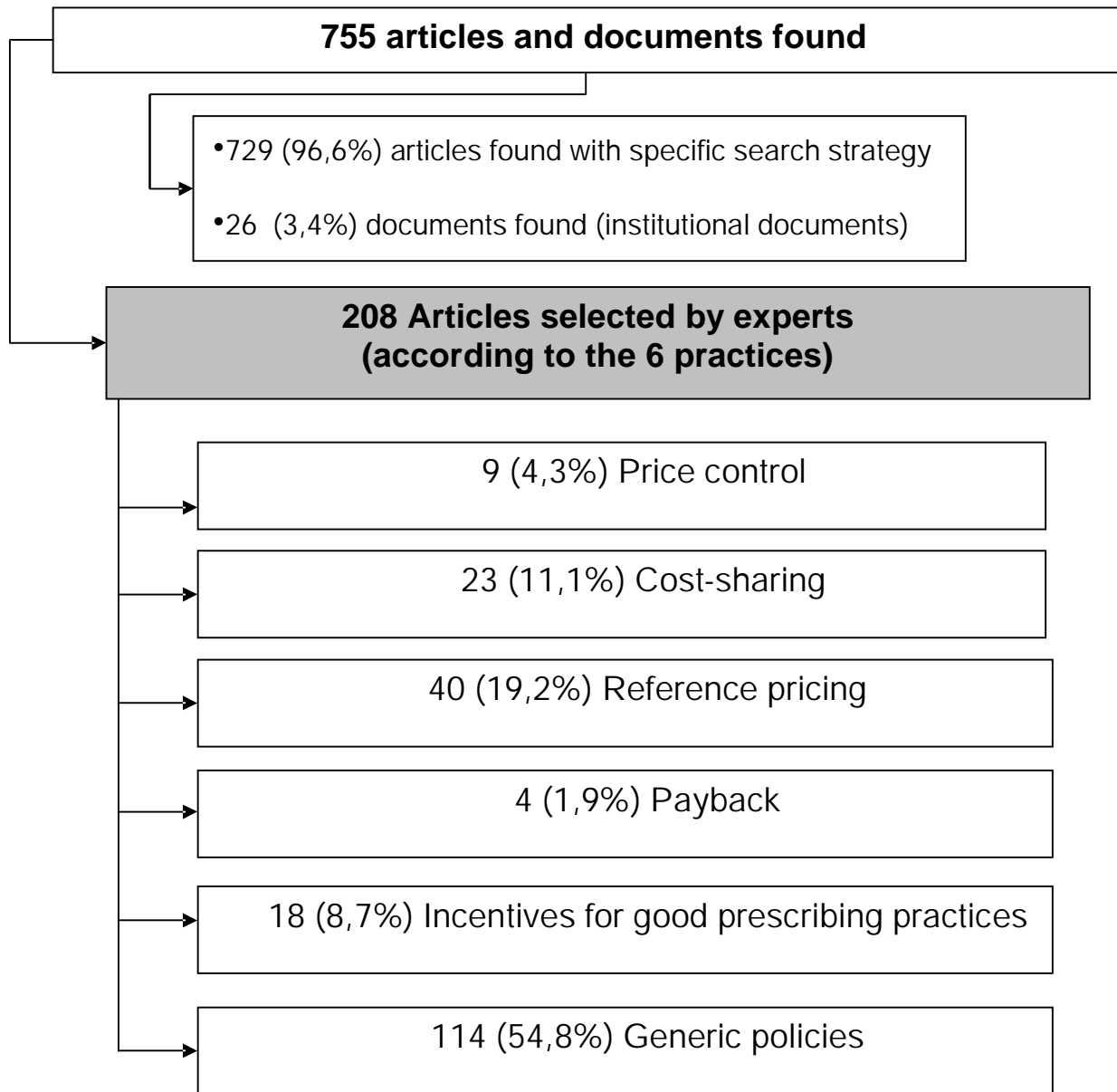
- § Study Reference
- § Objectives
- § Evaluated Policies
- § Evaluated Impact/Effect
- § Applied Methodology
- § Used Data (nature, source, countries, period...)
- § Results, Conclusions and Recommendations

1.6. Data synthesis

As a result, a database has been created using the software Reference Manager, version 10.

The analysis and the synthesis of the studies are reflected in the report of this project.

2 Summary of search results



3 Price control. Methodology for the specific structured review

3.1 Search strategy

For the evaluation of Price Control the most suitable MeSH terms in combination with principal and secondary key words directly related to “price control” were checked.

Principal Key word	Secondary key word	Principal MeSH term	Secondary MeSH term
Price control	§ Pric* and Reimbursement § Pharmaceutical policies	§ Cost Control § Drug Costs	§ Pharmacy Administration § Reimbursement Mechanisms § Pharmaceutical Services /economics § Pharmaceutical Services /legislation & jurisprudence § Pharmaceutical Preparations /economics Legislation, drug /economics § Pharmaceutical Preparations /supply & distribution § Economics, Pharmaceutical

For this specific review, the search strategy follows this sequence integrated boolean operator.

Combination of Principal term			OR	Any secondary term	
Principal Key word	AND	Principal MeSH term		Secondary key word	Secondary MeSH term

3.2 Search Results

3.2.1 Articles selection (Reference List)

The 23 specific references found about “Price Control” are:

1. Abbott TA. The impact of price controls on pharmaceutical R&D investment. *Value in Health* 2004; 7(3):380.
2. Anderson GF, Shea DG, Hussey PS, Keyhani S, Zephyrin L. Doughnut holes and price controls. *Health Aff* 2004; 23(5):396-404.
3. Ault A. Call for tightening of US drug price controls. *Lancet* 1998;

4. Bernstein J. Consequences of price controls. *Orthopedics* 2001; 24(1):14.
5. Borrell JR, Merino-Castello A. [Perverse effects of pharmaceutical regulation in Spain. How much will it affect price competition?]. *Gac Sanit* 2006; 20(Supl.2):41-50.
6. Butler SM. Medicare price controls: The wrong prescription. *Health Aff* 1998; 17(1):72-74.
7. Calfee JE. Pharmaceutical price controls and patient welfare. *Ann Intern Med* 2001; 134(11):1060-1064.
8. Chang S. Ambiguous social welfare effects of price regulation under imperfect competition. *Journal of Economics-Zeitschrift fur Nationalokonomie* 2004; 81(1):53-60.
9. Chen P. Setting price controls while facing variable or uncertain market conditions. *International Economic Review* 1999; 40(3):617-634.
10. Dickson M. The pricing of pharmaceuticals: an international comparison. *Clin Ther* 1992; 14(4):604-610.
11. Hassett KA. Pharmaceutical Price Controls in OECD Countries. 4-8-2006.
12. Jacobzone S. Pharmaceutical policies in OECD countries: reconciling social and industrial goals. 2000. *Labour Market And Social Policy - Occasional Papers No. 40*.
13. Kessler DP. The Effects of Pharmaceutical Price Controls on the Cost and Quality of Medical Care: A Review of the Empirical Literature. 2006.
14. Langwell K. Price controls: on the one hand ... and on the other. *Health Care Financ Rev* 1993; 14(3):5-10.
15. Nakagawa B. More the same than different: worldwide drug policy issues. *J Ambul Care Manage* 2004; 27(3):194-201.
16. Reekie WD. How competition lowers the costs of medicines. *Pharmacoeconomics* 1998; 14 Suppl 1:107-113.
17. Salonen R, Idanpaan-Heikkila J. [The effect of price control on drug expenses in Finland]. *Nord Med* 1975; 90(3):90-91.
18. Santerre REJA. A Cost-Benefit Analysis of Drug Price Controls in the U.S. 2004. AEI-Brooking Joint Center for Regulatory Studies.
19. Slinn J. Price controls or control through prices? Regulating the cost and consumption of prescription pharmaceuticals in the UK, 1948-67. *Business History* 2005; 47(3):352-366.
20. Thomas LG, III. Pricing, regulation, and competitiveness. Lessons for the US from the Japanese pharmaceutical industry. *Pharmacoeconomics* 1994; 6 Suppl 1:67-70.

21. Vernon JA. The relationship between price regulation and pharmaceutical profit margins. *Applied Economics Letters* 2003; 10(8):467-470.
22. Vogel RJ. Pharmaceutical patents and price controls. *Clin Ther* 2002; 24(7):1204-1222.
23. Vogel RJ. Pharmaceutical pricing, price controls, and their effects on pharmaceutical sales and research and development expenditures in the European Union. *Clin Ther* 2004; 26(8):1327-1340.

Of these 23 articles, 9 articles (in italics) of Price Control were selected according to the quality assessment and criteria selection explained.

4 Cost-sharing. Methodology for the specific structured review

4.1 Search strategy

For the evaluation of cost-sharing, the MeSH term Cost-sharing and most suitable MeSH terms in combination with principal and secondary key words directly related were checked.

Principal Key word	Secondary key word	Principal MeSH term	Secondary MeSH term
§ Co-payment § Co-insurance § User and Fee	§ Pharmaceutical policies § Interventions* § Practices*	§ Cost sharing	§ Cost Control* § Drug Costs § Legislation, drug/economics § Economics, Pharmaceutical § Pharmacy Administration § Reimbursement Mechanisms § Pharmaceutical Services/ economics § Pharmaceutical Services/ legislation & jurisprudence

For this specific review, the search strategy follows this sequence integrated boolean operator.

Combination of Principal term			AND	Combination of secondary terms		
Principal MeSH term	OR	Principals Key word		Pharmaceutical terms	OR	Intervention terms*

4.2 Search results

There were checked the titles of 143 references. When the title was not describing directly cost-sharing, the abstract was checked. Of these 143 references, there were selected 23 references according to the quality assessment criteria explained before

4.2.1 Articles selection (Reference List)

The selected studies included: Impact of co-payment; Side-effects of cost-sharing; Co-payment in three-tier formulary; Benefit packages with different co-payment; Impact of removing co-payment to the poor; Comparison of three-tier packages; Impact of cost-sharing regarding patient answers; Impact of co-payment in the Netherlands; and Impact of plans with different cost-sharing arrangements.

1. Aaserud M, Dahlgren AT, Kusters JP, Oxman AD, Ramsay C, Sturm H. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. *Cochrane Database Syst Rev.* 2006 Apr 19;(2):CD005979. Review.
2. Balkrishnan R, Byerly WG, Camacho FT, Shrestha A, Anderson RT. Effect of prescription benefit changes on medical care utilization in a Medicare HMO population. *Am J Manag Care.* 2001 Nov;7(11):1093-100.
3. Chawla M, Ellis RP. The impact of financing and quality changes on health care demand in Niger. *Health Policy Plan.* 2000 Mar;15(1):76-84.
4. Chisadza E, Maponga CC, Nazerali H. User fees and drug pricing policies: a study at Harare Central Hospital, Zimbabwe. *Health Policy Plan.* 1995 Sep;10(3):319-26.
5. Cunningham PJ. Prescription drug access: not just a Medicare problem. *Issue Brief Cent Stud Health Syst Change.* 2002 Apr;(51):1-4.
6. Diop F, Yazbeck A, Bitran R. The impact of alternative cost recovery schemes on access and equity in Niger. *Health Policy Plan.* 1995 Sep;10(3):223-40.
7. Fairman KA, Motheral BR, Henderson RR. Retrospective, long-term follow-up study of the effect of a three-tier prescription drug copayment system on pharmaceutical and other medical utilization and costs. *Clin Ther.* 2003 Dec;25(12):3147-61; discussion 3144-6.
8. Federman AD, Adams AS, Ross-Degnan D, Soumerai SB, Ayanian JZ. Supplemental insurance and use of effective cardiovascular drugs among elderly medicare beneficiaries with coronary heart disease. *JAMA.* 2001 Oct 10;286(14):1732-9.
9. Hassell K, Atella V, Schafheutle EI, Weiss MC, Noyce PR. Cost to the patient or cost to the healthcare system? Which one matters the most for GP prescribing decisions? A UK-Italy comparison. *Eur J Public Health.* 2003 Mar;13(1):18-23.
10. Hill-Smith I. Sharing resources to create a district drug formulary: a countywide controlled trial. *Br J Gen Pract.* 1996 May;46(406):271-75.
11. Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Muriel AC, Frank RG. Impact of 3-tier formularies on drug treatment of attention-deficit/hyperactivity disorder in children. *Arch Gen Psychiatry.* 2005 Apr;62(4):435-41.
12. Huttin C, Andral J. How the reimbursement system may influence physicians' decisions results from focus groups interviews in France. *Health Policy.* 2000 Nov 17;54(2):67-86.

13. Joyce GF, Escarce JJ, Solomon MD, Goldman DP. Employer drug benefit plans and spending on prescription drugs. *JAMA*. 2002 Oct 9;288(14):1733-9. Erratum in: *JAMA* 2002 Nov 20;288(19):2409.
14. Karkee SB, Tamang AL, Gurung YB, Mishra G, Banez-Ockelford J, Saunders P, Rai C. Improving access to drugs by poor households through a cost sharing drug scheme: a wealth ranking approach. *Nepal Med Coll J*. 2005 Jun;7(1):26-31.
15. Liu SZ, Romeis JC. Changes in drug utilization following the outpatient prescription drug cost-sharing program--evidence from Taiwan's elderly. *Health Policy*. 2004 Jun;68(3):277-87.
16. Lurk JT, DeJong DJ, Woods TM, Knell ME, Carroll CA. Effects of changes in patient cost sharing and drug sample policies on prescription drug costs and utilization in a safety-net-provider setting. *Am J Health Syst Pharm*. 2004 Feb 1;61(3):267-72.
17. Motheral B, Fairman KA. Effect of a three-tier prescription copay on pharmaceutical and other medical utilization. *Med Care*. 2001 Dec;39(12):1293-304.
18. Motheral BR, Henderson R. The effect of a copay increase on pharmaceutical utilization, expenditures, and treatment continuation. *Am J Manag Care*. 1999 Nov;5(11):1383-94.
19. Schafheutle EI, Hassell K, Noyce PR, Weiss MC. Access to medicines: cost as an influence on the views and behaviour of patients. *Health Soc Care Community*. 2002 May;10(3):187-95.
20. Starmans B, Janssen R, Schepers M, Verkooijen M. The effect of a patient charge and a prescription regulation on the use of antihypertension drugs in Limburg, The Netherlands. *Health Policy*. 1994 Jan 15;26(3):191-206. Review.
21. Tamblyn R, Laprise R, Hanley JA, Abrahamowicz M, Scott S, Mayo N, Hurley J, Grad R, Latimer E, Perreault R, McLeod P, Huang A, Laroche P, Mallet L. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001 Jan 24-31;285(4):421-9.
22. Tseng CW, Brook RH, Keeler E, Mangione CM. Impact of an annual dollar limit or "cap" on prescription drug benefits for Medicare patients. *JAMA*. 2003 Jul 9;290(2):222-7.
23. Wouters A. Improving quality through cost recovery in Niger. *Health Policy Plan*. 1995 Sep;10(3):257-70. PMID: 10151843

Of these 23 articles, only 6 selected studies (in italics) contained important aspects of cost-sharing.

5 Reference pricing. Methodology for the specific structured review

5.1 Search strategy

For the assess of reference pricing, most suitable MeSH terms in combination with principal and secondary key words directly related were checked.

Principal Key word	Secondary key word	Principal related MeSH term	Secondary MeSH term
§ Reference pricing	§ Pharmaceutical policies § Interventions* § Practices*	Not found	§ Cost Control* § Drug Costs § Legislation, drug/economics § Economics, Pharmaceutical § Pharmacy Administration § Reimbursement Mechanisms Pharmaceutical Services/ economics § Pharmaceutical Services/ legislation & jurisprudence

For this specific review, the search strategy follows this sequence integrated boolean operator.

Combination of Principal term	AND	Combination of secondary terms		
Principal Key word		Pharmaceutical terms	OR	Intervention terms*

5.2 Search results

There were checked the titles of 183 references. When the title was not describing directly reference pricing, the abstract was checked. Of these 183 references, there were selected 40 references of which the complete articles were looked.

5.3 Articles selection (Reference List)

40 articles selected were selected according to the quality assessment criteria. They are:

1. Aaserud M, Dahlgren AT, Kusters JP, Oxman AD, Ramsay C, Sturm H. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. *Cochrane Database Syst Rev.* 2006 Apr 19;(2):CD005979. Review.

2. Abel-Smith B, Mossialos E. Cost containment and health care reform: a study of the European Union. *Health Policy*. 1994 May;28(2):89-132.
3. Ausejo Segura M. [The new reference prices: an opportunity for efficient management of medication]. *Aten Primaria*. 2005 Feb 15;35(2):64-6. Spanish.
4. Bourgault C, Elstein E, Le Lorier J, Suissa S. Reference-based pricing of prescription drugs: exploring the equivalence of angiotensin-converting-enzyme inhibitors. *CMAJ*. 1999 Aug 10;161(3):255-60.
5. Danzon PM, Ketcham JD. Reference pricing of pharmaceuticals for Medicare: evidence from Germany, The Netherlands, and New Zealand. *Front Health Policy Res*. 2004;7:1-54. Review.
6. Dickson M, Redwood H. Pharmaceutical reference prices. How do they work in practice? *Pharmacoeconomics*. 1998 Nov;14(5):471-9.
7. Duetz MS, Schneeweiss S, Maclure M, Abel T, Glynn RJ, Soumerai SB. Physician gender and changes in drug prescribing after the implementation of reference pricing in British Columbia. *Clin Ther*. 2003 Jan;25(1):273-84.
8. Gibson TB, Ozminkowski RJ, Goetzel RZ. The effects of prescription drug cost sharing: a review of the evidence. *Am J Manag Care*. 2005 Nov;11(11):730-40. Review.
9. Giraud A. [Opposable medical references in perspective] *Therapie*. 1996 May-Jun;51(3):237-9. French.
10. Giuliani G, Selke G, Garattini L. The German experience in reference pricing. *Health Policy*. 1998 Apr;44(1):73-85.
11. Hazlet TK, Blough DK. Health services utilization with reference drug pricing of histamine(2) receptor antagonists in British Columbia elderly. *Med Care*. 2002 Aug;40(8):640-9.
12. Ioannides-Demos LL, Ibrahim JE, McNeil JJ. Reference-based pricing schemes: effect on pharmaceutical expenditure, resource utilisation and health outcomes. *Pharmacoeconomics*. 2002;20(9):577-91. Review.
13. Jonsson B. Pricing and reimbursement of pharmaceuticals in Sweden. *Pharmacoeconomics*. 1994;6 Suppl 1:51-60.
14. Kanavos P. Financing pharmaceuticals in transition economies. *Croat Med J*. 1999 Jun;40(2):244-59.
15. Kerpel-Fronius S. [Medical problems associated with the national reference pricing system in Hungary] *Orv Hetil*. 2004 Apr 25;145(17):913-8. Hungarian.
16. King DR, Kanavos P. Encouraging the use of generic medicines: implications for transition economies. *Croat Med J*. 2002 Aug;43(4):462-9. Review.
17. Koopmanschap MA, Rutten FF. The drug budget silo mentality: the Dutch case. *Value Health*. 2003 Jul-Aug;6 Suppl 1:S46-51.
18. Lofgren H. Generic drugs: international trends and policy developments in Australia. *Aust Health Rev*. 2004;27(1):39-48.

19. Lopez-Casasnovas G, Puig-Junoy J. Review of the literature on reference pricing. *Health Policy*. 2000 Nov 17;54(2):87-123. Review.
20. Marshall JK, Grootendorst PV, O'Brien BJ, Dolovich LR, Holbrook AM, Levy AR. Impact of reference-based pricing for histamine-2 receptor antagonists and restricted access for proton pump inhibitors in British Columbia. *CMAJ*. 2002 Jun 25;166(13):1655-62.
21. McLaughlin PR. Reference based pricing for provincial drug benefit programs. *Can J Cardiol*. 1996 Jan;12(1):16, 25-6.
22. Menon D. Pharmaceutical cost control in Canada: does it work? *Health Aff (Millwood)*. 2001 May-Jun;20(3):92-103.
23. Mrazek MF. Comparative approaches to pharmaceutical price regulation in the European Union. *Croat Med J*. 2002 Aug;43(4):453-61. Review.
24. Puig-Junoy J. What is required to evaluate the impact of pharmaceutical reference pricing? *Appl Health Econ Health Policy*. 2005;4(2):87-98.
25. Ranwella S. Sri Lankan students campaign for rational medicine: the story of SIRHA. *Essent Drugs Monit*. 1993;(16):10.
26. Rigter H. Recent public policies in The Netherlands to control pharmaceutical pricing and reimbursement. *Pharmacoeconomics*. 1994;6 Suppl 1:15-21.
27. Rocchi F, Addis A, Martini N; Working Group of the National Drug Utilisation Monitoring Centre (OsMed). Current national initiatives about drug policies and cost control in Europe: the Italy example. *J Ambul Care Manage*. 2004 Apr-Jun;27(2):127-31.
28. Rothberg AD, Blignault J, Serfontein CB, Valodia B, Eekhout S, Pels LM. Experience of a medicines reference-pricing model. *S Afr Med J*. 2004 Mar;94(3):183-8.
29. Schneeweiss S, Soumerai SB, Maclure M, Dormuth C, Walker AM, Glynn RJ. Clinical and economic consequences of reference pricing for dihydropyridine calcium channel blockers. *Clin Pharmacol Ther*. 2003 Oct;74(4):388-400. (7)
30. Schneeweiss S, Maclure M, Dormuth C, Avorn J. Pharmaceutical cost containment with reference-based pricing: time for refinements. *CMAJ*. 2002 Nov 26;167(11):1250-1.
31. Schneeweiss S, Maclure M, Soumerai SB, Walker AM, Glynn RJ. Quasi-experimental longitudinal designs to evaluate drug benefit policy changes with low policy compliance. *J Clin Epidemiol*. 2002 Aug;55(8):833-41. (8)
32. Schneeweiss S, Soumerai SB, Maclure M. Reference drug pricing. *CMAJ*. 2002 Jul 23;167(2):126-7; author reply 127-8.
33. Schoffski O. Consequences of implementing a drug budget for office-based physicians in Germany. *Pharmacoeconomics*. 1996;10 Suppl 2:37-47. Review.
34. Segu Tolsa JL, Zara Yahn C. [Impact and applicability of the system of reference prices] *Aten Primaria*. 2001 Sep 30;28(5):340-8. Spanish.

35. Simoens S, De Bruyn K, Bogaert M, Laekeman G. Pharmaceutical policy regarding generic drugs in Belgium. *Pharmacoeconomics*. 2005;23(8):755-66. (154)
36. Stargardt T, Schreyogg J, Busse R. [Pharmaceutical reference pricing in Germany: definition of therapeutic groups, price setting through regression procedure and effects] *Gesundheitswesen*. 2005 Jul;67(7):468-77. German.
37. Towse A. The efficient use of pharmaceuticals: does Europe have any lessons for a Medicare drug benefit? *Health Aff (Millwood)*. 2003 May-Jun;22(3):42-5.
38. Ulrich V, Wille E. Healthcare reform and expenditure on drugs. The German situation. *Pharmacoeconomics*. 1996;10 Suppl 2:81-8.
39. von der Schulenburg JM. Management of cost and utilization of pharmaceuticals in Germany. *Health Policy*. 1997 Sep;41 Suppl:S45-53.
40. Woollard RF. Opportunity lost: a frontline view of reference-based pricing. *CMAJ*. 1996 Apr 15;154(8):1185-8.

Of these 40 articles, 10 selected studies (in italics) were read in depth and included in the study. For this practice a Cochrane Review (Aaserud 2006) was found.

6 Payback. Methodology for the specific structured review

Due to is a relatively recent mechanism, it doesn't found specific articles on the topic.

6.1 Search results.

Some article and institutional literature has treated the matter. However, in most of the cases they provide only economic data.

1. *European Pharmaceutical Pricing and Reimbursement Strategies*. National Centre for Pharmacoeconomics. March 2005
2. *IMS Pharma Pricing & Reimbursement (2005 and 2006)*
3. Le Pen C. The drug budget silo mentality: the French case. *Value Health* 2003; 6 Suppl 1:S10-S19
4. *Jacobzone S. Pharmaceutical policies in OECD countries: Reconciling social and industrial goals. Labour market and social policy - occasional papers No. 40. OECD 2000*

Payback is relatively new and not a common-established practice; therefore evidence on its impact is scarce or lacking

7 Incentives for good prescribing practices. Methodology for the specific structured review.

7.1 Search strategy

A search for articles on the Incentives for good prescribing practices, as a pricing and reimbursement system and cost containment practice" published was carried out. For the evaluation of incentives for good prescribing practices most suitable MeSH (Medical Subject Headings) terms were checked in combination with principal and secondary key words directly related to "prescribing behaviour or prescribing practices"

Principal Key word	Secondary key word	Principal MeSH term	Secondary MeSH term
Prescribing behaviour	§ Pric* and Reimbursement § Pharmaceutical policies	§ Cost Control § Drug Costs § Legislation, Drug/economics § Pharmaceutical Preparations/supply & distribution § Economics, Pharmaceutical	§ Pharmacy Administration § Reimbursement Mechanisms § Pharmaceutical Services /economics § Pharmaceutical Services /legislation & jurisprudence § Pharmaceutical preparations/economics

For these specific review, the search strategy follows this sequence integrated Boolean operator.

Combination of Principal term		OR	Any secondary term	
Principal Key word	AND		Principal MeSH term	Secondary key word

7.2 Search Results

7.2.1 Articles selection (Reference List)

The 31 articles selected are:

1. Akkerman AE, Kuyvenhoven MM, van der Wouden JC, Verheij TJ. Prescribing antibiotics for respiratory tract infections by GPs: management and prescriber characteristics. *Br J Gen Pract* 2005; 55(511):114-118.
2. Anderson GM, Lexchin J. Strategies for improving prescribing practice. *CMAJ* 1996; 154(7):1013-1017.
3. Anton C, Nightingale PG, Adu D, Lipkin G, Ferner RE. Improving prescribing using a rule based prescribing system. *Qual Saf Health Care* 2004; 13(3):186-190.

4. Armstrong D, Reyburn H, Jones R. A study of general practitioners' reasons for changing their prescribing behaviour. *BMJ* 1996; 312(7036):949-952.
5. Ashworth M, Lea R, Gray H, Rowlands G, Gravelle H, Majeed A. How are primary care organizations using financial incentives to influence prescribing? *J Public Health* 2004; 26(1):48-51.
6. Ashworth M, Lea R, Gray H, Gravelle H, Majeed A. The development of prescribing incentive schemes in primary care: a longitudinal survey. *Br J Gen Pract* 2003; 53(491):468-470.
7. Bateman DN, Campbell M, Donaldson LJ, Roberts SJ, Smith JM. A prescribing incentive scheme for non-fundholding general practices: an observational study. *BMJ* 1996; 313(7056):535-538.
8. Carthy P, Harvey I, Brawn R, Watkins C. A study of factors associated with cost and variation in prescribing among GPs. *Fam Pract* 2000; 1(17):36-41.
9. Chaix-Couturier C, Durand-Zaleski I, Jolly D, Durieux P. Effects of financial incentives on medical practice: results from a systematic review of the literature and methodological issues. *Int J Qual Health Care* 2000; 12(2):133-142.
10. Cockburn J, Pit S. Prescribing behaviour in clinical practice: patients' expectations and doctors' perceptions of patients' expectations--a questionnaire study. *BMJ* 1997; 315(7105):520-523.
11. Davis DA, Thomson MA, Oxman AD, Haynes RB. Changing physician performance. A systematic review of the effect of continuing medical education strategies. *JAMA* 1995; 274(9):700-705.
12. Denig P, Witteman CLM, Schouten HW. Scope and nature of prescribing decisions made by general practitioners. *Qual Saf Health Care* 2002; 11(2).
13. Dormuth CR, Maclure M, Bassett K, Jauca C, Whiteside C, Wright JM. Effect of periodic letters on evidence-based drug therapy on prescribing behaviour: a randomized trial. *CMAJ* 2004; 171(9):1057-1061.
14. Galán HS, Delgado Marroquín MT, Altisent TR. Análisis de la relación entre el médico de atención primaria y la industria farmacéutica. [Analysis of the relationship between primary care doctors and the pharmaceutical industry]. *Aten Primaria* 2004; 34(5):231-237.
15. Gill PS, Makela M, Vermeulen KM, Freemantle N, Ryan G, Bond C et al. Changing doctor prescribing behaviour. *Pharm World Sci* 1999; 21(4):158-167.
16. Gill PS, Freemantle N, Bero L, Haaijer-Ruskamp F, Markela M, Barjesteh KP. GPs' prescribing behaviour may be affected by drug promotion. *BMJ* 1996; 313(7053):367.
17. Gómez Martínez ME, Ruiz Romero JA, Martínez Olmos J. Políticas de uso racional del medicamento en Europa. *Revista de Administración Sanitaria* 1999; 3(9).

18. Gray J. Changing physician prescribing behaviour. *Can J Clin Pharmacol* 2006; 13(1):81-84.
19. Helin-Salmivaara A, Huupponen R, Klaukka T, Hoppu K. Focusing on changing clinical practice to enhance rational prescribing--collaboration and networking enable comprehensive approaches. *Health Policy* 2003; 66(1):1-10.
20. Henriksen K, Hansen EH. The threatened self: general practitioners' self-perception in relation to prescribing medicine. *Soc Sci Med* 2004; 59(1):47-55.
21. Jacoby A, Smith M, Eccles M. A qualitative study to explore influences on general practitioners' decisions to prescribe new drugs. *Br J Gen Pract* 2003; 53(487):120-125.
22. Jaye C, Tilyard M. A qualitative comparative investigation of variation in general practitioners' prescribing patterns. *Br J Gen Pract* 2002; 52(478).
23. Lagerlov P, Loeb M, Andrew M, Hjortdahl P. Improving doctors' prescribing behaviour through reflection on guidelines and prescription feedback: a randomised controlled study. *Qual Health Care* 2000; 9(3):159-165.
24. Laing R, Hogerzeil H, Ross-Degnan D. Ten recommendations to improve use of medicines in developing countries. *Health Policy Plan* 2001; 16(1):13-20.
25. Levine MA, Pradhan A. Can the health care system buy better antibiotic prescribing behaviour? *CMAJ* 1999; 160(7):1023-1024.
26. Lexchin J. Interactions between physicians and the pharmaceutical industry: what does the literature say? *CMAJ* 1993; 149(10):1401-1407.
27. Martens J, Winkens R, van der Weijden T, de Bruyn D, Severens J. Does a joint development and dissemination of multidisciplinary guidelines improve prescribing behaviour: a pre/post study with concurrent control group and a randomised trial. *BMC Health Services Research* 2006; 6(1):145.
28. Soumerai SB, McLaughlin TJ, Avorn J. Improving drug prescribing in primary care: a critical analysis of the experimental literature. *Milbank Q* 1989; 67(2):268-317.
29. Walton RT, Harvey E, Dovey S, Freemantle N. Computerised advice on drug dosage to improve prescribing practice. *Cochrane Database Syst Rev* 2001;(1):CD002894.
30. Wessling A, Boethius G, Sjoqvist F. Prescription monitoring of drug dosages in the county of Jamtland and Sweden as a whole in 1976, 1982 and 1985. *Eur J Clin Pharmacol* 1990; 38(4):329-334.
31. Windmeijer F, de Laat E, Douven R, Mot E. Pharmaceutical promotion and GP prescription behaviour. *Health Economics* 2006; 15(1):5-18.

Of these 31 articles, 18 (in italics) was selected according to the quality assessment criteria for incentives for good prescribing practice

8 Generics Policies. Methodology for the specific structured review

8.1 Search strategy

For the evaluation of generic policies, as a pricing and reimbursement system and cost containment practice, the MeSH term Drugs, Generic and Health policy are associated with most suitable MeSH terms. This combination, with principal and secondary key words directly related, was checked.

Principals Key words	Secondary key word	Principal MeSH term	Secondary MeSH term
§ Generic Pharmaceutical Expenditure § Generic Products § Generic Patent § Generic (Patent Expiry) § Generic Penetration § Generics Incentive § Generics Prescribing § Generics Pharmacies § Generics Registration § Generics Policies § Generics Payment § Generics Substitution	§ Pharmaceutical policies § Interventions* § Practices*	§ Drugs, Generic § Health policy	§ Cost Control* § Drug Costs § Legislation, drug/economics § Economics, Pharmaceutical § Pharmacy Administration § Reimbursement Mechanisms § Pharmaceutical Services/economics § Pharmaceutical Services/legislation & jurisprudence

For this specific review, the search strategy follows this sequence integrated boolean operator.

Combination of Principal term			AND	Combination of secondary terms		
Principal MeSH term	OR	Principals Key word		Pharmaceutical terms	OR	Intervention terms*

8.2 Search results

There were checked the titles of 339 references. After applying the search strategy, 302 references were obtained. In addition, included 37 references checking the related links suggested by PUBMED. When the title was not describing directly generics policies, the abstract was checked.

Of these 339 references, there were selected 114 references of which the abstract were read. Of this 114 abstracts, were selected 20 complete articles for this review.

8.2.1 Articles selection (Reference List)

The 20 selected studies included are:

1. Andersson K, Bergstrom G, Petzold MG, Carlsten A. Impact of a generic substitution reform on patients' and society's expenditure for pharmaceuticals. *Health Policy*. 2006 Aug 29;
2. Andersson K, Sonesson C, Petzold M, Carlsten A, Lonnroth K. What are the obstacles to generic substitution? An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden. *Pharmacoepidemiol Drug Saf*. 2005 May;14(5):341-8.
3. Borrell JR, Merino-Castello A. [Perverse effects of pharmaceutical regulation in Spain. How much will it affect price competition?] *Gac Sanit*. 2006 Apr;20(Supl.2):41-50. Spanish.
4. Christian-Herman J, Emons M, George D. Effects of generic-only drug coverage in a Medicare HMO. *Health Aff (Millwood)*. 2004 Jul-Dec;Suppl Web Exclusives:W4-455-68.
5. Garattini L, Tediosi F. A comparative analysis of generics markets in five European countries. *Health Policy*. 2000 Apr;51(3):149-62.
6. Haas JS, Phillips KA, Gerstenberger EP, Seger AC. Potential savings from substituting generic drugs for brand-name drugs: medical expenditure panel survey, 1997-2000. *Ann Intern Med*. 2005 Jun 7;142(11):891-7. Summary for patients in: *Ann Intern Med*. 2005 Jun 7;142(11):130.
7. Joyce GF, Escarce JJ, Solomon MD, Goldman DP. Employer drug benefit plans and spending on prescription drugs. *JAMA*. 2002 Oct 9;288(14):1733-9. Erratum in: *JAMA* 2002 Nov 20;288(19):2409.
8. Kaplan WA, Laing R. Paying for pharmaceutical registration in developing countries. *Health Policy Plan*. 2003 Sep;18(3):237-48.
9. King DR, Kanavos P. Encouraging the use of generic medicines: implications for transition economies. *Croat Med J*. 2002 Aug;43(4):462-9. Review.
10. Klok RM, Boersma C, Oosterhuis I, Visser ST, de Jong-van den Berg LT, Postma MJ. Switch patterns before and after patent expiry of omeprazole: a case study in The Netherlands. *Aliment Pharmacol Ther*. 2006 Jun 1;23(11):1595-600.
11. Lee YC, Yang MC, Huang YT, Liu CH, Chen SB. Impacts of cost containment strategies on pharmaceutical expenditures of the National Health Insurance in Taiwan, 1996-2003. *Pharmacoeconomics*. 2006;24(9):891-902.
12. Lexchin J. The effect of generic competition on the price of brand-name drugs. *Health Policy*. 2004 Apr;68(1):47-54. (184)
13. McManus P, Birkett DJ, Dudley J, Stevens A. Impact of the Minimum Pricing Policy and introduction of brand (generic) substitution into the Pharmaceutical

- Benefits Scheme in Australia. *Pharmacoepidemiol Drug Saf.* 2001 Jun-Jul;10(4):295-300.
14. Rothberg AD, Blignault J, Serfontein CB, Valodia B, Eekhout S, Pels LM. Experience of a medicines reference-pricing model. *S Afr Med J.* 2004 Mar;94(3):183-8.
 15. Sagardui-Villamor JK, Lacalle Rodriguez-Labajo M, Casado-Buendia S. [Substitution of generic for brand medicines in primary care. Factors associated to refuse the change] *Aten Primaria.* 2005 Nov 30;36(9):489-93. Spanish.
 16. Simoens S, De Bruyn K, Bogaert M, Laekeman G. Pharmaceutical policy regarding generic drugs in Belgium. *Pharmacoeconomics.* 2005;23(8):755-66.
 17. Tilson L, Bennett K, Barry M. The potential impact of implementing a system of generic substitution on the community drug schemes in Ireland. *Eur J Health Econ.* 2005 Sep;6(3):267-73.
 18. Tilson L, McGowan B, Ryan M, Barry M. Generic drug utilisation on the General Medical Services (GMS) scheme in 2001. *Ir Med J.* 2003 Jun;96(6):176-9.
 19. Tseng CW, Brook RH, Keeler E, Steers WN, Waitzfelder BE, Mangione CM. Effect of generic-only drug benefits on seniors' medication use and financial burden. *Am J Manag Care.* 2006 Sep;12(9):525-32.
 20. Vieira FS, Zucchi P. [Price differences between generic and innovator medicines in Brazil] *Rev Saude Publica.* 2006 Jun;40(3):444-9. Epub 2006 Jun 23. Portuguese.

Of these 20 articles, the 7 marked articles (in italics) represent important aspects of generics policies.