Healthcare/Pharmaceutical Spending
and
Pharmaceutical Reimbursement Policy in Turkey

Pharmaceutical Reimbursement Policy in Turkey

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FOREWORD

The main objective of the healthcare system is to improve the health status of the Turkish community. In order to achieve this, it is necessary to ensure equity, increase productivity, improve the quality of services provided and guarantee patient satisfaction, as well as ensure the continuity of healthcare service provision. For this purpose, there is always a need for evidence based information so as to use available sources effectively and efficiently to attain improved healthcare outcomes.

The Turkish people have waited for several years for equitable and improved access to quality health care services. Within this context, the government's Transformation in Health Programme is a momentous policy initiative and is expected to set things in motion in the desired direction of sickness fund consolidation, improved access and equity. It is obvious that all stakeholders in this sector should contribute to this process through constructive dialogue and evidence-based study. Non-governmental organizations also have an important role to play in this issue.

Within this context, the New Hope in Health Foundation (SUVAK) has conducted a comprehensive study on "Pharmaceutical Reimbursement Policy in Turkey" with the participation of and contribution from national and international experts. This study analyzes the pharmaceutical policy environment from a Turkish and international perspective and proposes pharmaceutical reimbursement policy reform options in Turkey. Its objective is to contribute to the health care policy determination process by expanding the available evidence base and provide scientifically documented analysis. We hope that this study will offer a toolkit for policy makers and will contribute to the reform discussions currently under way in Turkey.

I would like to gratefully acknowledge the assistance of senior government officials in providing their time and their technical support and expertise in every stage of this study.

In this study, Prof. Dr. Patricia Danzon has been the Principal Technical Coordinator; Prof. Dr. Mehmet Tokat and Prof. Dr. Mehtap Tatar have been the members of the Review Committee. Prof. Dr. Peter Berman has contributed significantly in different stages of the study. I would like to express my sincere thanks to all of them.

I would also like to thank the valuable experts Assoc. Prof. Dr. Panos Kanavos, Prof. Dr. İsmail Üstel, and Dr. Joan Costa-Font for all their efforts in authoring a study which is believed to be an important reference for those who are interested in health and drug policies.

Prof. Dr. A. Murat Tuncer
Chairman of the Board
New Hope in Health Foundation (SUVAK)

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Panos Kanavos, İsmail Üstel, Joan Costa-Font

September 2005

TABLE OF CONTENTS

TABLES

FIGURES

BOXES

The appendices of this report can be reached from the SUVAK web site (www.suvak.org.tr):

Appendix 1. Summary of Drug Policy Measures in Selected OECD Countries
Appendix 2. Data Sources and Databases
Appendix 3. Guideline for Economic Evaluation (Pharmacoeconomy)

ABBREVIATIONS

AFFSAPS:	French Medicines Regulatory Agency
ADR:	Adverse Drug Reaction
ATC:	Anatomical Therapeutic Classification
BIG:	Budget Implementation Guidelines (Turkey)
CCOHTA:	Canadian Coordinating Office for Health Technology Assessment
CE:	Cost Effectiveness
CEPS:	Comite Economique des Produits de Sante (France)
CPP:	Characteristics of Pharmaceutical Product
DDD:	Defined Daily Dose
DTC:	Direct-To-Consumer
DUR:	Drug Utilisation Review
EMEA:	European Medicines Evaluation Agency
EU:	European Union
FDA:	Food and Drug Administration
GAO:	General Accounting Office (USA)
GCP:	Good Clinical Practice
GDP:	Gross Domestic Product
GDPP:	General Directorate of Pharmaceuticals and Pharmacies (Turkey)
GDRP:	Good Drug Reimbursement Practice
GHI	General Health Insurance
GMP:	Good Manufacturing Practice
GPRD:	General Practice Research Database (UK)
HIT:	Health in Transition
HTA:	Health Technology Assessment
IMSR:	Improvement in Medical Service Rendered (France)
IPRP:	Intellectual Property Rights Protection
INN:	International Non-proprietary Name
LPD:	Local Product Documents
MHRA:	Medicines and Healthcare Products Regulatory Agency (UK)
MoF:	Ministry of Finance
MoH:	Ministry of Health
MoLSS:	Ministry of Labour and Social Security (Turkey)
NICE:	National Institute for Clinical Excellence (UK)
NPC:	National Prescribing Centre (UK)
OOP:	Out-Of-Pocket
OTC:	Over the Counter
PCT:	Primary Care Trust (UK)
PE:	Pharmacoeconomics
PHC:	Public Health Care
POM:	Prescription-Only-Medicine
PPA:	Prescription Pricing Authority (UK)
PPP:	Purchasing Power Parity
PPRS:	Pharmaceutical Price Regulation Scheme (UK)
RMO:	References Medicales Opposables (Medical References – France)
QALY:	Quality-Adjusted Life Year
SPC:	Supplementary Protection Certificate
SSI:	Social Security Institution (Turkey)
SSK:	Social Insurance Organisation (Turkey)
TADMER:	Turkish Centre for Monitoring and Evaluation of Adverse Drug Reactions
TMA:	Turkish Medical Association
TUFAM:	Turkish Pharmacovigilance Centre
WHO:	World Health Organisation

EXECUTIVE SUMMARY

1. **Objectives.** The objectives of this study are to (a) review pharmaceutical financing/reimbursement policies in Turkey and other comparator countries with reference to access to medicines, cost of medicines to individuals and public payors, and intellectual property rights and identify problems and caveats; and (b) to describe and discuss cost containment measures and assess their outcomes in relation to policy goals and their applicability in Turkey. By drawing on the above, this study provides recommendations for a sound and sustainable pharmaceutical financing/ reimbursement policy in Turkey.
2. **Methods**. The analysis in this study was based on both primary sources (interviews and meetings with policy-makers and stakeholders) as well as secondary sources (peer review articles and papers, government reports, other published and unpublished material, including official statistics and IMS data sources).
3. **The Turkish pricing and reimbursement system.** The caveats in the Turkish drug reimbursement system include among others: (i) a centralized but fragmented system, although current reform initiatives aim at reducing fragmentation. Arguably, health care reform and the introduction of a generalised health insurance cover will address this problem in the medium- to long-term, whereas in the short-term (significant) costs of adjustment may be expected; (ii) one of the major bottlenecks is the insufficiency of the human resources profile in some fields such as health/pharmacoeconomics (iii) a relative deficiency in strategic priority-setting at macro level; (iv) the present underlying philosophy of the drug reimbursement system focuses on minimizing drug expenditure rather than promoting cost-effectiveness; (v) the roles and responsibilities of the drug reimbursement decision bodies could benefit from better definition; (vi) the assumption that drug reimbursement decisions are based on evidence, whether clinical or cost-effectiveness, is rather patchy; (vii) the drug reimbursement criteria are not sensitive to innovative drugs; (viii) the drug reimbursement system does not take into account the optimization of public health needs and the pharmaceutical sector strategic expectations; (ix) the clinical guidelines and clinical algorithms do not have any enforcing power at all. In fact, enforcement of legislation appears to be a more generalised problem within the context of health policy in Turkey; (x) the generic (or internal) reference pricing system is far from being dynamic and flexible enough to satisfy the needs of the drug reimbursement stakeholders and may be the case that health insurance pays premium prices for commodity (patent-expired) drugs; (xi) a knowledge management system

selective and sensitive enough to monitor, evaluate, and analyse the intended and adverse effects of the drug reimbursement instruments is not in place; (xii) the "policy - implementation - policy research" cycle does not exist, making it almost impossible to feed-in the lessons learned; (xiii) the drug reimbursement system has still a large potential to improve on governance philosophy and social dialogue practice; (xiv) the benchmarking approach is far from depicting the external drug reimbursement practices in detail to enable the policy makers understand the models as a whole and predict the long-term effects of the interactions among the contextual dynamics; (xv) there is no in-depth analysis of the current policy, making it difficult to understand the impact of different drug reimbursement policy interventions on the impact of pharmacotherapy and drug expenditure; (xvi) fieldwork and meetings with stakeholders suggest that the data collected at prescribing or dispensing level are either non-existent or not used for policy analysis.

4. **The evidence from the international experience.** There are many different approaches to regulating pharmaceuticals that affect public policy objectives to control costs while improving efficiency, quality of care and equity. International comparisons may contribute to a better understanding of how different measures and policies are implemented. However, there are significant limitations to the relevance and transferability of lessons and policies across countries. Contextual factors such as the social, economic, medical, healthcare and political environment as well as constraints of history and institutional frameworks play a major role on how policies are developed and implemented in practice. This is particularly important in the EU because of the co-existence of national as well as supra-national regulation. Therefore, a policy adopted in one country may not necessarily work, or at least not to the same degree, in another and may need to be modified to the new context. It is often difficult to be clear on which component of a diverse range of measures undertaken was most successful. Given these two factors, deriving any sense of which of the many possible interventions are most effective is difficult. A further complication is that governments must consider those policies already in place and their effects before new policies are adopted. Trade-offs between competing policy objectives (e.g. health versus industrial policy) or the needs of different stake-holders (patients, health professionals, and industry) are inevitable.

5. Governments in OECD countries are all faced with rising pharmaceutical expenditures but have taken widely divergent approaches to tackling these. Some government policies

that enhance quality of care or cost-effectiveness or access may decrease the ability to contain expenditures. Rising expenditures by themselves may not be a problem if they are accompanied by health gain or by a similar rise in government revenues. In practice, the added health gain for added expenditure is often unclear, and the rate of rise of expenditure often exceeds revenue, so governments are forced to act. At the same time, they must aim not just to ***contain costs*** but to improve the ***cost-effectiveness*** and ***quality*** of the health service, and preserve or enhance ***equity***. Consequently, any approach to cost containment has to be evaluated in terms of its effects in these four dimensions.

6. The analysis has suggested that no single policy approach acts without a trade-off on the impact along these four dimensions, in addition to competing trade-offs between the objectives of the policies themselves. Thus, a policy maker needs to be clear what primary impact is desired, but conscious of where a subsequent negative impact of any policy may arise in other dimensions; if the impact of the trade-off along the other evaluative areas out-weighs the gains in the primary indicator, a policy must be reconsidered.
7. Polices aimed solely at cost containment might reduce *equity and access*, but if the aim of cost containment is to reduce unnecessary expenditure so as to allow access to other therapies, then cost containment would increase equity and access. In general, policies for the rational use of medicines would be expected to result in improvements in equity at an aggregate level. Policies such as generic (internal) reference pricing and prescription co-payments may reduce equity, unless there are exemptions to protect more vulnerable patients: used carefully these interventions can increase efficiency and decrease cost, without damaging quality and with minimal disruption to equity.
8. It is observed that strict cost control policies can have an effect in decreasing drug prices; but price controls alone are not necessarily associated with an efficiency improvement or the control of total expenditures. Demand side measures and rational drug utilization can deliver results when considered with and accompanied by concomitant measures in efficiency, equity and quality improvements.
9. **Prioritising drug sector reforms in Turkey.** In light of the research conducted, the evidence provided, and the stakeholder analysis, the study proposes several reforms that could be act on the supply-, the proxy demand- and the demand-side. Clearly, these policy options cannot be implemented in their entirety in the short-term. Unavoidably, as the government seeks to unify health care coverage and gradually extend prescription

drug coverage to the entire population in sweeping reforms, choices need to be made in the short-term in order to put in place a functional pharmaceutical policy that will endeavour to meet cost-effectiveness, equity, quality, and access criteria.

10. **Principles of regulation and intellectual property rights protection.** It is important that, from a systemic and regulatory perspective (including registration and intellectual property rights), the prevailing EU principles should not only be applied, but also enforced. New drugs and changes in product mixture will result in an increase in drug expenditure in the future. Policy makers should determine how the "innovative drug" concept will be defined in terms of clinical value and how these drugs are to be encouraged in order to ensure community benefit from drug utilization.
11. **Pricing of pharmaceutical products.** Pricing of pharmaceutical products should be separated from that of their reimbursement decisions. Pricing of in-patent products, generics and OTCs should be treated separately.
12. With regards to in-patent products, the short-term proposal is to maintain external referencing, whereas health insurance and the other competent authorities should put in place the mechanisms that would allow a more rational decision-making process, suitable to the Turkish conditions in the longer term. These would include, among others, criteria for assessing the innovative potential of new drugs and cost-effectiveness.
13. With regards to generics, there can also be a short-term and long-term policy. In the short/medium-term, the 30% mark-up on the lowest priced generic could be abandoned and referencing could take place of the lowest segment in the market (e.g. average of two or three lowest). However, given the transitional nature of intellectual property rights in Turkey, particularly the recent developments in data exclusivity, it is suggested that this to be handled in the medium-term and within the framework of a phased road map. Over the longer-term, health insurance might wish to re-consider the existing regulation since it links the prices of generics to those of originator drugs and probably results in high prices for generics. Instead, competition could be allowed to take place among generic producers and reimbursement to be set either at the lowest generic that can meet a significant proportion of domestic demand, or at some average of the lowest priced generics within a molecular cluster (again, a version of [internal] reference pricing as above). Monitoring of the system should be continuous and reference prices reconsidered on a frequent basis. The primary objective of health insurance when reimbursing generics should be to seek cost savings as opposed to subsidizing generic products.

14. With regards to OTCs, health insurance should first of all define what OTCs are and put in place a framework for their (selective) delisting from reimbursement. In the absence of an environment that encourages delisting, the short-term objective would be to introduce high co-payments in products for minor ailments (transferring these products to a lower reimbursement status). Whereas in the longer term these products could altogether be delisted and with a few exceptions not be reimbursed at all. If this is achieved, then the prices of delisted, non-reimbursed products should also be allowed to be free.

15. **Reimbursement of pharmaceutical products - Principles**. Reimbursement policy should be characterized by transparency, flexibility, robustness and regular policy updating to account for new treatments and evidence. The first tasks that health insurance is faced with are (a) the setting up of a reimbursement committee that will decide on which treatments are going to be reimbursed, at what rate and the likely price-volume tradeoffs that may arise and (b) the composition of a national positive list which will include drugs that health insurance will reimburse (partially or fully). In the selection of drugs which will be in the positive (reimbursement) list, scientific evidence, particularly clinical cost-effectiveness, should be followed.

16. **The use of health economics and health technology assessment**. Health technology assessment approach has to be coordinated with the training initiatives of the decision-makers, physicians, pharmacists, and the patients on matters pertaining to health economics. Graduate curricula in pharmacy and medicine need to be adapted and incorporate health economics and management. HTA is only a useful tool which should not result in total disregard of patients/citizens choice. It is critical to ensure involvement of patients in evidence-based decisions. Patient associations could be formally involved in the HTA processes to ensure wider societal consensus. Along with the use of health economics and cost effectiveness, it is recommended that an agency be created with the remit of assessing the (clinical) cost effectiveness of new treatments. This can be a medium- to long-term policy objective.

17. **Government-Industry agreements**. A negotiation model between relevant government agencies and sectoral stakeholders is strongly advocated, so that a decision making mechanism for which buy in of all stakeholders be ensured within the framework of common sense could be designed. Price-volume trade-off agreements, budget ceiling agreements and payback are examples of priority agenda items within this framework.

18. **Physicians**. Policies towards physicians should be a key area of focus by health insurance from the very beginning. Health insurance must initiate changes in the following areas: (a) physician prescribing behaviour, (b) rational drug use, (c) establishment and dissemination of clinical guidance, and (d) strengthening the incentive structure so as to influence physician prescribing decisions. Each of these areas would require integrated and immediate attention for the right policies to be implemented and enforced.

19. In order to monitor and evaluate prescribing, physicians should be provided with timely feedback on their prescribing behaviour. This would require a national prescribing database, which would include, among other things, patient diagnosis and utilization data. Based on this, positive (e.g. additional performance scores) and/or negative incentives could be imposed on physicians.

20. Unbiased and uninterrupted comparative information policies are of paramount importance in terms of eradicating the prescribing patterns that are incompatible with the national drug policy. Drug formularies including evidence-based comparative evaluation of drugs from a clinical and economic perspective are examples to this end.

21. Cost effective and evidence-based prescribing should be keywords to be stressed at all times underlining the range from awareness to accountability. Prescription quality management tools like "good prescribing practice" guidelines focusing on minimum requirements should be considered to influence physician decision-making. Another example targeting prescribing quality improvement is the clinical decision support systems that generate patient-specific pharmacotherapeutic roadmaps

22. **Rational drug use.** Policies on rational drug use have a long-term horizon, combined with an element of continuity. They comprise changes in national education curricula of medical, dental and pharmacy students, improved and objective sources of information for prescribers, continuing education for practitioners, monitoring and evaluation of prescribing patterns at the national level and promoting consumer/patient awareness of public health issues.

23. **Pharmacists and pharmacy practice**. Governmental institutions and professional organizations should work collaboratively in this context. Pharmaceutical services and counselling function of pharmacists should be emphasized. In this frame, healthcare professionals primarily physicians on the one hand and consumers/patients on the other should be made conscious on rational drug use. "Muvazaa", which is both against the

law and negatively affects community benefiting from pharmaceutical services, should definitely be abolished.

24. **Pharmacy remuneration and discounts.** Drug dispensing, should focus on optimizing drug expenditures by generic substitution. This approach can be supported by providing financial incentives to pharmacists. This practice can also be supported by paying a flat fee per prescription for pharmaceutical service. A thorough review and evaluation of pharmacy income should be undertaken to throw light on the potential adverse effects of discounts and free goods on regressive margins. The use of a clawback and/or the institutionalisation of a flexible generic referencing system could be considered for regulating profits in case the evidence indicates that the discounts and free goods are found to be interfering with the regressive margin policy tool.
25. **Patient cost sharing**. Another way of optimizing drug expenditure is transferring certain drugs and/or indications to lower reimbursement status. Naturally, this application will increase the co-payment for these drugs.
26. A differential co-payment system can be considered as another policy tool for branded and generic drugs with different cost sharing options. A lower co-payment for generic drugs when compared to branded drugs may encourage patients to purchase generic drugs.
27. In short term for OTC products, a higher co-payment procedure should commence (i.e. +50%-75%). In the longer term, however, the reimbursement of these products should altogether cease by excluding them from the positive list.
28. **Supporting self medication**. Governmental institutions in charge of reimbursement decisions should develop a more effective OTC policy that encourages self-medication. A class of OTC products could be created and could be dispensed with pharmacists' assistance. For this to take place, pharmacists should be staffed by pharmacists at all times.

1. Introduction

1.1. Background – The Context and Issues Arising

Turkey is a middle-income country on its course towards full EU membership. The most recent and internationally comparable estimates from the National Health Account study indicate that Turkey spent, in 2000, US$13.1 billion on healthcare (or US$30.4 billion at PPP) corresponding to US$194 (or US$ 443 at PPP) per capita. The share of total health expenditures in GDP was estimated at 6.6%. Of the total healthcare spending 63% was made out of public purse (of the total health expenditures of which 37% came from social security organizations). Out-of-pocket expenditures constituted 27.6% of total health expenditures (OECD, 2004).

The major healthcare problems that the country is facing are as follows (Tatar and Kanavos, 2005):

- Poor health status indicators compared to other countries with comparable economic development levels, e.g. IMR and MMR.
- High regional disparities in health status.
- Inadequate and divergent healthcare coverage.
- Highly fragmented structure both in provision and financing with resultant inefficiencies.
- Weak management capacity at both macro and micro levels.
- Irregular flows of patients and resources between public and private practice resulting in waste of public resources for private purposes.
- Problems of accessibility especially for the deprived population.
- An ineffective and under-funded public health care (PHC) system with lack of a functioning referral system resulting in excessive and inappropriate use of hospital services.
- Inequitable geographical distribution of human resources.
- Inefficient use of hospital resources with highly underutilized capacity.
- Dissatisfaction of the health workers and public with the current health system.

These problems have urged governments to embark on health sector reforms since the early 1990s with limited success. However, recent attempts have begun to reshape the entire healthcare policy and system. The introduction of a General Health Insurance (GHI) Scheme is the major reform initiative on the financing side**.** Health care financing in Turkey is very complex and fragmented and that also includes access to and consumption of pharmaceuticals. Current social security systems have different benefit packages both in terms of quality and coverage. The indigents are covered by the government financed Green Card scheme whose benefits have only recently been expanded to cover ambulatory care and pharmaceuticals in addition to hospital care. Although in theory the majority of the population is assumed to be covered by these existing schemes, recent studies show that nearly 30% of the population does not have any coverage (Ministry of Health and Başkent University, 2003; Ministry of Health, 2004). The underinsurance phenomenon arising from the deficiencies of the existing schemes is another issue to be addressed. The high level of out-of-pocket expenditures even by the publicly insured population can be regarded as a reflection of this phenomenon.

The proposed GHI scheme merges all existing schemes under one scheme with special emphasis on preserving all the current benefits. The premiums of those under the poverty line will be paid by the government and the people will be free to choose from family practitioners and hospitals. The Scheme with its monopsonic power will be the major purchaser of services from competing healthcare providers from both public and private sectors. All provisions of the Act are to come into effect gradually until 2008.

1.2. The Terms of Reference

Within the context of sweeping health care reforms, the remit of this report is to analyse pharmaceutical financing and reimbursement policies in Turkey with the assistance of international comparisons and provide policy recommendations to inform the debate on drug sector reform. In so doing, component 2 addresses the following issues;

1. Review of pharmaceutical financing/reimbursement policies in Turkey and other comparator countries with reference to
    - Access to medicines,
    - Cost of medicines to individuals and public payors, and
    - Intellectual property rights.

2. Description of cost containment measures and assessment of their outcomes in relation to policy goals and their applicability in Turkey.
3. This report provides recommendations for a sound and sustainable pharmaceutical financing/reimbursement policy for Turkey taking into account:
    - Availability, accessibility, cost-effectiveness
    - Requirements for success of this effort (organizational, managerial, infrastructural)

1.3. Methodology

1.3.1. Data and Methods

The report has benefited from primary sources as well as a wealth of secondary sources. It has also included the international experience, by reviewing and cross-comparing drug policy tools and their implementation in a number of selected countries, particularly drawing upon the European experience.

With regards to primary sources, material was collected these were twofold:

a) Meetings and interviews in Ankara with decision-makers as well as experts on drug policy.

b) Meetings and interviews with other experts on regulatory issues and intellectual property rights issues also contributed to this effort.

Interviewees have included:

1. Prof. Dr. Sabahattin Aydın, Deputy Under-Secretary, Ministry of Health
2. Mr. A. Tuncay Teksöz, President, Social Security Institution, Ministry of Labour and Social Security
3. Dr. Füsun Sayek, President, Turkish Medical Association
4. Mr. Hayati Gökçe, Deputy General Director, Ministry of Finance - General Directorate of Budget and Fiscal Control
5. Dr. Salih Mollahaliloğlu, Director, Ministry of Health School of Public Health
6. Assoc. Prof. Dr. Bülent Gümüşel, General Secretary, Ankara Pharmacists' Association
7. Ms. Hülya Çaylı, European Patent Consultant, Paragon Consultancy Co.

This study has also benefited from comments and views expressed, in various meetings, by many others including those who have mentioned in the Acknowledgement. Secondary sources have included, among others:

- A study on informal payments in Turkey (Tatar, et al., 2003)
- Legislation and draft regulations
- Other secondary sources on the Turkish health care system and pharmaceutical policy.

In presenting the international experience on drug policy (regulatory and intellectual property rights, pharmaceutical pricing and reimbursement, policies towards physicians, pharmacists and patients), we drew upon evidence from OECD countries, particularly those in the European Union. We believe that our selected countries have a wealth of information and allow us to draw useful inferences and examples about the process of drug sector reform in Turkey.

1.3.2. Policy Objectives

Within the context of health and pharmaceutical sector reform, the policy objectives that characterise drug policy are fourfold:

a) **Macro-economic efficiency**, in the sense that budgets are finite and due consideration should be given to optimal allocation and prudent as well as effective utilisation of scarce resources.

b) **Micro-economic efficiency** (resource allocation); the environment and dynamics for health care reform and the extent to which there is silo budgeting in individual parts of the health care economy; the inter-relationship between pharmaceuticals and other sectors of the health care economy;

c) **Access** to medicines and impact on the **quality** of care, avoidable mortality and ways these can be improved;

d) **Assessing the dynamics of policy trade offs,** in particular those between health policy trade policy and industrial policy, and their application in the Turkish case; of interest, among other things, are the long-term dynamics of policy trade offs, particularly in connection with cost containment and industrial policy (e.g. incentives for R&D, attracting pharmaceutical investment in Turkey, etc)

1.4. Report Outline

This report consists of six chapters. The aim, scope and method of the study are covered in chapter 1 (Introduction). Chapter 2 presents an in-depth situation analysis of Turkish pharmaceutical sector. Chapter 3 discusses drug policy in a number of countries within the OECD area. Chapter 4 presents a detailed review of Turkish drug policy addressing problems pertaining both the system and policies. Chapter 5 outlines a number of comprehensive policy recommendations on drug sector reform in Turkey. Finally Chapter 6 offers concluding remarks and policy recommendations.

2. Analysis: The Pharmaceutical Sector in Turkey

2.1. Health System Background and Key Indicators

Turkey's population of approximately 70 million is relatively young when compared to the population profile of the EU countries. Estimates of life expectancy are lower than EU countries, while infant and maternal mortality rates are much higher. The main cause of death in infants is infectious diseases. On the other hand, ischemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease - COPD, and lower respiratory infections are the main causes of death among adults (MoH School of Public Health, Burden of Disease Study, December 2004). The State Planning Organization is responsible for strategic planning of the health care system. The Ministry of Health is the coordinating body for the health care delivery activities. However, the centralized yet fragmented character of health care delivery makes it difficult to manage the system effectively and efficiently. Until recently, the Ministry of Health owned and operated approximately 60% of the hospitals; another 20% were owned by other public agencies, mainly by the Social Insurance Organization (SSK). As part of the ongoing health care reforms and the implementation of a generalised health insurance scheme, the ownership of most public hospitals including all SSK's, has now been transferred to the Ministry of Health as of February 2005.

The main sources of health care financing are:

a) The general government budget funded by tax revenue;

b) Contributions obtained from members of the social security schemes, namely "SSK", "Bağ-Kur", and "Emekli Sandığı";

c) Out-of-pocket payments.

The State Planning Organization data on the numbers of valid health cards indicate that the social security systems cover around 59% of the population. There is a system of multiple insurance schemes. In addition to above-mentioned systems there is also the Green Card scheme, financed directly by the state, covering about 19% of the population under a certain income threshold.[1] Total expenditure on health care as the proportion of GDP (6.6% for the year 2000) is low relative to 15 EU member states (OECD, 2004).

[1] Coverage of population by SSK, Bağ-Kur and Emekli Sandığı are respectively 34.45% (23.02 million), 13.69% (9,15 million), and 15.04% (10.05 million). The number of Green Card holders was about 13 million at the time (Source: Ministry of Labour and Social Security, Proposal for Reform in Social Security, April 2005. p 36 in Section 5.1.6). According to State Statistics Institute data, the total population of 2000 was 66.83 million.

The Act on the Socialization of Healthcare Services of 1961 was the milestone of health care reforms in the 1960s. Later, effectively beginning from 1987 with the enactment of Basic Law on Health Services in that year, a renewed attempt on reforming the system began. Establishment of a universal health insurance scheme, decentralization and strengthening primary care level based on a family practitioner system have been the key policy elements of this period. These reform proposals due to a host of political, technical and managerial reasons have not been implemented thus far. More recently, the government has announced its "Health Transformation Programme" to be implemented over the next few years. The programme's main objective is to ensure that health services are organized, funded and delivered in an effective, efficient and equitable way. The main components of the proposed programme are as follows:

- restructuring of the Ministry of Health to enhance its core functions of setting priorities, ensuring quality and managing public health processes, including preventive services;
- introducing compulsory statutory health insurance for the whole population, with the possibility of supplementary voluntary health insurance operated by private insurers;
- increasing access to health care by making use of private facilities where necessary, strengthening primary care, improving the referral system and giving institutions more administrative and financial autonomy;
- improved and more appropriate training for doctors, nurses and administrators and better incentives to encourage a more even distribution of personnel across the country;
- establishing a school of public health and a national quality and accreditation agency;
- supporting more rational use of drugs and medical devices through the establishment of a national drug agency and a medical device agency;
- improving health information systems.

As a result, the Turkish health care system is undergoing significant change at this juncture. The changes are driven by a strengthened national commitment to deliver healthcare in a fair and equitable manner to all citizens. An unbalanced social structure and a significant

gap in income distribution, mean that the needs of urban and rural areas are vastly different in Turkey. Drug utilization varies greatly between urban and rural areas and detailed evidence on that has been presented in the other SUVAK study conducted by Liu and others. Physicians are attracted to urban areas for cultural, educational, and financial reasons. In urban areas, private-sector physicians and dentists earn more money, and private-sector hospitals enjoy much higher revenues. Many of these hospitals are now serving foreign patients as well. This economic imbalance of the country is reflected in the state of government-run hospitals. Some have been reported to be poorly equipped and staffed that patients usually need to bring their own medical supplies.

SSK, Emekli Sandığı and Bağ-Kur are among the prime purchasers of pharmaceutical products. In addition, MoH and other public sector hospitals, university hospitals, and private hospitals are main pharmaceutical purchasers for use in inpatient care.

Table 2.1 shows some of the key health and expenditure indicators in Turkey whereas Table 2.2 compares these with a number of other countries. In 2002, there were 1,156 hospitals in Turkey with a total bed capacity of 162,235, or 1 bed per 429 people (calculated) (State Institute of Statistics, 2004). Average capacity utilization was 61.3% (excluding Ministry of Defence hospitals) (MoH, 2002), therefore, on average fairly low, although it varies from hospital to hospital or from hospital type to hospital type. Usually, hospitals that were formerly owned by SSK, work with much higher utilisation rates with respect to MoH or other special government hospitals (military hospitals, ministry of education hospitals, etc). Unification of ownership status under the MoH will probably address this issue in the medium- to long-term. There are 95,190 doctors, 79,059 nurses (excluding midwives), and 17,108 dentists (State Institute of Statistics, 2004). The number of patients per doctor is 731 while the population per dentist is 4,070 (both calculated from State Institute of Statistics, 2004).

Doctors are mostly affiliated and accredited with hospitals even if they have private offices, while most dentists operate in their private offices and can therefore prescribe from the supplier of their choice without cumbersome tender procedures that hospitals must follow.

The majority (about 66%) of drug purchases in monetary terms throughout the country are reimbursable through public sector agencies such as the Emekli Sandığı and SSK while the remaining 34% is met by individuals either by co-pays or direct purchase from the

supplier of their choice (OECD, 2004). Unification of reimbursement scheme across all insurance funds is currently underway and will be fully harmonized in the coming years.

Table 2.1. Relevant economic, demographic and health related characteristics of Turkey, 1980 - 2001

Characteristic	1980	1985	1990	1995	1999	2001
Life expectancy – male	55.80	59.80	63.90	65.70	67.00	-
Life expectancy – female	60.40	64.30	68.50	70.30	72.10	-
Infant mortality[a]	95.40	88.90	58.00	44.40	40.00	36.00
Human Development Index	0.62	0.65	0.69	0.72	0.73	0.74
Inflation rate	-	45.00	60.30	93.60	64.90	54.40
GDP/capita (US$)	1,539	1,330	2,682	2,759	2,880	2,540
Health spending per capita (US$ PPP)	75.00	74.00	165.00	184.00	392.00	446.00[d]
Health spending as % of GDP	3.30	2.20	3.60	3.40	6.44	6.60[d]
Total Public expenditure % of Health Expenditure	27.30	41.80	61.00	70.30	61.10	62.90[d]
Pharmaceutical spending as % of Health Spend	10.20	13.20	20.50	31.60	24.30	24.80[d]
Pharmaceutical spend per capita (US$ PPP)	9.00	10.00	35.00	60.00	95.00	110.00
Cancer prevalence (%)	0.02	0.03	0.05	0.05	0.04	-
Chronic pulmonary diseases (%)	0.08	0.11	0.14	0.19	0.22	0.23
Traffic accidents[c]	-	70.52	99.35	108.94	112.02	97.95
Smoking rates %	-	44.00	-	35.00	-	-
Hospital beds per 100,000 population	258.65	239.77	243.41	250.73	263.25	235.52
Physicians per 100,000 population	61.26	72.89	90.21	114.42	127.44	127.16
% Private in-patient hospital beds	2.23	2.38	2.89	4.06	6.72	7.48
Bed occupancy rate (%)	39.50	52.10	57.20	55.40	57.80	58.80
Hospital spend as % of total health spending	-	35.80	33.40	28.70	21.30	36.38[d]

[a] Infant deaths per 1,000 live births
[b] Maternal deaths per 100,000 live births
[c] Road traffic accidents with injury per 100,000 population.
[d] Year 2000.

Source: World Health Organisation, 2003.

Table 2.2. Relevant economic, demographic and health related characteristics of Turkey compared with other European Countries (latest available data)

Characteristic	UK	Ger	Fra	Spa	Ita	Gre	Pol	Cze	Tur
Life expectancy – male	75.90	75.69	79.35	76.28	77.11	76.34	70.25	72.12	**67.00**
Life expectancy – female	80.60	81.59	83.15	83.32	83.22	81.66	78.48	78.66	**72.10**
Infant mortality[a]	5.48	4.31	4.38	4.08	4.67	5.05	7.67	3.97	**36.00**
Human Development Index	0.93	0.92	0.93	0.92	0.92	0.89	0.84	0.86	**0.74**
Inflation rate	1.80	2.00	2.40	3.20	2.70	3.00	5.50	4.70	**54.40**
GDP/capita (US $)	24,219	22,422	22,129	14,150	18,788	11,063	4,561	5,554	**2,540**
Health spending per cap (US$ PPP)	2,012	2,735	2,588	1,567	2,107	1,670	629	1,083	**446[d]**
Health spending as % of GDP	7.50	10.80	9.40	7.50	8.30	9.40	6.00	7.30	**6.60[d]**
TPE[b] as % Health Expenditure	83.00	78.60	75.90	71.30	76.00	53.10	71.90	91.40	**62.90[d]**
Pharma spend as % of health spend	15.80	14.30	20.90	21.20	22.40	15.60	9.20	21.90	**24.80[d]**
Pharma spend per capita (US$ PPP)	-	402	537	209	493	211	-	242	**110**
Cancer prevalence (%)	-	-	1.34	-	2.40	-	-	3.03	**0.04**
Chronic pulmonary diseases (%)	-	0.24	0.20	-	0.30	0.29	-	-	**0.23**
Traffic accidents[c]	391.48	455.85	196.37	247.19	366.92	186.35	139.23	254.56	**97.95**
Smoking rates %	27.00	34.50	27.00	34.40	24.10	37.60	32.00	23.30	**35.00**
Hospital beds per 100,000	417.10	901.06	793.17	394.35	446.81	487.80	549.45	857.55	**235.52**
Physicians per 100,000	220.16	330.70	329.67	324.34	612.08	453.28	224.13	344.50	**127.16**
% Private in-patient hospital beds	4.51	22.82	34.45	32.81	23.13	29.40	1.17	10.38	**7.48**
Bed occupancy (%)	80.80	80.10	77.40	76.10	76.00	-	-	70.50	**58.80**
Hospital spend as % of THE	-	36.10	41.70	27.90	41.50	-	-	36.60	**36.38[d]**

[a] Infant deaths per 1,000 live births.
[b] Total Public Expenditure.
[c] Road traffic accidents with injury per 100,000 population.
[d] Year 2000.

Source: World Health Organisation, 2003.

2.2. Key stakeholders and Responsibilities in Pharmaceutical Policy

In Turkey, the Ministry of Health, General Directorate of Pharmaceuticals and Pharmacies (GDPP) is the sole authority in charge of registration, marketing approval/authorisation, pricing of pharmaceuticals, legal classification and inspection. In particular, the role of this authority is to provide for registration, marketing approval/authorisation and pricing of pharmaceutical products, to define rules to be followed

as well as to control the advertisement of pharmaceutical products, to undertake inspection of pharmaceutical products and pharmaceutical production plants in Turkey. The Directorate General's duties and responsibilities are laid down in Decree Law on the Organisation and Duties of the Ministry of Health (Official Gazette No. 18251, 14.12.1983) and the Basic Law on Health care Services (Law No: 3359 Official Gazette, 14.05.1987).

In its tasks, the Ministry of Health is assisted by a number of "internal" commissions (Advisory Commission for the Registration of Medicinal Products for Human Use, Advisory Commission for Technology – Pharmacology, Bio-availability – Bio-equivalence Evaluation Commission and Radio-pharmaceutical Advisory Commission) composed of university professors, pharmacologists, pharmaceutical technologists, clinicians, and representatives of the Ministry and other related experts. The duties and functions of these commissions/committees are regulated in the Regulation on setting the duties of Scientific Advisory Board and Commissions for Medicinal Products for Human Use (Official Gazette no: 25254, 9.10.2003). These commissions actually operate as consulting bodies of the Turkish Ministry of Health in the handling of marketing approval applications submitted by pharmaceutical products manufacturers. According to the information gathered, these commissions need to be consulted before a marketing authorisation/approval is given. An application needs subsequent "green light" of each one of these committees before it can be dealt with by the next one.

In terms of procedures, the regime/process as described above applies to all pharmaceutical products to be put on the market in Turkey, whether imported or locally produced. The marketing authorisation/approval details are laid down in the Licensing Regulation for Pharmaceuticals (Official Gazette No: 22218, 2.03.1995).

Apart from certain procedural differences (between research-based and generic products to be explained below in connection to the issue of data protection), the requirements for a registration dossier for pharmaceutical products are standard and applicants must comply with them. Article 8 of the Licensing Regulation for Pharmaceutical Products specifies a list of documents that should accompany the application. Accordingly, a summary of the dossier, chemical, pharmaceutical and biological information, pharmacological – toxicological documents and clinical documents (tests) should be provided. The Appendix of the Licensing Regulation for Pharmaceutical Products provides a full list of information and documents that need to be included in the dossier for the registration of medicinal products. Furthermore and in order to assist applicants, the Turkish Ministry of Health, in addition to WHO and FDA

guidelines and recommendations, has produced a special check list (Guideline of Evaluation of Authorisation Applications) where the items to be included in the registration dossier are listed.

Following the opinion of the advisory commissions/committees as above, a report is being prepared and submitted to the General Directorate of Pharmaceuticals and Pharmacies of the Health Ministry. If the notification requires the applicant to submit additional information, the applicant has to provide it within a period defined in the given notification. Article 17 of the Licensing Regulation (Notifications and Objections) lays down the right of objection for the applicant in case of refusal of its application. If the license application is rejected, the applicant shall be notified of the decision with reasons. The applicant is entitled, in case of refusal, to have recourse to judicial remedies before the competent administrative courts.

In terms of deadlines, there are no specific and binding deadlines for the conclusion of the processing of marketing approval applications. On 3 December 2003, though, the Ministry of Health issued a Notice (No: 49221) to the Pharmaceutical Industry Manufacturers Association (IEIS) where they declared that their intention was to complete the registration/marketing approval within 210 days for all products.

On 19 January 2005 MoH issued a Notice harmonizing the registration process with EU Directive 2001/83 (details in "*2.3.2.1 Granting Marketing Authorisation").* Amendments according to the new EU Directive 2004/27 shall be made after accession to EU. Regulation Regarding the Variations on Medicinal Products for Human Use With Registration or Pending Registration is publicized on 23 May 2005, (effective from 30 December 2005) setting forth the rules and principles to be used in applications about variations in medicinal products for human use that are already registered, or with registration pending.

Finally, the criteria considered by the Ministry of Health when evaluating applications for registration of pharmaceutical products are efficacy and safety under proposed administration conditions, whether introduction of the product into the market will be beneficial, whether the product has suitable technical and pharmacological specifications and whether its price is reasonable. This is clearly stated in the Law on Medicinal Products for Human Use (Law No: 1262, Official Gazette No: 809, 26.05.1928) and the Licensing Regulation for Pharmaceutical Products of 1995.

In other words, pricing determination is an integral part of the marketing/registration approval process in Turkey and there have been no instances where a marketing approval was granted without a previous pricing determination.

2.3. Obtaining Market Access in Pharmaceuticals

2.3.1. Intellectual Property Rights Protection

New licensing regulations that closely resemble European Union regulations came into force recently, and a national patent law has been in effect since January 1st, 1999, implemented retrospective from January 1st, 1995. The Turkish patent law currently does not include provisions for marketing exclusivity or a Supplementary Protection Certificate (SPC). However, The MoH has recently (January 19, 2005) modified its Registration Regulations where a 6 year of marketing exclusivity under certain conditions is allowed. Accordingly, marketing exclusivity will not be implemented retrospectively and will provide protection only for new molecules registered in Turkey after 1 January 2005 where the protection term will effectively begin from the first registration date in any of the EU Customs Union Zone countries. This protection term is limited with the patent term of the concerned molecule, and as prescribed in the Regulations, is also applicable to molecules registered from 1 January 2001 if only there was no generic in the marketplace in Turkey or no generic application as of 31 December 2004 for these molecules. These conditions are still under debate among stakeholders.

2.3.2. Registration and Market Authorization

2.3.2.1.Granting Marketing Authorisation

MoH regulations stipulate that product registration can only be granted to a firm registered in Turkey. To obtain MoH product approval, a company should have as much information pertaining to safety, efficacy, bio-equivalence (for generics), bio-availability (for originals), and active ingredient information as possible. Documentation used in acquiring FDA, the European Union (EMEA) and other recognized authorities approvals should also provide sufficient information to receive drug market approval but this has not been a prerequisite. According to the new registration regulation of 19.01.2005, which was originally come into force from 30.12.2005, submission of CPP (Characteristics of Pharmaceutical Product) is obligatory to inform the MoH the countries in which the drug is registered. Depending on the completeness of the application dossier, the drug approval process could in practice vary up to twenty-four months depending on the drug and this period embraces drugs' inclusion in the reimbursement list. According to the same Regulations, registration

period is to be completed within 210 days excluding the period for inclusion in the reimbursement list, pricing and analysis process. However, due to ambiguity of the definition of OTCs, there are uncertainties in the approval process.

The current regulations limit the distribution of drugs solely through pharmacies and hospitals, and make it illegal to sell or distribute pharmaceuticals elsewhere. Pharmaceutical registration fees vary for domestically manufactured and imported products and the validity period of a drug registration is five years. For renewal, the licensee must submit an application to the MoH at least six months prior to the expiration date.

The process of drug approval follows the steps below:

- The Board is comprised of around 20 permanent members including specific clinicians, pharmacologists, technologists and pharmacognosia specialists and ad hoc specialists for the application of different category of pharmaceuticals, which are chosen from a list of which is to be updated regularly. Review by this board takes approximately 3 – 4 months.
- In the second phase of product registration, the entire pharmaceutical approval dossier is evaluated by the Technical and LPD (Local Product Documents) Review Commission. It is this board that generally undertakes technical assessment of dossiers and compares them with EMEA and FDA approved prospectus. The Board, if necessary, requires additional information on drug safety. Registration process for the generic products starts at this stage. Evaluation of the pharmaceutical dossier takes approximately 6 to 8 months.
- Following laboratory testing, the drug approval dossier was submitted to the Pricing Board of the MoH. According to the current practice, Turkish pricing authorities request lowest of the minimum ex-manufacturer price among five pre-selected EU countries (Spain, France, Portugal, Italy and Greece), country of origin and current local price is set as the new price. Prices should be approved approximately within 1 month as prescribed in the pricing regulations but in practice it lasts between 3 – 6 months and even longer.
- After pricing approval, for original products information due to bio-availability and for generic products information on bio-equivalence shall be reviewed in the Bio-availability and Bio-equivalence Commission. Afterwards the drug application is returned to the Registration Board with stamps and approvals confirming every step

had been followed as noted above. The company is then granted "Marketing Authorization". This stage may take between 2– 4 weeks.

- Together with the registration approval barcode is granted.
- The final step is the granting of the “Sales Permission”. This is issued following the issuance of a barcode and verification that the product meets the appropriate labelling regulation. The sales permit is issued approximately 14 days.

MoH Technical and LPD Review Commissions are formed by different members according to the original and generic products.

2.3.2.2.Bio-Equivalence for Generics

Applicants must now submit bio-equivalence data in support of generic products as part of the approval process. Already registered and in-market generics without a bio-equivalency certificate are now obliged to submit such certificates. The deadline for submission was originally set for January 2003 but it has now been extended to December 2005. At the end of 2002 there were reportedly around 600 branded generics on the market without bio-equivalence certification. Almost 300 products have since been granted certification, while data in support of a further 250 was being evaluated. With bio-equivalence data now mandatory for all new drugs, the market should be free from non-compliant products in the near-future.

2.3.2.3.The New Drug Agency

The recently announced Health Transformation Programme includes a component for the establishment of a National Drug Agency. A draft law setting out its framework of operation is also available. The status of the new agency, degree of autonomy, governance, and type of accountability are currently under debate. A new law on the status of the new agency is currently under preparation and will not be implemented before a proposed Ministry of Health and a general public sector re-structuring, take place. The new law also suggests that the new agency be autonomous within the overall MoH structure and be funded exclusively by user fees. In the current model, the MoH has exclusive responsibility for drug registration and approval, as well as pricing of medicines.

2.4. The Pharmaceutical Market in Turkey

2.4.1. Market Size and Consumption

There are, as of May 2005, 1388 active ingredients and 3667 products with different forms (about 7000) currently available on the Turkish market. The market is exclusively served by either branded original products, or by branded generics. Unbranded generics are completely absent from the Turkish market.

There are 33 multinational companies operating in Turkey some with owned manufacturing capacity while others predominantly utilizing local generic facilities as toll-manufacturers. The 167 generic and mostly domestically owned companies focus on the generic market either as manufacturers or importers. Pharmaceutical expenditure in Turkey is lower than that of Western Europe. In 2000, per capita pharmaceutical expenditure (PPP) was $110 in Turkey where it ranged from 189 in Ireland to $491 in France in Western Europe (WHO, 2003).

2.4.2. Price Levels of Medicines in Turkey and Elsewhere

Official Ministry of Health data on prices for a number of branded original products in Turkey and a number of other European countries in 2004 suggest that Turkish prices for branded originator products are generally lower than the same prices in all reference countries (France, Italy, Portugal, Spain, and Greece) (see Table 2.3). This is not surprising as the pricing rule that the Turkish Ministry of Health follows suggests that the price of a drug in Turkey should be the lowest among a basket of these reference countries. The comparative price levels of older medicines (older than 20 years) have not been studied here since they are not subjected to the new pricing rule of “generics could receive a price up to 80% of the original”.

Table 2.3. Comparative Prices of Selected Top-selling Products in Turkey (As of June 2005)

Product	Molecule	Reference Price (EURO)	Reference Country	Ex-Man Price TL (Excluding VAT)	Reference Price (TL)	Price Difference
Seretide Inhaler 125 Mcg 120 Dose	Salmeterol + Flutikasone	38.21	Greece	66,091,004	67,800,244	-2.52%
Plavix 28 Film Tab.	Clopidogrel Hydrogen Sulfate	37.70	Spain	64,163,311	66,895,295	-4.08%
Lustral 50 Mg 28 Tab.	Sertralin	17.82	Greece	27,233,202	31,620,004	-13.87%
Lipitor 20 Mg 30 Film Tab.	Atorvastatin Calcium	32.64	Greece	34,907,767	57,916,775	-39.73%
Norvasc 5 Mg 30 Tab.	Amlodipine Besilate	10.02	Portugal	16,627,091	17,783,147	-6.50%
Zyprexa 10 Mg 28 Tab.	Olanzapine	87.89	Spain	143,926,343	155,952,983	-7.71%
Fosamax 70 Mg 4 Tab.	Alendoronate Sodium	26.16	Greece	38,627,511	46,418,592	-16.78%
Co Diovan 160/25 Mg 28 Film Tab.	Valsartan +H.thyaside	16.49	France	29,259,010	29,260,037	0.00%
Viagra 25 Mg 4 Film Tab.	Sildenafil Citrate	19.24	Greece	29,701,508	34,139,668	-13.00%
Lansor 30 Mg 28 Cap.	Lansoprazole	21.81	Italy	17,512,086	38,699,904	-54.75%
Symbicort 60 Dose Inhaler	Budesonid	24.40	Portugal	43,287,563	43,295,628	-0.02%
Ketek 400 Mg 10 Film Tab.	Telitromycine	20.00	Italy	35,481,631	35,488,220	-0.02%
Tavanic 500 Mg 1 Vial	Levofloxacin	33.91	Greece	36,138,463	60,170,277	-39.94%
Singulair 4 Mg 28 Tab.	Montelukast Sodium	29.32	Spain	48,908,663	52,025,731	-5.99%
Karvezide 300 Mg/12.5 Mg 28 Tab.	İrbesartan + H.thyaside	20.46	Italy	36,290,571	36,304,449	-0.04%
Actonel 5 Mg 28 Film Tab.	Risedronate Sodium	22.67	Italy	40,217,736	40,225,897	-0.02%
Diamicron Mr 30 Mg 30 Tab.	Gliclazide	4.00	Portugal	7,088,005	7,097,644	-0.14%
Foradil 12 Mcg 60 Cap.	Formoterol Fumarate	21.20	Greece	37,064,942	37,617,513	-1.47%
Foradil 12 Mcg Inhaler	Formoterol Fumarate	35.08	Italy	58,401,337	62,246,338	-6.18%
Hyzaar Forte 14 Tab.	Losartan Potassium +H.thyaside	12.51	Portugal	22,185,965	22,197,882	-0.05%
Celebrex 200 Mg 30 Cap.	Celecoxib	23.27	Italy	30,233,888	41,290,544	-26.78%
Cipralex 10 Mg 28 Tab.	Escitalopram	15.64	Spain	27,744,839	27,751,788	-0.03%
Avandia 8 Mg 28 Film Tab.	Rosiglitazone	30.45	France	54,025,333	54,030,815	-0.01%
Beloc Zok 100 Mg 20 Tab.	Metoprolol Succinate	4.51	Spain	7,991,845	8,002,594	-0.13%
Nexium 20 Mg 7 Tab.	Esomeprazole	5.95	France	10,556,579	10,557,745	-0.01%
Xenical 120 Mg 84 Cap.	Orlistat	52.54	Greece	83,419,137	93,227,554	-10.52%
Cefamezin Im/Iv 500 Mg 1 Vial	Cefazolin Sodium	2.79	Italy	2,133,877	4,950,607	-56.90%
Inhibace Plus 5 Mg 28 Tab.	Cilazapril+ H.thyaside	10.42	Greece	18,480,049	18,489,363	-0.05%
Zocor 10 Mg 28 Tab.	Simvastatin	4.55	Spain	8,066,599	8,073,570	-0.09%

Note:

1. Currency: 1 EURO=1,774,411 TL.
2. One form from each product is chosen.
3. If list price was set before the effective date of the regulation and is lower than the lowest of the minimum ex-manufacturer price among five pre-selected EU countries (Spain. France. Portugal. Italy and Greece) pharmaceutical company can not increase.
4. MoH erases the last four digits and rounds the number to the lowest and this makes the price difference.
5. Source: MoH General Directorate of Pharmaceuticals and Pharmacy web site (http://www.saglik.gov.tr/sb/default.asp?sayfa=birimler&cid=1&sid=1065) (Accessed on 27 June 2005)

2.4.3. Prescribing Practices

All patients with social insurance coverage have the right of access to public primary (health posts, centres), secondary or tertiary care services and physicians free of charge. Under certain rules and conditions free access also allowed to private healthcare facilities. Physicians are not contracted individually with a particular public insurance scheme; rather, it is institutions (i.e. hospitals) that are contracted these insurance schemes.

Physicians always prescribe by brand name (whether this is a generic or an original product). Although the MoH, through its School of Public Health, has prepared and published (2003) guidelines for drug use in primary care, these are not yet enforced. In addition, there are no financial ceilings for prescribing, no drug utilisation reviews by any of the insurance funds. There are no direct incentives to prescribe certain medications and, by the same token, there are no disincentives (penalties) for over-prescribing. One of the limitations on prescribing is a ceiling determined by the sickness funds in terms of number of medicines per prescription. It appears, therefore, that monitoring of prescribing and evaluation of what is being prescribed, are missing, and so is financial accountability.

Although there is a general guidelines provided by the Ministry of Finance (MoF) through its annual Budget Implementation Guidelines, there is no comprehensive and systematic source of information available to physicians on which to base their prescribing. An updated National Formulary does not exist, although MoF has recently issued a positive list, the criteria for the inclusion of (new) drugs have not been published yet.

The lack of a systematic source of information makes the physicians almost fully dependent on commercially available sources of information to aid their prescribing. There are also no sources of independent information to physicians; the government is proposing to fill this gap by publishing a bulletin to be distributed to all physicians, but this is still pending.

Regarding corporate promotional activities to physicians, there are currently no official (government) limits on company rep visits to physicians. Limits on product samples do not exist and physicians may receive unlimited numbers of free samples from company reps. It is also understood that physicians may receive gifts in kind (invitations to attend conferences, symposia, workshops), which may influence their prescribing habits to favour prescribing of certain products over others, although the extent and frequency of such practices has not been documented in detail and remains anecdotal. Pharmaceutical promotional activities are regulated by the MoH GDPP's Regulations on Promotional Activities for Pharmaceuticals. Our understanding is that the Turkish Medical Association

(http://www.ttb.org.tr/ilac/ilke.htm Accessed on August 29, 2005) as well as the Pharmaceutical Manufacturers Association (http://www.ieis.org/tr/endustri/index2.htm Accessed on September 7, 2005) and the Association of Research-Based Pharmaceutical Companies (AIFD, 2004) have published codes of practice to their members[2] but our interviews suggest that none of these are enforced effectively.

2.4.4. Reimbursement

Currently, all social insurance organizations have positive lists for prescriptions. The SSK has a positive list (formulary) of 748 molecules covering the entire range of diseases. Emekli Sandığı, Bağ-Kur and civil servants are also subject to positive list (formulary) as a part of MoF Budget Implementation Guidelines (BIG) (Official Gazette No: 25702, 09.02.2005) comprising 6747 different forms of drugs in commercial names and basic features are;

- drugs not included in the positive list will not be reimbursed
- new drugs could be reimbursed upon approval of the reimbursement committee
- reimbursement committee convenes at latest in 3 months (currently more often due to backlog)

It is understood that SSK's positive list and BIG will merge by 2006 when all public reimbursement scheme would implement one single list with the same rules and procedures.

2.4.5. Dispensing

Pharmaceutical companies sell drugs to pharmacies, through pharmacy co-operatives and through wholesalers. Pharmacies are all "owned" and are in principle operated and managed by a pharmacist. Nevertheless, a pharmacist may not be present in the pharmacy at all times. There are also phenomena of "pharmacy-degree hiring" (muvazaa), which essentially suggest that the pharmacy may unofficially be owned by a third party and be operated by a "technician", without a qualified pharmacist being present. This phenomenon is said to be more widespread in the Eastern and South-eastern provinces of Turkey. Technicians, who are in many instances solely responsible for dispensing, have no formal training or qualifications in pharmacy or pharmacy practice and this is the norm throughout the country.

[2] A code of practice is a document containing guidance to those who agree to adhere by it, including, for instance, guidance for ethical behaviour.

A system of green and red prescriptions is used to control the sale of certain medicines, including psychotropic medicines (green prescriptions) and narcotic substances (red prescriptions). Chain pharmacies are not allowed in Turkey.

Pharmacists can substitute reimbursed outpatient products if they are below the reference price and the product to be dispensed is a lower-priced than the prescribed one. There is no "dispense as written" box on the prescription, and patients may actually prefer the branded original than the (branded) generic product. The generic for substitution should be listed officially to be one of the equivalent drug products. Since 2001, a nationwide information system allows pharmacists to obtain information on the equivalency profile of generic drugs for substitution for all drug reimbursement schemes.[3]

In the current environment, where (generic) substitution is allowed, the principal factor affecting the decision of the pharmacist concerning substitution is purely commercial. That is, the pharmacist is heavily influenced by the financial incentives such as industry/wholesaler discounts (which are allowed), the distribution of free goods ("mal fazlası"), and a flexible pay back period when it comes to the selection of the equivalent generic substitute among alternatives.[4] The actual scope and size of these incentives have not been studied but the total monetary value of these incentives may be highly significant requiring close attention, research and policy action.

In the presence of company discounts to pharmacy and (generic) substitution being allowed, pharmacies may have an incentive to dispense whichever product offers them the highest discount, taking also into account their (regressive) margin, although the latter may be a weaker incentive in the presence of discounts and free goods.

2.4.6. Prescription Monitoring

Currently, Emekli Sandığı and Bağ-Kur operate nation-wide computerised systems at pharmacy level that identify patients and their utilisation patterns, thereby potentially monitoring utilisation. It is nevertheless unknown whether policy-makers use the information therein to monitor and evaluate policies as well as follow up. It is understood that systematic prescription monitoring, audit and providing feedback to physicians are missing from the

[3] However, there is effectively a number of non-bioequivalent drugs on the Turkish market which are also on the reimbursement list. These products are either still to submit a bio-equivalency certificate until the deadline or have submitted one but await for the completion of the evaluation process by the MoH.

[4] The international experience suggests that pharmacists are either paid on the basis of fixed margins (negotiated with health insurance/the government) or operate on the basis of discounts. If the former, then discounts are officially disallowed and in fact forbidden, although they occur but their extent is very small. If the latter, then there are no fixed fees in place.

Turkish policy environment. However, discussions with senior officials have revealed that ground work is underway for a comprehensive monitoring and evaluation system some of whose supportive elements are to be piloted in the near future.

2.5. Pharmaceutical Pricing and Reimbursement Policies

2.5.1. Pharmaceutical Pricing

The decree on the Pricing of Medicinal Products for Human Use, which was issued by the Ministry of Health on 6 February 2004 (N° 2004/6781 and published on the Official Gazette of 14 February 2004 N° 25373) has now come into effect. This Decree was later modified by the Decision Amending the Decree Relating to the Pricing of Human Medical Products N° 2004/7124 dated 5th April 2004 and published in the Official Gazette of 14th April 2004. Parallel to these two legal acts, the Turkish authorities also published two explanatory Notifications.[5] Recently, the MoH has published a Decree (which has come into effect on 13 June 2005 - Official Gazette of 28th April 2005 N° 25799) where a 10% premium price allowed for products using domestically produced raw materials is no longer applicable.

In terms of pricing, Article 3 of the Decree, as amended by the related subsequent Decision provides for a basket of five EU countries (Italy, France, Spain, Portugal, and Greece for 2005) to be determined each year to be used as the basis for establishing the price of the original products. According to this amendment, the price of the original drug could be maximum of the ex-factory price of the country with the cheapest of the five reference countries. In case no ex-factory price is available, it could be as much as the sale price to the wholesaler as calculated from the consumer price of the same country by deducting VAT and mark-ups for wholesalers and pharmacies. If the ex-factory price in the country from where it is imported is lower than the designated reference price, the ex-factory price in the country of importation shall be taken as the reference price. The public sale price shall be determined upon adding the envisaged wholesalers and pharmacy mark-ups and VAT to the sale price to the wholesaler.

For generic products, the reference price is determined at 80% of the reference price determined for the originals (100% of the cheapest ex-factory sales price among the reference 5 countries). Similarly to the original products, if the ex-factory sales price of the product under pricing in the country of importation is lower than the generic product reference price,

[5] Respectively 3 March 2004 and N° 25391 and 22 April 2004 N° 25441.

the ex-factory price in the country of importation shall be taken as the reference price of that generic product. The final public price shall be determined upon adding the applicable wholesaler and pharmacy margins to the sale price to the wholesaler.

The Pricing Decree as amended by the relevant Decision and clarified by the above mentioned Notifications envisages the conclusion of the whole pricing process (pricing transaction) within 90 days upon the submission of all the necessary documentation by the company concerned. In case of heavy workload, this period may be extended by 60 days.

Finally, the Pricing Decree also envisages more structured, streamlined and time limited procedures not only for pricing but also for pricing adjustments of prices following price variations of the products in the reference (basket) countries or for re-determination of prices of products already in the market.

2.5.2. Price Revisions

Manufacturers and importers shall apply to the Ministry together with their requests for obtaining, increasing or decreasing a price. When the product is registered for the first time, if the price application of the company in question is not regarded as suitable by the Ministry, the concerned company shall complete the valid documents and submit its application; the pricing transaction shall take place within 90 working days as of the application date. The registration date of the price request of the concerned company in the documents of the Pharmaceutical General Directorate shall be regarded as the beginning of the 90 working days. The allowed period will be frozen on the date the non-acceptance decision is declared. The time will re-start as of the registration of the document in reply on the documents of the Pharmaceutical General Directorate. In case of failure of the concerned companies to submit their valid documents, the price determined by the Ministry shall be retained valid. In case of failure of the Ministry to issue any notification within 90 working days, the price requested by the concerned company shall be retained valid. But, in case of an accumulation of applications, if the company is notified by the Ministry before the use of the additional 90 days, the additional period of 60 days may be used. Anecdotal evidence suggests that these periods in practice are not effectively observed.

In case of a decrease of 5% or more in the price of the original product in the reference countries, the company manufacturing or importing the product shall be obligated to apply to the Ministry within 3 months to obtain a new price. A second degree withdrawal transaction shall be implemented on the products for it is determined by the Ministry that no such notification has been made and the registration shall be suspended for a period three times

longer than the period in which no notification has been made, including 3 months. The suspension transaction shall be annulled by issuing the new price at the end of this period.

2.5.3. Reimbursement Policies

2.5.3.1.General Principles

The public reimbursement system in Turkey mainly consists of SSK, Emekli Sandığı, and Bağ-Kur as well as Green Card scheme for individuals with income below the poverty level. In addition, there is a separate system for active civil servants which are financed by the Ministry of Finance. The Green Card scheme used to provide coverage for only inpatient care; the policy has now changed where the coverage has now been extended to outpatient care including drugs as of February 2005. There are about 700,000 private health insurance policy holders (about 1% of the population) who would also have publicly provided healthcare coverage.

There is co-finance arrangement for all state reimbursed systems (SSK, Emekli Sandığı, Bağ-Kur, Green Card, and active civil servants). Accordingly, those who are in active employment and the Green Card holders co-pay 20% of the price of the product; while retired beneficiaries, irrespective of their age, contribute 10%. The respective social security system picks up the remaining 80-90% of the established price. Retirement was up until recently defined on the basis of service years, rather than age, although, recently a retirement age limit of 55 for women and 60 for men has been established. As in most countries, there are exemptions to co-payment requirements for especially chronic diseases. Inpatient pharmaceutical costs for the insured population are by law fully reimbursed by respective social security institutions.

2.5.3.2. Reimbursement by Bağ-Kur

Bağ-Kur serves principally the self-employed and represents around 20% of the pharmaceutical market by value. Until the end of 2001 Bağ-Kur patients could obtain their prescribed drugs from private pharmacies with no limitations. In February 2002, Bağ-Kur switched to a generic referencing policy when it started to reimburse only the cheapest price plus up to 30% more. Some manufacturers in order to compensate the revenue loss and surmount prescription restrictions introduced different pack sizes and formulations of existing products. If the cheapest generic is 30 then the amount reimbursed would be equal to 39 (=1.30*30). A list of the molecules subjected to reference pricing by Bağ-Kur is presented in Table 2.4 below (now Bağ-Kur implement the same policy and has adopted Emekli Sandığı list which currently has 6747 different forms of drugs listed by commercial names). It is

understood that if the patient insists on the prescribed brand, then s/he would have to pay the difference out-of-pocket. It is understood that in subjecting molecules shown on Table 2.4 to reference pricing was decided mainly on the basis of total expenditure for each molecule. This list was limited and did not include all product categories.

Table 2.4. List of Molecules Subjected to Reference Pricing - Bağ-Kur (2004)

1. Amicacin Sulfate	20. Ciprofloxacin (excl. collyre)	40. Meloxicam
2. Amoxicillin Trihydrate	21. Clarithromycin	41. Metronidazole
3. Amoxicillin +Potassium Clavulanate	22. Clindamycin HCL	42. Naproxen
4. Ampicillin	23. Diclofenac Potassium	43. Naproxen Sodium
5. Ampicillin Sodium+Sulbactam Sodium	24. Diclofenac Sodium	44. Ofloxacin (excl. collyre)
6. Acyclovir	25. Enalapril	45. Omeprazole
7. Atorvastatin	26. Erythromycin	46. Opipramol HCL
8. Azithromycin	27. Etodolac	47. Ornidazole
9. Bacampicillin	28. Famotidine	48. Pantoprazole
10. Cefaclor Monohydrate	29. Finasteride	49. Pentoxifyllin
11. Cefadroxil	30. Flucanazole	50. Piracetam
12. Cefazolin Sodium	31. Fluoxetine HCL	51. Ranitidine
13. Cefotaxime Sodium	32. Ginkgo	52. Roxithromycin
14. Ceftazidime	33. Indapamide	53. Sertraline HCL
15. Ceftriaxone Disodium	34. Itraconazol	54. Simvastatin
16. Cefuroxime	35. Cetoconazole	55. Sulpiride
17. Cefuroxime Axetil	36. Cetotifen	56. Tenoxicam
18. Cephalexin	37. Lansoprazole	57. Tiamfenicol
19. Cetirizine HCL	38. Lisinopril	58. Trimethoprim+Sulphamethoxazole
	39. Loratadine	

2.5.3.3. Reimbursement by SSK

SSK operates under the Ministry of Labour and Social Security and serves principally employees of the private sector and blue-collar workers of public sector. SSK is providing social security coverage to almost 33 million people, including pensioners, comprising 48% of the Turkish population. However, the effective health coverage is reported to be around 34% of the entire population (MoLSS, 2005). In 2003, the SSK pharmaceutical expenditure approached US$1.4 billion a significant of which (14% in 2002) was related to the reimbursement of antibiotics. SSK had (until 19 February 2005) its own hospitals and pharmacies within hospitals. Until then, SSK used to procure most of its pharmaceuticals directly from wholesalers via tenders and dispense to its outpatients from its own hospital pharmacies.

According to the SSK reimbursement policy which was adopted in 1993 and remained in force until February 2005, SSK purchased the cheapest alternative from available products with the same active ingredient or the same therapeutic class. Consequently, the cheapest alternative (generic or original) of each molecule was purchased by SSK to be serviced to its patients at SSK pharmacies. If an SSK pharmacy was not available then the patient could

purchase the prescribed drug at private pharmacies where the SSK reimbursed them on the basis of the cheapest generic plus up to 30% more. “The cheapest plus 30%” rule, the essence of this policy, is still in force with some modifications which are mentioned below. This has been changed since 19 February 2005 due to transfer of all SSK hospitals to MoH, all SSK members receive prescribed drugs for outpatient care from private community pharmacies.

SSK has a positive drug list of 748 drugs in operation. The drug reimbursement decisions, that is the inclusion of drugs and conditions for reimbursement is reached by the SSK drug committee. The criteria for addition to the list include the therapeutic need, added value, and financial burden issues. The composition of this decision body includes physicians from different specialty areas and institutional pharmacists. This committee which is responsible for the technical principles and procedures for drug reimbursement meets -at least- twice a year. Of course, this reimbursement committee will be replaced by a MoLSS equivalent as part of the generalised health insurance implementation.

2.5.3.4. Reimbursement by Emekli Sandığı

Emekli Sandığı (Government Pension Fund) serves people retired from public service. Emekli Sandığı reimbursement system was exactly the same as the Bağ-Kur System before the reimbursement system changed in 2002, in which the generic and innovative products were all reimbursed as long as the doctors prescribed them by the brand. In March 2003, however, Emekli Sandığı also switched to a generic reimbursement policy based on the arithmetic average of all registered generics prices and the original product price. This system is called the “average reference price”. The example below shows how the system works:

Original product price	100
Generic A product price	50
Generic B product price	30
Emekli Sandığı maximum reimbursement price:	*60 = (100+50+30)/3*

There is always the danger that the application of a reference pricing system may result in a switch towards products that are not covered by the system, therefore increasing expenditure considerably, rather than containing its rate of growth, but robust evidence on this is not available.

The above system was discontinued in March 2004, following a court ruling. Emekli Sandığı, together with all other public reimbursement system began to implement a

reimbursement system similar to Bağ-Kur's. The details are presented in the following section.

Civil Servants drug reimbursement system is also subject to Budget Implementation Guidelines as mentioned above and funding is provided from ministerial budget.

2.5.3.5.The New Reimbursement System

It is understood that as part of preparation towards General Health Insurance and the reform process, the Social Security Institution (SSI), currently part of the Ministry of Labour and Social Security, has started to take over the major responsibility for the conduct of drug policy in Turkey. During a meeting with Mr. Tuncay Teksöz, President of the SSI, it is also understood that the new drug policy in Turkey operates on the basis of:

- A unified positive list that provides access to all insurees.
- An inter-ministerial reimbursement committee under the presidency of the MoF has been established according to the Pharmaceutical Pricing Decree. The Committee comprises of representatives of MoF (Emekli Sandığı), MoH (General Directorate of Curative Services and General Directorate of Pharmaceuticals and Pharmacy), MoLSS (SSI, SSK, Bağ-Kur).
- The government also plans to implement in detail, policies that will affect physician prescribing and overall authorising behaviour, although at the time of writing it is not known what form this will take, or what precise measures will be implemented. These may include (but are not explicitly confined to) drug utilisation reviews.

In the meantime, important amendments to the reimbursement policy for 2005, taking into account the unified health insurance scheme which will come into operation from 2005 onwards, were announced on December 14th, 2004. These amendments included the rebate from pharmacy, implemented from February 1st, 2005. The aim of this policy is to reduce the (informal, but significant) discounts that manufacturers offer to pharmacies, via their wholesalers, and resembles a clawback policy, similar to those currently in operation in the UK and the Netherlands. Until the General Healthcare Insurance is enforced, SSK, Bağ-Kur and Emekli Sandığı will continue to cover currently paid drugs and comply with the payment conditions of these drugs, in the year 2005 as well. These drugs will be listed according to their commercial name.

The policy stipulates that rebates will be applied by all public funds for drugs covered by these funds. These rebates will be as follows:

a. A 14.5% rebate will be applied on the pharmacy sale price for all generic drugs. The 3.5% portion of this rebate will be covered by the pharmacist, whereas the 11% portion will be covered by the manufacturer or importer.

b. The rebates to be applied on original drugs will be differentiated according to two drug groups:

   Group 1: With regard to drugs which have not completed 6 full years as of the first registration date of the relevant pharmaceutical molecule or a new chemical formula in Turkey, a 7.5% rebate will be applied over the pharmacy sale price. The 3.5% portion of this rebate will be covered by the pharmacist, whereas the 4% portion will be covered by the manufacturer or importer.

   Group 2: With regard to original drugs not falling into the first group and older than 6 full years, a 14.5% rebate will be applied over the pharmacy sale price. The 3.5% portion of this rebate will be covered by the pharmacist, whereas the 11% portion will be covered by the manufacturer or importer.

   The share of the rebate to be covered by manufacturers or importers (4% or 11%) may be invoiced to the wholesalers over the sale price to wholesalers. In such a case, wholesalers and pharmacies will reflect their current profit margins over the purchase prices and the pharmacy rebate may be carried out on the final price obtained. With regard to original products, in drugs the prices of which remain below the maximum prices dated June 15, 2004, determined with the Decision on the Pricing of Medicinal Products for Human Use, the rebate to be applied by the manufacturer or importer shall be less, in proportion with the amount remaining below the reference price.

c. With regards to drugs with a pharmacy sale price of 3 NTL and below, a 7.5% rebate shall be applied. The 3.5% portion of this rebate will be covered by the pharmacist, whereas the 4% portion will be covered by the manufacturer or importer.

In their equivalent drug purchases, all institutes will continue to reimburse the cost of those drugs at an amount of up to 30% more than the cheapest drug in the same reimbursement group. These cheapest drugs must be available on the market. The drug

designated as the cheapest drug taken as the ceiling, should be available in the market for at least 5 months.

2.6. Current Demand-Side Policies

Table 2.5 shows the actual (out-patient) consumption by therapeutic group in Turkey, with antibiotics, analgesics and anti-rheumatics accounting for more than 40% of total drug consumption. Cough and cold preparations as well as vitamins account for just under 15% of total consumption in Turkey. Some of these products are reimbursed by individual sickness funds, and there is great ambiguity of what products should be classified as OTC in Turkey. A relevant regulation has been published which is to come into effect on 31 December 2005. It is understood that lists of OTCs could be announced by the end of the year according to this Regulation. Reimbursed products also include other dietary supplements (such as Tebokan®, a Ginkgo-Biloba preparation) or nasal decongestants (e.g. Sterimar® or Liomer®, which contain pressurised salt water).

Table 2.5. Leading Therapeutic Groups by Pharmaceutical Consumption (2002)

Therapeutic Class	% of Total Consumption
Antibiotics	18.1
Analgesics	12.3
Antirheumatics	11.0
Cough and cold	8.4
Vitamins, minerals, antianaemics	6.4
Cardiovascular	6.1
Dermatologicals	5.3
Antacids, stomatologicals	5.2
Hormones and gynaecologicals	4.5

Source: IEIS, 2003.

2.6.1. Physicians

All physicians are paid on a salary basis with a revolving fund supplement, determined by additional revenues of hospitals. Additional revenues, and, therefore, the revolving fund, are generated by the authorising behaviour of physicians (e.g. laboratory tests, procedures, diagnostic tests, etc). In the MoH hospitals (which now also include all SSK hospitals from February 2005), for full time public sector practitioners, two-thirds of the total annual physician income comes from the revolving fund and one third from the salary determined by the government. There is, therefore, an explicit case of supplier-inducement, in that physicians have an incentive to authorise as many of these tests as possible, since they

determine their final salary. Understandably, health insurance organisations may have the power (or will have the power under the unified health insurance system) to change the pricing of the most widely authorised items, but this by no means eliminates the supplier-inducement phenomenon.

Some physicians, mostly senior, further supplement their incomes through private practice. Private practice is often used as a means to determine access and jump any waiting lists in the public system. Private practice fees are in principle paid either by the patient directly or by his/her private insurance if the latter exists. It is understood that physician and service fees in private practice are not regulated by the government, but it is understood that they are regulated by the Turkish Medical Association.

Prescription monitoring by private insurers has traditionally been tighter than scrutiny in the public sector, though explicit limits on prescribing in the private health market are relatively limited. The three state-run insurance funds have begun to increase controls on prescribing behaviour more recently – albeit largely through indirect measures such as the introduction of tighter reimbursement criteria.

The SSK, limited the number of products that may be prescribed by GPs in 2000. Resistance to similar controls is expressed more vocally by affiliates of the Emekli Sandığı and Bağ-Kur, but stricter controls will be necessary to ensure the financial viability of a merged public health insurance scheme. Common approaches to prescribing and reimbursement policy will be either encouraged or demanded in the run-up to a potential merger.

Central government has targeted prescription volumes as part of its cost-containment policy in recent years. Measures have included reimbursement delisting of certain expensive drugs (previously in the positive list) by transferring them to the Negative List of the BIG. Restrictions on the prescribing of certain therapeutic groups have also been introduced.

Other recent initiatives include the introduction by Emekli Sandığı and Bağ-Kur of computerised systems designed to rationalise dispensing of prescriptions. There is no evaluation of what these systems have achieved; interviews with decision makers suggest that there is no prescription monitoring, evaluation, audit and follow-up. The transfer of SSK hospitals to the MoH should encourage broader application of similar technology in the hospital sector.

Limits on the number of items that can be included in outpatient prescriptions in the public sector have recently been reduced from five to four. No such limits are imposed by most private insurers, and while prescription monitoring is more sophisticated in the private sector, branded drugs will remain a benchmark of quality for higher-income patients, and will be prescribed and dispensed much more widely in the private sector.

Generic substitution in Turkey is not mandatory in the public sector, but restrictions on reimbursement offered by state-run insurance funds have increased its frequency. Local generic manufacturers will attempt to drive rates of substitution by offering higher discounts and other incentives to pharmacists willing to dispense their products. Low levels of purchasing power among the majority of the population will also drive substitution rates.

MoH hospital managers are bound by guidelines from the MoH Directorate of Curative Services. Thus, as per the guidelines, a maximum of 50% of the funds (part of the overall revolving fund) can be used for topping up salaries, if the hospital has no other outstanding bills. The amount of these payments (salary supplements) is based on performance evaluations. Facilities collecting the revolving funds can use the receipts in different ways.

2.6.2. Wholesalers and Pharmacists

Official mark-ups for locally manufactured products were abolished at the beginning of 2002, leading to an effective 10% drop in prices. Previously, discounts passed along the distribution chain were sanctioned by the government during price negotiations. This had led to a situation where retail margins on some products were in excess of 30%, however, and with manufacturers also allowed to mark up their wholesalers' selling price by 14% as part of the discounting procedure retail prices had been seriously inflated. The wholesale and retail margins as well as their ranges for the (ex-manufacturer) price of the product are shown on Table 2.6 and 2.7 respectively.

Widespread protests by pharmacists, who had also been affected by a reduction in import margins introduced in 2001, prompted manufacturers to reinstate a 4% discount on local products (this has since raised to 5%). Wholesalers offered a further 1%, subsequently increased to 2%, giving back retailers a total 7% discount. Pharmacy margins were also preserved by a cut in discounts offered to the government, which fell from 5% to 2.5%.

Discounts on all drugs are legal even in low-volume transactions. Local companies have incorporated discounting and free goods as part of their bargaining strategy in the

current market environment, since failure to offer such incentives could lead to the loss of sales volumes. Discounting is likely to retain its popularity driven by competition for access to reimbursement lists.

Margins on imported products were cut in 2001, negatively impacting both importers and the retail pharmacy sector, where the contribution of imported products to turnover has fallen sharply. Pressure on retailer margins is also exerted by payment delays from the state-run insurance funds to pharmacists, who are required to settle their own accounts with distributors on a monthly basis.

Table 2.6. Pharmaceutical Sector Margins for Imported Products (Before 2004)

Components	Mark-Up Levels as %	
	Before 2001	After 2001
Cost margins	20	6
Manufacturer	14	10
Distributor	9	7
Pharmacist	25	20*

* Calculated in relation to the ex-factory price; if calculated on the retail price basis, pharmacy margin actually reduced to 16.6%.

Currently, a standard-level value-added-tax (VAT) of 8% applies to both prescription and OTC-type medicines. This rate was 18% prior to 1 March 2004.

Table 2.7. Wholesaler and Pharmacy Margins (Since 2004)

Ex-Manufacturer's Price (in NTL)	Wholesaler (%)	Pharmacy (%)
The part ≤ 10	9	25
The part between 10-50	8	24
The part between 50-100	7	23
The part between 100-200	4	16
The part >200	2	10

Consumer prices are calculated by adding to the ex-factory prices wholesaler and pharmacy mark-ups and VAT. Wholesaler and pharmacy mark-ups are of digressive nature. As shown in Table 2.7, mark-ups decrease as the ex-factory price increases. The Ministry of Health is authorized to review these rates by taking into consideration the annual wholesale price index of chemical products of the State Statistics Institute of the former year and the allocation of the total sales of medicinal products in the last 3 years.

More than 400 companies are registered as pharmaceutical wholesalers, but less than 100 are active in the market. Major players include Hedef Alliance (50% owned by UK-based Alliance UniChem), and Selçuk Ecza, which account together for over 70% of the market. Regional pharmacy co-operatives are also a significant factor in the market, with organisations in Bursa, İzmir and İstanbul holding an estimated 10% of the market and serving around 5000 outlets between them. The number of wholesalers will fall over the coming years, due to a combination of tighter pricing regulations and distribution standards as well as rising competition within the sector.

Pharmacists have begun to play a more prominent role in the market following the introduction of reimbursement ceilings by state-run insurance funds leading to increased rates of generic substitution.

2.7. Other Elements of Drug Policy

2.7.1. Hospital Tenders

Early in 2003 the government began to purchase drugs used across the SSK network mostly through a centralised drug tender. As SSK was required to honour individual annual contracts signed in previous months with various pharmaceutical manufacturers, the introduction of the system caused initial confusion. According to the new tender law, wholesalers are also able to bid for contracts, and some have been created specifically for this purpose.

For purchases of lifesaving drugs at values up to NTL150,000 SSK can deal directly with the relevant companies, meaning that most transactions are carried out via tenders anyway. The change from a system based on bidding by individual hospitals was, however, deemed necessary following substantial mismanagement of the fund, and the subsequent accrual of losses, which have been blamed partly on unethical practices by some suppliers.

The centralised tendering process has failed to achieve significant savings. Factors blamed for this include lack of foresight on the part of the administration, which has introduced the system without proper planning and especially without piloting. Additionally, SSK has not reduced the total amount of drugs its hospitals procure, and has also suffered a negative impact of price increases. Prior to the introduction of the single tender, SSK hospitals had an average discount of 7% and were able to obtain reductions on the price of original brands. These discounts are no longer applicable.

Although some early problems have been solved, the tender system is still regarded as cumbersome and inefficient by the pharmaceutical industry. Invitations for tendering are sometimes announced late (or even not announced at all), giving little time for companies to prepare their bids, while price has emerged as the decisive factor in most tender decisions.

Nevertheless, tendering is likely to continue. The SSK remains deeply in debt, and still often fails to meet payment terms to suppliers. As a result, wholesalers prefer cash only purchases. The improvement of payment terms is considered a priority.

Many small distributors compete for business in the public hospital tendering sector, and a number of specialist companies have been established explicitly for this purpose following the introduction of centralised tendering. Established players in retail distribution sector have found it difficult to come to terms with the bureaucratic nature of the new tendering process, but are expected to seek broader involvement as teething problems with new procedures are addressed. Direct distribution is only allowed between manufacturers and hospitals that have licensed pharmacies on their premises.

Individual manufacturers usually deal with three or more wholesalers, partly in order to achieve reasonable geographical coverage of the market, but also in order to maximize profits. Electronic ordering systems have yet to become commonplace, although the standard and speed of service offered by major distributors is reasonably high. Deliveries are prompt and frequent, especially to retail pharmacies, many of which have been forced to limit stocks as a result of delayed payment for products reimbursed in the state-run insurance sector.

2.7.2. The OTC Sector

2.7.2.1.Stylised Facts in the Turkish OTC Market

Non-prescription or over-the-counter medicines (OTCs) are sold without prescription and are used to treat minor ailments and considered to be safe for self-medication often on the advice of pharmacists. OTCs concentrate chiefly in the following therapeutic classes: Analgesics, Antiseptics, Vitamins and Minerals, Cough Cold, Digestive System remedies, Laxatives, Dermatologic products, Ophthalmologic products and Sleeping Regulators. To be classified as OTC, a medicine should be assessed on the basis of various criteria including indications, side effects, routes of administration, dosage and length of use. The prices and marketing approval of what would normally be classified as OTC are controlled by the Ministry of Health. Except for a limited number of OTCs, almost all OTCs are reimbursed by the social sick funds/programs. About 70% of all OTCs in Turkey belong to nine ATC classes. These are in order of significance: Cough & cold preparations (16%); Analgesics

(15%); Cerebral/Peripheral Vaso-therapeutics (Ginkgos) (9%); Nasal Decongestants and Anti-infectives (7%); Vitamins (6%); Mineral Supplements (4%); Systemic Antihistamines (3%); and Topical Anti-rheumatics (3%).

Estimates of the OTC market, based on a number of assumptions (including that there would be no OTCs dispensed in the ***hospital market*** where the majority of the medicines are used for inpatients), suggest that in 2003, the total ex-factory value of medicines that could be classified as OTC was US$807 million. Of this total US$126 million worth of drugs were excluded from the reimbursement list (the "negative list" of the BIG). Therefore, the total ex-factory value of reimbursable OTCs was US$681 million and US$924 million at consumer prices (wholesaler and pharmacist margins as applied to locally manufactured products together with VAT are included). The total OTC market, at consumer prices would be about US$1.1 billion. It is assumed here that of the total reimbursable OTC market 42% is paid out of pocket by consumers (the remainder, 58% is met by the state). When this is reflected in the calculations together with adjustments for VAT and co-pays, the net share of the public sector is estimated to be around US$484 million (consumer prices).

Table 2.8. Size of OTC Market and Financial Burden of the State in Turkey, 2003

Ex-Factory Prices (US$ thousand)			
	IMS Market	**SSK** (Estimate)	**Total**
A – Total OTC	608,177	199,040	807,216
B – Reimbursable	513,250	167,973	681,223
Consumer Prices (US$ thousand)			
	IMS Market[1]	**SSK**[2] (Estimate)	**Total**
A – Total OTC	879,628	214,963	**1,094,591**
B – Reimbursable	742,332	181,411	923,743
C – Share of social security organizations[3] **(B–Co-pays)**	368,494	154,199	522,693
D – Total share of public sector[4] **(C–VAT)**	341,198	142,777	**483,975**

[1] In calculating consumer prices; wholesaler margin: 8%, pharmacy margin: 24%, VAT: 18%.
[2] Only VAT of 18% added.
[3] The social security organizations represented about 58% of the total OTC market based on a market survey. Patient co-pay is taken as 15% on average.
[4] VAT is deducted.

2.7.2.2.Caveats

It is widely estimated that the state pays for 80% of all pharmaceutical spending in Turkey. Insofar as OTCs are concerned, however, the state finances about 58% of the total OTC market. Based on the evidence presented above, it is seen that OTC financing places a significant financial burden on the public budget. In 2003, the total state burden is estimated to be around US$523 million.

The evidence presented in the previous section indicates that OTC reimbursement is responsible for an estimated burden of US$484 million for the state budget. This can be allocated elsewhere, given that the vast majority of OTC products are for minor ailments are no longer routinely reimbursed in the majority of EU Member States.[6]

Pharmacists seem to have played a pivotal role in "blocking" proposals to establish an explicit OTC drug category in the late 1990s, but pressure for the introduction of similar measures has increased in recent years and the profession is unlikely to be successful in defeating anticipated government proposals this time around. The current administration has already withdrawn many OTC-type products from state reimbursement lists. The creation of an explicit OTC classification will offer considerable cost-savings to the government. Assuming that an OTC classification is introduced, such products will be restricted to distribution through pharmacy outlets in the near future. The profession fears the eventual liberalisation of OTC drug supply, however, leading to the introduction of direct competition from supermarkets and other powerful non-pharmacy retail chains.

With no separate legal classification for OTC medicines, most OTC-type products are currently required to undergo the same registration procedures as other prescription drugs, and are available only through pharmacy outlets.[7] Moves towards the creation of an explicit OTC category are under way, however. In December 2003 the government lifted direct-to-consumer (DTC) advertising restrictions on non-prescription products in a move that was widely regarded as the first step towards the establishment of a separate, non-reimbursable OTC drug category. Turkish Pharmacists' Association opened a lawsuit against this situation and this was later accepted by the court and implementation was rejected.

[6] With the exception of a number of new accession countries in Eastern Europe, which are currently trying to minimize the impact from OTC reimbursement on their pharmaceutical budgets.

[7] There are currently a limited number of products classified as OTC based on decisions of the by-product commission.

It is suggested that products which are likely to be listed in OTC category be gradually delisted from the reimbursement list. It is not clear whether the government will entertain such an idea, however, and the cost-cutting implications of immediate de-listing are likely to prove attractive in the current financial environment.

2.8. Out-of-pocket and informal payments by Turkish patients[8]

A recent study aiming to identify the extent and reasons of informal payments in the health sector in a medium size city in Turkey revealed a number of interesting facts about the existence of such payments and coercion on the side of patients. Of the total payments made to the public sector, 62% was formal and 38% was informal. The figures for the private sector were 78% and 22% respectively. As Table 2.9 shows, in the public sector, the majority of both the formal and informal payments occurred for drugs. For the informal payments this is followed by the physicians' surgical services and donations. Donations are the amount that is paid to associations and foundations attached to hospitals or health centres. These payments are not linked to any specific service or purpose. As its name suggests, donations should be based on the willingness of the person to donate something to the hospital or the health centre. However, in practice, these amounts are forced on individuals to pay and are, therefore, regarded as informal. The effect of under-insurance and "knife payments" can also be seen in the table too. So far as the private sector is concerned, not surprisingly, the informal payments were for physicians' medical services. This reflects the influence of "part-timers"[9] in the health sector. The negative influence of part-timers on the health sector has long been discussed in various quarters. It is a well-known fact that part-timers offices usually serve as a bridge for public services. Part-timers can work half day in the public hospital and half day in their private clinics. It is very widely known among the patients that if they visit the private office of the doctor first, they will get better treatment, as well as jump the queue for tests and surgery. That is why although covered by a health insurance scheme giving the right to utilize free public services, patients refer to private practice first.

[8] This section builds on a recent study by M. Tatar et al (2003). Informal payments include all non-statutory payments made by insured patients to the service providers either in cash or in kind. These include the so-called "knife-payments (bıçak parası)" as well as out of pocket payments, other than statutory co-pays, made by say an SSK beneficiary for a medicine. Moreover, it should be noted that those medications to be used for hospitalized patients are also classified under informal payments if acquired from community pharmacies according to OECD-SHA methodology.

[9] In Turkey, the definition of "part-timers" may not be so clear. However, the term here has been used to refer to the actual situation/practice.

Table 2.9. Out-of-Pocket Payments According to Purpose for Public and Private Providers (%)

Purpose	Public Providers		Private Providers		Total
	Formal	Informal	Formal	Informal	
Donation	-	11.1	-	-	1.3
Physicians' medical services	9.2	2.3	29.8	99.0	32.6
Physicians' surgical services	8.2	23.5	-	-	4.4
Drugs	70.3	50.5	49.7	1.0	46.7
Nurses' /other staff's care	-	1.5	-	-	0.2
Laboratory/ imaging tests	8.1	-	12.2	-	8.2
Other services	4.0	11.1	8.3	-	6.6
Total	100.0	100.0	100.0	100.0	100.0

Source: Tatar, et al., 2003.

The study also shows that:

1. Informal payments comprised of 25% of out-of-pocket (OOP) payments.
2. Payments for drugs accounted for the majority of the formal payments. Informal payments for medicines include payments made mainly OOP (other than statutory co-pays) by insured individuals and particularly medicines acquired from community pharmacies for in-patients.
3. The majority of the informal payments were in the form of cash payments. Gift and in-kind payments also existed to a lesser degree.
4. Physician office visits and payments for surgery (i.e. the so-called knife-payments) arose as the most important types of informal payments. Both the influence of part-timers on the health sector and extra payments for surgeons have been discussed by all the parties related with the health sector for a long time. It is widely acknowledged that in Turkey if a patient wants to get a prompt and better service s/he has to visit the private office of the doctor first. In addition, some surgeons ask for extra money for performing surgery ("knife payments"). The evidence from this study suggests that these two practices are the main reasons for informal payments.
5. The under insurance phenomenon ("double billing") is raised as an important issue for health policy makers in this survey. Under insurance occurs when a

patient pays for the services although he is already covered by a scheme. This issue is verified by the fact that the insured population also paid informal payments especially in physicians' offices and physician services in the public hospitals. Thus, health insurance coverage does not mean that OOP payments both formal and informal are avoided.

6. Even Green Card holders, who theoretically constitute the poorest section of the population, had to pay for informal payments. The majority of these payments occurred ironically in the public facilities where the MoH facilities had the largest share. The knife payments also had a large share for the Green Card holders.

7. For the hospitalized patients the majority of the informal payments were for in-kind contributions which comprised drug purchases, food, medical supplies, and expenditures for the accompanying person. These payments occurred predominantly in MoH facilities. Furthermore, Green Card holders were the major payers of informal payments in MoH facilities where they are supposed to get care free of charge.

8. In the public sector the poor paid more informal payments per capita than the wealthier segments of the population. The elderly also paid more informal payments per capita then the young. The unemployed also paid more informal payments per capita in the public sector then the rest. The findings were further exacerbated with the analysis of the reasons for not seeking, delaying or interrupting treatment. A significant number of people did not seek treatment for lack of money even among the insured population. For interrupting treatment, the lack of money was the main reason for 93.3% of Green Card Holders and 73.3% of the insured population.

2.9. Access to Medicines by the General Population

Access to medicines in Turkey by the general population does not present significant problems for the insured population. With a recent policy change (1 January 2005) Green Card holders now benefit from outpatient healthcare coverage including pharmaceuticals.

Although access issues are less important, there seem to be are issues of quality of care and issues of appropriate prescribing. According to two recent studies[10], 45% of the total number of prescriptions (by volume) and 55% by value are thought to be inappropriate.

Finally, the phenomenon of informal payments is less prominent in pharmaceuticals. However, this may hinder access to health care services among the less privileged segments of society (e.g. Green Card holders).

2.10. Concluding Remarks and Issues Arising

The situation analysis has taken place at a critical and very dynamic juncture in Turkish health care reform, with sweeping systemic changes occurring across the board. The timing is therefore right for any inconsistencies and problems that have been identified to be debated and rectified. In particular, the situation analysis has highlighted a number of issues, which, in many cases, generate problems in the implementation of a national drug policy in Turkey.

Pricing

- While the lowest of the five prices from a basket containing 5 EU countries appears to be a logical way of devising a pricing strategy in Turkey, the same cannot be said about the pricing methodology for generic products. The current maximum ceiling of 80% of the originator price may lead to high prices for generic products.
- The non-existence of pure generic (non-branded) products does not necessarily allow for the implementation of a robust generics policy, although, understandably, generics may still need a further vote of confidence by prescribers and patients alike.

Reimbursement

- Although up until recently there was no unified reimbursement system, the government is gradually implementing such a principle, working from bottom upwards. This will eliminate differences across insurance schemes and will increase equity in access by less privileged social groups, i.e. Green Card holders. The downside to this development is the cost, which, according to some estimates

[10] Meeting with Dr. S. Mollahaliloğlu, Ankara.

may be as low as $800 million (conservative estimate) and as high as $2.5 billion.[11]

- It is unclear at this point whether the unified reimbursement system (as applied by Bağ-Kur) based on haphazard and selective price referencing yields any benefits or is robust to take account of market dynamics. Indeed, a general evaluation of this system has suggested that it may at times be cheaper for Bağ-Kur to even reimburse originator branded products than to reimburse generic versions of these products.
- It is unknown what principles guide the admission of (new) products into the reimbursement list and how robustly these are followed. There is also little information on the experts involved in reimbursement decisions and their respective contribution. Indeed, the roles and responsibilities of drug reimbursement decision makers not clearly defined.
- It appears that several medications, which should in principle be available as over-the-counter, are actually reimbursed by insurance funds. This may lead to waste of scarce resources by health insurance and could be done on a selective basis initially, before being altogether abolished (with few exceptions) in the long-run.
- It also appears that other elements of Turkish reimbursement policy are not robust; for instance, in addition to the positive list and the criteria for inclusion, our interviews suggest that there is little being done on rational drug use, on monitoring physician prescribing, audit, or drug utilisation review.

Proxy demand-side

With regards to policies influencing physician behaviour, we have identified several problems, which affect quality and appropriateness of care and may also lead to waste of scarce resources. The problems outlined below reflect the situation in physician prescribing and authorising behaviour.

- Physicians always prescribe by brand name; although pharmacists can substitute for a (theoretically cheaper) generic, the entire system may not necessarily create any savings worthwhile mentioning.

[11] Both figures come from individual statements in meetings with key experts and specialists who are currently involved in the health care reform process. They represent broad "guesstimates" and should therefore be treated with caution.

- There is a multi-tier system with some physicians also practicing privately
- Enforcement of available clinical guidelines by clinicians remains non-existent.
- Physicians and other health care professionals working in hospitals and primary care centres are considered to be civil servants and their productivity is thought to be low.
- At the other end of the spectrum, an increase in "productivity" is thought to occur through physicians' supplementary payments. Physician authorising behaviour in hospitals is explicitly linked with the size of the hospital revolving fund, from which physicians draw a significant proportion of their salary; there is, therefore, an explicit occurrence of supplier-induced demand, which may lead to a waste of scarce resources because of the financial incentives to physicians from this practice. Some of the decision makers believe that the Turkish population is potentially under-using the (publicly funded and provided) healthcare system; service provision through revolving fund is encouraged and this would lead to improved service utilization. However, this practice may have distortionary and potentially disastrous effects in the long-run.
- In terms of human resources, there are urgent needs in more practicing physicians in the country on the basis of (i) increasing patterns of utilisation; (ii) increases in population; (iii) small number of general practitioners; and (d) physicians who retire.
- There are great challenges in terms of management team training in hospitals to run the reforms; there are currently very few, if any, hospital managers and most hospitals are run by lead physicians.

Pharmacies

- The "muvazaa" practice and the lack of skills among dispensers undervalue the contribution of the pharmacy profession and its role as providing, among others, proper counselling to patients.
- A further "devaluation" of the pharmacy profession is underwritten by the near complete absence of any regulation regarding pharmacy location, geographical distribution and the total number of pharmacies in the country. While this policy was probably important up until this point in order to enable more pharmacies to

offer services to patients, policy makers would probably need to address the problem from now on.

- Pharmacists are paid on a regressive margin basis from health insurance funds, but they also receive (unknown but thought to be generous) discounts and free goods from manufacturers. It is thought that the reimbursement authorities are not aware of the extent of such discounts and free goods. An evaluation of pharmacy income as well as target income for the official dispensing (Rx) business has never taken place.

Other

A key general problem is the enforcement of legislation; this is thought to lead to the continuation of old and persisting problems on the demand-side but also the supply-side. These phenomena relate to prescribing, dispensing, as well as the existence of informal payments, as discussed in previous sections. A key task for the present government will be to enforce legislation, if reforms are to succeed, despite the political cost it may imply.

3. Pharmaceutical Policy from an International Perspective: A Comparative Analysis

3.1. Introduction

Governments try to regulate few markets as much as they do the pharmaceutical market. They have to balance contrasting objectives. First, governments must secure health policy objectives: protecting public health; guaranteeing patient access to safe and effective medicines; improving the quality of care; and ensuring that pharmaceutical expenditure does not become excessive so as to undermine these and other government objectives. Equity and efficiency (i.e. making best use of limited resources to increase population health), and meeting patient need are therefore perhaps the prime objectives. Health economists might equate efficiency with quality: doctors and patients would define quality as treating the patient appropriately, i.e. as the patient needs for their condition, and with only limited, if any, consideration of cost or cost effectiveness. One of the roles of government in pharmaceutical policy is to provide the funding and framework that allows that efficiency as well as quality of care is promoted.

Cost containment is thus not a main health policy objective in itself but is one of the few tools that governments employ in their attempts to manage pharmaceuticals and to achieve a balance between these conflicting demands. Governments therefore have often seemed to concentrate on this as a regulatory measure, especially targeting the supply-side of the market, namely the pharmaceutical industry; demand-side instruments are now also increasingly used. The success of these policies is varied and in many countries pharmaceutical expenditures nevertheless continue to rise. The impact of these cost containment policies on efficiency and quality of care and prescribing is also often unclear. Governments may seek ideas for solutions from the experience of other countries, bearing in mind the different contexts in which they work. There are also concerns about future developments - for example, the impact of new technologies (such as the developments in pharmacogenomics) and of course, the impact of demographic shifts in ageing populations.

Second, governments must also balance these health policy objectives against those of industrial policy, i.e. encouraging drug research and development, continued employment in the pharmaceutical sector, and a positive balance of trade with regard to drug exports.

A variety of controls and incentives are used in different countries to try to balance effective and efficient spending on drugs against the need to promote a major industry.

Regulating pharmaceutical markets is complex and involves a dynamic interplay between government and multiple actors, not just the prescribing physician. Pharmacists have an active role not only in dispensing but also in selecting multi-sourced products and in product procurement. Wholesalers can affect the final retail price. The pharmaceutical industry itself has an extremely important influence in terms of not only product development and pricing, but also on levels of drug utilisation as a result of marketing and information dissemination. Finally, patients today are more informed about their own health and treatments, and in some countries have been given financial disincentives to make them more aware of their pharmaceutical consumption. All of these must be taken into account in trying to regulate pharmaceutical expenditures.

Many of these trade-offs, market structures and regulations do not exist for any other industrial sector. The pharmaceutical market is unique with regard to the extent and depth of its failure to meet the criteria for a perfect market (Jacobzone, 2000; Dukes, et al., 2003). There are market imperfections in both supply (generally related to patent protection, the process and length of regulatory approval and brand loyalty) and demand sides (there is a four-tiered structure of demand where the physician prescribes, the pharmacist dispenses, the patient consumes and a third-party pays). Other fundamental characteristics of pharmaceutical and healthcare markets that make it less ideal for allocation solely by market mechanisms include the existence of indivisibilities and externalities.

In this section, we provide an overview of the policies and the systems by which countries try to address these problems. It is difficult to assess which has been the most effective, as measures and policies are rarely applied singly, and it is often impossible to disentangle the influence of each in an overall effect. Many of the effects observed may be context specific, and may not indicate a universal truth as to which approaches are the most likely to bring about a change. Even where interventions have been studied individually, the quality of the evidence may be weak: this will be considered for each approach in turn. Finally, we focus on issues relating to pharmaceutical pricing, reimbursement and access issues rather than the pure regulatory aspects of marketing authorisation, approval and intellectual property rights protection, although some of these aspects have been dealt with within the Turkish context.[12]

[12] Intellectual property rights protection has a common broad framework under the TRIPs Agreement. Within the European framework, particularly that of the EU, Turkey must have adopted and also implemented a standard marketing exclusivity clause and a Supplementary Protection Certificate (SPC), when the time comes to join the EU. Marketing Authorisation in Europe subscribes to the framework set out by the European Union and

3.2. Trends in Pharmaceutical Expenditure

Although most healthcare in EU member states is publicly funded, this is not universally the case in the pharmaceutical sector, where levels of private expenditure are often high (Table 3.1). A significant proportion of pharmaceutical expenditure is private in Belgium, Italy, Greece and Denmark (OECD, 2004). Between 1980 and 2000, the public share of total expenditure on pharmaceuticals declined in 9 out of 14 EU member states for which data exists, largely because of attempts to contain healthcare costs (Mossialos and Le Grand, 1999). The decline was small in Sweden, the Netherlands, Portugal and the United Kingdom, but substantial in Italy and Belgium. Conversely, some countries saw an increase in the share of public expenditure on pharmaceuticals – significant in Ireland, more modest in France and Spain. Countries with low total pharmaceutical expenditure as a percentage of GDP include Ireland, Luxembourg, and Denmark, while those with high pharmaceutical expenditures in terms of GDP as well as percentage of total health expenditures include Italy, Portugal, France, Spain, and Greece.

Between 1995 and 2002, most countries increased their public pharmaceutical spending as a percentage of total health expenditure; the exceptions being Belgium, Denmark, and Luxembourg (Table 3.1). Looking back over the last two decades, between 1990 and 2002 the unweighted average of per capita pharmaceutical expenditure (in US$ PPPs) in the EU member states (excluding Austria) increased by 79.9%, prompting much greater attention to drug expenditures during the 1990s.

Most data on pharmaceutical spending, however, do not distinguish between different types of private expenditure. As a result, it is difficult to determine how much private expenditure arises from direct payments, such as spending on over-the-counter (OTC) products or prescribed products that are not reimbursed by the statutory healthcare system, and how much arises from user charges, i.e. co-payments for reimbursed products. Although OTC drugs are usually relatively inexpensive and consumed by a large proportion of the population, the distributional impact of OTC drug expenditure is not easy to measure.

Additional methodological problems exist when performing cross-country comparisons of pharmaceutical expenditure and prices; biases include exchange rate fluctuations, differences in pharmaceutical prices between countries, and variations in private

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the European Medicines Evaluation Agency (EMEA) in particular. Turkey must implement this framework for pharmaceutical product approvals and adjust its policies to become aligned with this framework. Indeed, the Turkish regulatory authorities do participate in Europe-wide initiatives, such as PEFRAS, to inform and assist them in their national policies.

(out-of-pocket) and public coverage. To eliminate price level differences in inter-country comparisons, conversions using Purchasing Power Parities (PPPs) equalise currencies to allow the purchase of the same basket of goods and services in different countries (although, even PPPs present problems from a comparative perspective). In addition, there are challenges in separating out factors that influence drug prices caused by the structure of the market in each country: different health system structure and financing, divergent regulatory and pricing policies, drug subsidies, production costs and product mix variations. Furthermore, consideration must be given to where price information is taken from within the distribution chain, as wholesale and retail prices are marked-up from the manufacturer's price – ideally it should always be taken from the same point in each country, but this is not always possible.

Table 3.1. Pharmaceutical expenditure in EU member states (1980-2003*)

	Total expenditure on pharmaceuticals (% GDP)					Total expenditure on pharmaceuticals (% of total health expenditure)					Public expenditure on pharmaceuticals (% of total pharmaceutical expenditure)					Total per capita expenditure on pharmaceuticals (US$ PPPs)				
	1980	**1985**	**1990**	**1995**	**2003***	**1980**	**1985**	**1990**	**1995**	**2003***	**1980**	**1985**	**1990**	**1995**	**2003***	**1980**	**1985**	**1990**	**1995**	**2003***
Austria	-	-	-	-	1.5	-	-	13.2	10.4	16.1	-	-	-	-	74.9	-	-	-	-	358
Belgium	1.1	1.1	1.1	1.4	1.6	17.4	15.7	15.5	16.3	16.2	57.3	51.0	46.8	43.0	44.7	100	139	193	309	318
Denmark	0.6	0.6	0.6	0.7	1.1	6.0	6.6	7.5	9.1	9.2	49.9	45.5	34.2	48.6	52.5	50	77	109	171	239
Finland	0.7	0.7	0.7	1.1	1.4	10.7	9.7	9.4	14.0	15.9	46.7	44.5	47.4	45.3	53	54	82	122	199	309
France	-	-	1.4	1.7	2.5	-	-	16.8	17.5	20.8	-	-	61.9	61.4	67	-	-	254	346	570
Germany	1.2	1.3	1.2	1.3	2.2	13.4	13.8	14.3	12.3	14.5	73.7	71.9	73.1	72.3	74.8	110	172	228	269	408
Greece	1.2	1.1	1.1	1.5	1.5[1]	18.8	-	14.5	17.3	15.3	60.0	-	70.3	70.0	71.5	65	83	104	195	278
Ireland	0.9	0.8	0.7	0.7	0.7	10.9	9.9	11.3	9.7	11.0	52.7	60.7	65.0	78.3	84.2	50	58	88	126	259
Italy	-	-	1.7	1.5	1.9	-	-	21.2	20.9	21.9	-	-	62.8	38.3	48.9	-	-	280	311	484
Luxembourg	0.9	0.9	0.9	0.8	0.9	14.5	14.7	14.9	12.0	11.6	86.4	86.0	84.6	81.7	82.5	88	132	223	255	355
Netherlands	0.6	0.7	0.8	0.9	1.6	8.0	9.3	9.6	11.0	10.4	66.7	63.3	66.6	88.8	60.6[2]	53	83	128	196	276
Portugal	1.1	1.5	1.5	1.9	1.9	19.9	25.4	24.9	23.2	23.4	68.6	64.7	62.3	63.3	66.1[2]	53	97	152	266	302
Spain	1.1	1.1	1.2	1.4	1.9	21.0	20.3	17.8	17.7	21.5	64.0	62.5	71.7	75.8	73.6	69	93	145	210	354
Sweden	0.6	0.6	0.7	1.0	1.4	6.5	7.0	8.0	12.5	13.1	71.8	70.1	71.7	71.4	69.3	55	82	120	202	329
U. Kingdom	0.7	0.8	0.8	1.1	1.2[1]	12.8	14.1	13.5	15.3	15.8	67.6	64.1	66.6	63.5	64.2	57	94	131	201	252[1]

* or latest available year
[1] 2002
[2] 2001

Source: OECD 2005; Economist Intelligence Unit 2005, WHO 2003

3.3. Regulating Pharmaceutical Prices

In the 1990s, pharmaceutical expenditures became a common target of healthcare cost-containment efforts. In general, such pharmaceutical policies are expected to yield lower costs in the subsequent year(s) while improving efficiency and equity. Policy-makers in a number of countries see controlling drug prices as less politically sensitive than cutting the salaries of health professionals or rationing particular medicines or other healthcare services. The implications of doing so at least on the incentives for innovation are part of a wider debate that is beyond the scope of this report.

Total pharmaceutical expenditure is a function of the quantity of drugs dispensed, multiplied by price. Increases in total pharmaceutical expenditures are driven by many factors including changing demographic patterns, changes in product mix, introduction of new often more expensive medicines, and an increasing number of 'me-too' drugs. Equally important are the imperfections in the supply and demand of pharmaceuticals that lead to market failure. In an attempt to correct for market imperfections, and control other factors driving rising drug expenditures, most western European governments have aimed much of their cost-containment effort at the supply-side of the market in the form of price controls, but demand-side measures such as financial incentives, quantity controls and educational initiatives for doctors have also been widely used with variable success.

Whether or how pharmaceutical prices are regulated varies among European Union (EU) countries, as shown in Table 3.2. The differing approaches reflect distinct national policy priorities: the need to contain pharmaceutical expenditures; whether and how the demand for pharmaceuticals is regulated; and the relative weights of health policy and industrial policy objectives (for example, promotion of pharmaceutical research and development, employment, a positive balance of trade). Measures for directly controlling pharmaceutical prices have commonly included negotiated prices, maximum fixed price, international price comparisons and price cuts or freezes. These direct methods have been included here under the term direct price controls. Alternative approaches include controlling reimbursement levels by trading off price decreases against volume increases. Indirect approaches include regulating profits or setting reference prices (reimbursement limits).

Table 3.2. Summary of Approaches to the regulation of Pharmaceutical Prices in EU Member States

	Market Segment	Free Pricing	Direct Price Controls	Use of International Price Comparisons	Profit Controls	Reference Pricing
Austria	In-patent		✓	✓		
	Off-patent		✓	✓		
Belgium	In-patent		✓	✓		
	Off-patent			✓		✓
Denmark	In-patent			✓		
	Off-patent			✓		✓
Finland	In-patent		✓	✓		
	Off-patent		✓	✓		
France	In-patent		✓			
	Off-patent					✓
Germany	In-patent	✓				
	Off-patent					✓
Greece	In-patent		✓	✓		
	Off-patent		✓	✓		
Ireland	In-patent		✓	✓		
	Off-patent		✓	✓		
Italy	In-patent		✓	✓		
	Off-patent					✓
Luxembourg	In-patent		✓	✓		
	Off-patent		✓	✓		
Netherlands	In-patent		✓	✓		✓
	Off-patent		✓	✓		✓
Portugal	In-patent		✓	✓		
	Off-patent			✓		✓
Spain	In-patent		✓	✓		
	Off-patent			✓		✓
Sweden	In-patent		✓	✓		
	Off-patent		✓	✓		
UK	In-patent				✓	
	Off-patent		✓			

Source: Kanavos and Gemmill, 2005.

This section examines the alternative approaches to regulating ex-manufacturers prices in EU countries and the evidence of their impact. The intention is not to engage in a

discussion of optimal pricing, but rather to consider the impact of government pharmaceutical price controls on overall drug expenditures. In addition, this report does not intend to present a price comparison between countries as doing so alone tell us little about the relative impact on drug expenditures of the particular measures used in a country. In fact, a number of studies attempt to either directly compare drug prices between countries (Pharmig, 2000; Productivity Commission, 2001; Department of Health, 2002; LIF, 2003), or to link price levels in different countries with the types of supply and demand-side policies in place. However, it is difficult to compare the results between studies as few adopt comparable methodologies. Common methodological differences include: the distribution chain point of comparison (ex-manufacturer, wholesale, or retail price); the pricing unit (per unit, dose or package); the range of products compared; the units of currency conversion (exchange rates or purchasing power of parities); the use of weights to account for a product's market share; and the use of bilateral or multilateral comparisons. Unfortunately, many comparative studies do not provide a full and clear description of the methodology employed.

Studies that do attempt to link a price level in a given country and the regulatory framework adopted do provide some interesting insights. A study by the United States General Accounting Office (GAO, 1994) found that prescription drug spending controls in France, Germany, Sweden and the United Kingdom in the late 1980s and early 1990s were effective keeping drug price increases lower than the overall inflation rate, but were unable to prevent the escalation of overall drug expenditures because of the volume effect. Similar evidence points to countries with strict price regulation ─ France, Italy and Spain ─ having systematically lower prices than countries with less stringent price regulation ─ Germany, Sweden and the United Kingdom (Jonsson, 1994; Garattini, et al., 1994; Rovira and Darba, 2001). Yet other studies that have analyzed both on-patent and off-patent drugs suggest that in markets with less regulation, such as Germany and the United Kingdom, prices have tended to be kept lower through competition (Reekie, 1998; Danzon and Chao, 2000). The discrepancies in these studies' findings reflect their different methodological approaches, including the range of products considered (particularly whether off-patent generics were included), the time period of the data, and the method of calculating the indices. Beyond the methodological difficulties that plague many international comparative pricing studies (Danzon and Kim, 1998; Kanavos and Mossialos, 1999), it is difficult to isolate causal effects in the cross-country comparisons because of the many factors influencing drug prices in a given market: differences in health system structure and financing, pharmaceutical subsidies,

cost-containment policies, product mix and production costs (Productivity Commission, 2001).

3.3.1. Direct Price Controls

Direct price controls amount to the setting of fixed maximum pharmaceutical prices. The definition of what is a reasonable maximum price varies from one country to another, and is dependent on a number of factors including budget limits, prescribing behaviour, patterns of utilization, and the importance of the pharmaceutical industry to the national economy. Direct price controls may apply broadly to all medicines whether or not they are reimbursed, or to specific groups of products (for example, reimbursed, inpatient/out-patient, on-patent/off-patent). In most EU countries, the regulated price is the market price since legislation often stipulates that a medicine may only be sold at a single price. All EU countries apply direct price controls to on-patent drugs, except Germany and the United Kingdom where new patented drugs can be freely priced at launch. Since 2003 free pricing was also introduced in France but only for products defined as innovative by the national Transparency Commission (based in the Ministry of Health and Social Security); nevertheless, the French Economic Committee (in the same ministry, but includes representatives of the Ministry of Economics and Finance and the National Health Insurance Fund for Salaried Workers) can register its opposition to the proposed price within 15 days of receiving the proposal. Moreover, cuts and freezes to these maximum fixed prices have been common in many of EU countries, often as regulators attempt to meet short-term budget constraints.

The various methods of directly controlling prices have as an objective to fix pharmaceutical prices at levels deemed "reasonable" and affordable to the healthcare system; how a reasonable price is defined is highly dependent on the importance of the pharmaceutical industry to the national economy. Either prices are directly controlled through negotiations (Austria, France, Italy, Portugal, and Spain) or are fixed by national authorities according to a list of factors, including discretionary criteria that are subjective, open to bias, and result in a lack of transparency. What factors are considered depends on whether the primary objective of the regulator is to achieve the lowest possible price as part of a cost-containment strategy or whether it is to achieve a price level that balances industry incentives and profitability with cost-containment goals. Some countries reward companies that contribute to the national economy or invest in research and development, but determining what contributions should be rewarded and how much is not necessarily evident. For

example, although Spain by law applies a cost-plus formula (manufacturer's costs plus a percentage margin) in the price control system, other factors such as therapeutic value and prices in other countries may be taken into account without being formally stated (Rovira and Darba, 2001).

Price comparisons between similar products within a country, or comparisons to identical or comparable products in other countries, especially other EU countries, are also used in price fixing. Table 3.3 provides examples of some approaches to cross-country price comparisons. In some countries, comparisons are used only as one factor in price determination, while in other countries (Greece, for example) they are the main factor, and prices cannot exceed the average of the compared countries. Finland also includes the prices of comparable parallel imports in its system of average price comparisons (Sirkia and Rajaniemi, 2001). Although price comparisons are meant to provide a basis to assess the fairness of the price setting process, comparisons may suffer from methodological problems and is complicated by the fact that even if a product is available in a given market there may be differences in the strength, formulation and package size of the product available across countries. Further, these comparisons may potentially be circular in derivation: country A looks at an average of prices in countries B, C, D; country B looks at an average of A, C, D or perhaps A, C and E. The price comparison mechanism is based on the assumption that the prices in the country being considered have a sound basis and/or that the factors leading to those prices are appropriate for the country doing the pricing on the basis of such comparisons, none of which may be true.

Table 3.3. Examples of International Price Comparisons in Price Setting Schemes in EU Member States

Belgium	Ex-manufacturers price in France, Germany, Luxembourg and Netherlands
Denmark	Average European ex-manufacturers price excluding Greece, Portugal, Spain and Luxembourg but including Lichtenstein
Finland	Average EU wholesale price
Ireland	Average wholesale price of Denmark, France, Germany, Netherlands, UK
Italy	Weighted average ex-manufacturers of EU prices (excluding Luxembourg and Denmark)
Netherlands	Average ex-manufacturers price of Belgium, France, Germany and UK
Portugal	Minimum ex-manufacturers price of identical products in France, Italy and Spain

Few countries now grant a reimbursement price "for life". Prices set at launch may be maintained for a period of time and then adjusted according to defined criteria. For example in France, prices are set initially for a period of five years, before being reassessed to take into account new indications, volume levels, or any pharmacovigilance problems (Pelen, 2000). In most countries price cuts have been more common than granting a price increase for a particular drug.

While direct price controls may have gone some way to tackling the price side of the expenditure equation by slowing the rise in drug prices or in fact lowering the prices of at least some drugs, pharmaceutical expenditures in these same countries often continued to increase; this increase is best explained by a rise in the quantity of drugs used and/or a change in the mix of drugs as newer drugs were added to reimbursement lists. A study of the effects of price, volume and new product introductions in the Netherlands between 1990 and 2002 found that year-to-year growth in the quantity of drugs used was the primary contributor to total turnover; prices actually decreased in several years of the period examined (Nefarma, 2002). In Sweden, real drug expenditures increased by 95% between 1974 and 1993, due to a 22% rise in the number of prescriptions ─ mainly due to newer more expensive products ─ while relative prices decreased by 35% (Jonsson, 1994). In France, numerous supply-side policies aimed at controlling drug prices have been used since 1975, achieving some of the lowest prices in Europe. However, with volumes unconstrained, pharmaceutical expenditures increased with the number of prescriptions (Le Pen, 1996; Lecompte and Paris, 1998). In Spain, the relative price of drugs decreased by 39% between 1980 and 1996, yet a 10% increase in the number of items prescribed, mostly for new products (there was a 442% increase in these) with little therapeutic gain, was associated with a 264% increase in real drug expenditures over the same period (Lopez-Batisda and Mossialos, 2000). A similar picture emerges from Greece, where from 1994 to 2000, despite a 17% decrease in relative prices, the number of prescriptions increased by 16% while drug expenditures grew by 204% (Kontozamanis, 2001). These examples serve only to emphasize that while direct price controls may be effective in lowering drug price, pharmaceutical expenditures may nevertheless increase. While the quantities of drugs used and mix of products may be necessary to meet patient need and off-set costs elsewhere in the system, it is nevertheless important that the use of medicines is rational.

3.3.2. Economic Evaluations and Drug Pricing

Several countries are using economic evaluation data alongside other criteria for reimbursement decisions. Finland is the only country to have officially adopted economic evaluation guidelines as part of the price setting mechanism. In most other countries, economic evaluation informs the pricing decision only to the extent that it aids in forming a judgment as to the costs and benefits offered by a product relative to a comparator product(s); in this sense it is a tool for price justification and potentially offers a margin for cost-effective innovation. Since the implementation of the Pharmaceutical Benefits Board in Sweden in 2003, evidence from comparative economic evaluations has been used to decide whether the price of the drug was too high and thus whether the drug should be excluded from reimbursement. The evidence of the effectiveness of using economic evaluation to secure "value prices" is limited. Some evidence from Sweden suggests that higher margins are gained by drugs considered to be innovative (Lundkvist, 2002), which may be a reflection of the use of economic evaluation. The case of the risk-sharing agreement for Multiple Sclerosis (MS) drugs in the United Kingdom (Box 3.1) is a unique example of a price directly linked to a cost per QALY ratio; however the implementation of the scheme has faced multiple challenges, such as the calculation and level of the cost per QALY threshold, patient selection and monitoring, and the implications for wider regulatory approaches within the UK NHS (Box 3.1).

Box 3.1. The Risk-Sharing Scheme for Multiple Sclerosis (MS) Drugs in The United Kingdom

Thanks to the advocacy efforts of patient groups and the pharmaceutical industry, Multiple Sclerosis patients in England and Wales, who meet certain criteria have been eligible to receive prescriptions for four products (Avonex, Betaferon, Copaxone and Rebif), since May 2002, paid for under a risk-sharing scheme operated by the National Health Service (NHS). The scheme evolved despite a negative ruling by National Institute of Clinical Excellence (NICE) in 2001 on the cost-effectiveness of these treatments. Under the scheme, the price for each product has been set according to evidence of its effectiveness derived from the outcomes obtained by patients participating in the scheme. If actual outcomes derived by a product fall short of targets within a margin of tolerance, the given company will have to make a repayment per a sliding scale agreed in advance. There are many caveats to this approach, including the calculation and level of the cost per QALY threshold, patient selection and monitoring, and implications for wider regulatory approaches of the NHS, such as the PPRS scheme (see below). Nevertheless, the risk-sharing scheme sets some precedence by linking price to volume to generate a performance-related price for reimbursement.

Source: Kanavos, 2004.

3.3.3. Profit Controls

The United Kingdom has had the Pharmaceutical Price Regulation Scheme (PPRS) in effect in various forms since 1957, indirectly regulating the prices of branded pharmaceuticals sold to the NHS by setting profit limits (Department of Health, 1999). The PPRS is the result of periodical negotiations between the Association of the British Pharmaceutical Industry and the Department of Health and is reviewed every few years. Its objective is to achieve a balance between securing medicines for the NHS at reasonable prices and encouraging a profitable pharmaceutical industry capable of competitive development of innovative medicines. As a 'reasonably priced' medicine is not defined in the PPRS, it leaves room for differing interpretations on the part of industry, government and tax payers.

Companies with NHS sales of £25 million are required to submit an annual financial return and any details on the capital employed by each company in supplying these medicines. The data are used to assess a company's overall profitability on NHS sales, and applications for price increases. New active substances may be priced at the discretion of the company on entering the market. Companies within the scheme have an allowable profit (or cap) of 21%, measured as a return on capital employed or return on sales for those companies that do not have major capital investments in the United Kingdom. If a company exceeds its target return, it can retain up to 40% over the originally permitted return if it has not received a price increase for any product in the same year. If profits exceed the margin of tolerance, the company must reduce profits by cutting prices, repaying the excess profit to the Department of Health or delaying or restricting previously agreed future price increases. The amount allowed for research and development can comprise up to 20% of total NHS turnover and companies are permitted an additional 3%, depending on their number of patented products sold in the United Kingdom. Companies are also allocated 6% of their NHS turnover for promotional spending.

The success of the PPRS in securing low prices of medicines for the NHS is undetermined. Some authors have argued that the PPRS has done little to control the prices of medicines for the NHS, as the pharmaceutical budget has increased approximately 10% per year from 1967 to 1997 (Maynard and Bloor, 1997; Bloom and van Reenen, 1998). United Kingdom prices are amongst the highest in the EU (Department of Health, 2002). This is despite one-off savings of GB£ 89.8 million resulting from 1993 price reductions (Borrell, 1999). This partly reflects the fact that the United Kingdom is most often included as a

reference country for international comparisons by other EU countries; its relatively free pricing means that companies are likely to establish their United Kingdom price first.

The PPRS is thought to have encouraged investment by maintaining a stable and predictable regulatory environment and allowing levels of research and development expenditures above the worldwide average (Mossialos, 1997). The limitations of the PPRS are not uncommon to other rate-of-return-type regulatory schemes, which provide little incentive for efficiency, as increased costs can be recovered through allowable price increases. Moreover, to the extent that returns are calculated as a percentage allowance on the capital invested, the company may over-invest in capital equipment or artificially inflate its asset base. This is similar to the Averch-Johnson-Wellisz effect associated with rate-of-return regulation of public utilities (Baldwin, 1995). Rate-of-return may also give firms incentives to shift production costs from an unregulated to a regulated division if they operate in several markets, as in the case of a firm manufacturing both PPRS-regulated patented medicines and generic medicines falling under another scheme. Finally, as target profits are negotiated and the process may not be transparent, there is the potential for "regulatory capture". The determination of the "proper or fair" rate of return essentially requires insight into the structure, conduct and performance of the industry. The transparency of the PPRS is limited, and the recently produced annual reports based on aggregate data (Department of Health, 2002) do not facilitate understanding of this complex and expensive policy.

3.3.4. Other Government-Industry Agreements

Government-industry agreements have commonly tried to make the industry responsible for overspending on public drug expenditure targets, resulting in price cuts and/or some repayment of the excess (Table 3.4). However, such agreements in Austria, Belgium, Denmark, Portugal and Spain have had a very limited impact in slowing the growth in public drug spending (OECD, 2002). In addition they have often been unpopular with industry as their objectives are often short-term.

Table 3.4. Examples of Government/Industry Agreements in EU Member States

Country	Type of Government/Industry Agreements
Austria	Agreement on drug expenditure targets for the Social Insurance Institution; growth to be slowed through price reductions.
Denmark	Agreement on reduction in overall price levels such that overall expenditure on subsidized pharmaceuticals is kept constant.
France	Sector based agreements on issues including exchange of information, promotion of compliance with national objectives, rational drug use, development of a generic market and others.
Ireland	Agreement on supply terms, conditions and prices of medicines for the health care services.
Portugal	Agreement with industry to cap the NHS drug expenditures and repay excess.
Spain	Multiple agreements covering price cuts, expenditure targets and company repayment targets are exceeded.
UK	Pharmaceutical Price Regulation Scheme (see above).

Some countries (Austria, France, Spain and Sweden) have negotiated price-volume trade-off agreements with individual companies. This mechanism works by setting prices according to expected or realized volume, such that if volume passes a threshold the price level will decrease and/or companies have to repay the government or health insurance plan. It is not known whether these schemes have been successful or respected by the industry. Furthermore, as summarized in Box 3.2, France has implemented both industry-wide and individual agreements with companies requiring repayments if government spending targets are exceeded. Such approaches are not uncontroversial. Belgium, for example, planned but never implemented price-volume contracts due to a debate between insurance funds and the pharmaceutical industry on how to classify products as innovative (Eggermont and Kanavos, 2001). Another concern is how such an approach may affect an appropriate increase in volume and how this should be defined. Finally, Finland and Italy do not have formal price-volume agreements, yet both consider the forecasts of the number of users and sales level of a product in their direct price-setting systems

Box 3.2. Sector-Wide and Agreements With Individual Pharmaceutical Companies in France

France has implemented both industry-wide agreements, as well as agreements with individual companies. Sector-wide agreements with the National Pharmaceutical Industry Union (LEEM - formerly SNIP) have been negotiated between the government and industry since 1994. These have generally defined common objectives including meeting national health expenditure targets, promoting rational drug use, reduced company advertising and the development of a generic drug market. Within these agreements if the health expenditure targets are exceeded the pharmaceutical industry must make a repayment to the sickness funds through a sliding scale tax based on each company's turnover; this rule applied only to 15 companies in 2001 as the remainder were exonerated by having signed individual agreements with the government.

The individual agreements set price-volume conditions for individual products. The price of a drug is set with regard to the improvement it provides compared to other drugs in the same therapeutic class on the positive list; the exception is for drugs which are defined as innovative which since mid-2003 can be freely priced. The Improvement of the Medical Service Rendered (IMSR) is evaluated by the Transparency Commission. The price of a drug can only be higher than other drugs in its class if the IMSR is higher. The Economic Committee for Medical Products (CEPS) then uses the IMSR along with cost-effectiveness analysis and other factors including the estimated sales volume, as well as the expected and actual conditions of its use in the negotiations with individual companies.

3.3.5. Reference Pricing Schemes

Reference pricing schemes set fixed reimbursement limits for products assigned to the same group. Their purpose is to limit the rise in pharmaceutical expenditures by requiring patients to pay any excess of the price of the prescribed drug over the reference price. This additional cost is anticipated to increase patient and physician awareness of the prescribed drug's price and possibly result in the patient being switched to a drug listed at the reference price. If switching occurs then a convergence of drugs in the same category to the reference price generally follows.

In the EU reference pricing has gained popularity because it can be effective in reducing price differences among drugs defined as therapeutic substitutes by improving market transparency (Giuliani, Selke and Garattini, 1998). Countries' schemes differ in coverage, pricing method and inclusion or exclusion of on-patent medicines. In general, reference pricing applies only to products that have been defined in the same category, having similar therapeutic mechanisms or clinical outcomes. However, if they are not generic equivalents, these classifications are often controversial (Rigter, 1994). In Denmark,

Germany, and Spain (and Sweden until October 2002) the reference pricing schemes include only off-patent drugs. Almost uniquely in Europe, the Netherlands includes patented drugs in its reference price scheme. Germany, which included patented drugs in the early stages of its reference price scheme, may do so again should proposals for a reform of pharmaceutical legislation proceed (Busse and Wörz, 2003).

Different mechanisms are used to calculate the reference price, as shown in Table 3.5. Evidence from studies in individual countries suggests that there is downward price convergence (Lopez-Casasnovas and Puig-Junoy, 2000). In Sweden, the market share of reference price drugs decreased from 13% by value at the start of the scheme in 1993 to 7.5% by 1996 (Nilsson and Melander, 2000); this was driven by a decrease in the price of both original brands and generic equivalents (Aronsson, Bergman and Rudholm, 1998; Bergman and Rudholm, 2001). Similar price decreases occurred in Germany after patients were switched to medicines at the reference price, sparing them the additional costs (Zweifel and Crivelli, 1996; Pavcnik, 2002). As a result, most companies in Germany reduced their prices and the label 'without co-payment' became one of the most important communication issues in physician-focused advertising campaigns (Vogelbruch, 1992). There is evidence of switching in other reference price schemes such as that in British Columbia (Canada), where seniors were switched from angiotensin-converting-enzyme (ACE) inhibitors listed above the reference price to lower cost alternatives (Schneeweiss, et al., 2002).

Table 3.5. Comparative Definitions of Reference Price in Selected EU Schemes

Country	Year Introduced	Definition of Reference Price
Germany	1989	Statistically derived median price for drugs of containing the same active substance and having comparable efficacy.
Netherlands	1991	Average price of drugs with similar pharmacotherapeutic effects.
Denmark	1996	Lowest priced generics equivalent available on the market.
Spain	2000	Arithmetic mean of the lowest cost-per-treatment-day grouped by formulation and calculated by DDD.
Belgium	2001	Equal to a price that is 26% lower than the price of the original brand for generic equivalent products.
Italy	2001	Lowest priced generic equivalent available on the market.
Portugal	2003	Lowest priced generic equivalent available on the market.

Even where reference pricing resulted in some savings on pharmaceutical expenditures, the effect was generally only short-term in the Netherlands (Lopez-Casasnovas

and Puig-Junoy, 2000), Germany (Nink, Schroder and Selke, 2001) and Italy (Donattini, et al., 2001). One explanation is that an increase in the volume and price of drugs outside the reference price system in general nullified any reductions in pharmaceutical expenditure from the scheme. Some German doctors, for example, preferred to prescribe products that were not included in the reference price scheme rather than sacrifice time to discuss co-payments with patients (Nink, Schroder and Selke, 2001). In fact, the price of drugs outside the reference price system increased by over 20% from the early stages of the German reference price system (Statistisches Bundesamt, 1998). A similar outcome of reference pricing in New Zealand led the government to supplement it with cross-product agreements, where securing a particular price on a new drug required prices of drugs in unrelated markets to be reduced (Woodfield, 2001).

As reference pricing is often targeted at generic medicines where price competition should be possible, the challenge in many of these systems has been how to stimulate demand-side cost awareness, which is essential for competition subsequently lowering the reference price. The lack of demand-side incentives in Norway was one reason given for the reference price scheme not achieving anticipated savings (ECON Centre for Economic Analysis, 2000); in fact, a lack of satisfaction with reference pricing has resulted in both Norway and Sweden abandoning their schemes. Germany has supplemented the reference price scheme with what is referred to as the downward price coil in an attempt to move prices below the reimbursement limit; as pharmacists were paid such that the absolute margin increases with product price they had little incentive to engage in discounting with wholesalers that would reduce a drugs market price. Despite the problems other countries have experienced with their reference pricing schemes, the practice continues to spread; Spain and Italy have also implemented a reference pricing scheme for off-patent drugs in 2000-2001.

There is a need for more thorough analysis of the impact of reference pricing systems, particularly in Europe. The evidence on reference pricing is for the most part based on aggregate data, and while these studies do contribute to our understanding of how such schemes work, few have controlled for the impact of other cost-containment measures. It is also important that studies of reference pricing consider the impact on clinical outcomes, the health status of patients, total health system costs and drug innovation (Kanavos and Reinhardt, 2003). Equity issues arising from the impact of reference pricing, particularly on the more vulnerable groups, needs also to be studied in more detail within a European

context; several studies from British Columbia have shown that some of the province's cost-savings on reference pricing have resulted in higher costs for seniors (Grootendorst, et al., 2001; Marshall, et al., 2002), as they had to pay out-of-pocket for their drug of choice if the latter was not the reference drug and its price was higher than the reference price.

3.3.6. Concluding Remarks on Drug Pricing and Reimbursement Issues

Price controls certainly can have an impact on either slowing price increases or lowering drug prices. However, the impact of price controls on drug expenditures may be mitigated by growth in the quantity of drugs used or in the mix of products that includes more expensive medicines. Countries continue to face the challenge of determining what a reasonable drug price is and how to decide on which drugs should be rewarded as cost-effective innovations; the latter is important so that it acts as a signal to influence the innovative process.

One debatable issue is to what extent pharmaceutical prices can be deregulated. Certainly for competition to generate lower prices there has to be cost-awareness on the demand side of the market for suitable alternative products. Financial incentives targeting physicians, pharmacists and patients have led to greater cost-awareness for off-patent drugs. The extent to which these same incentives motivate the selection of comparable substitutes and competition for on-patent drugs is not clear but is likely to be more limited than for generic drugs.

3.4. Monitoring and Influencing Physician Decision-Making

Since physicians are the key decision-makers on the demand-side of the pharmaceutical market, there is much interest in ensuring that they are engaging in good prescribing practices. 'Good prescribing' should encompass the appropriate choice of medicine not only from the perspective of the physician but also that of the patient, while at the same time aiming to maximise effectiveness, minimise risk, and minimise cost (Barber, 1995). Prescribers, patients and payers in different healthcare systems may have different perspectives on what constitutes good prescribing.

There are significant differences in the prescribing habits of individual practitioners and across countries. For instance, only 62.9% of consultations result in prescriptions in the Netherlands, whereas in Italy this figure is 94.5% (Nefarma, 2002). In 1996, only five medicines were common among the 50 most prescribed medicines of France, Germany, Italy, and the UK (Garattini and Garattini, 1998). It is, of course, premature to attribute these

differences only to prescribing culture, but clearly these discrepancies are significant (Nefarma, 2002). Study of good prescribing is difficult: the patient's "needs" are difficult to define and measure, and are not well captured by administrative data bases. Disentangling the complex interaction of factors that lead to a decision to prescribe a particular drug for a particular patient is difficult.

Various approaches have been made to monitor prescribing quality, including the use of a Medical Appropriateness Index and a review of detailed medical records. The Medical Appropriateness Index assesses prescribing suitability for an individual patient based on 10 dimensions. The use of medical records is the most accurate measure of performance quality, although it is not a realistic option for most European countries. Financial incentives also have been used to influence prescribing behaviour.

Prescribing data are used, in the UK for example, to provide doctors with reliable, regular and prompt information on their current prescribing in an effort to improve cost awareness, in theory leading to more effective and economical prescribing. In practice, the usefulness of such cost focused prescribing data in initiating change is limited because change dependents on the doctors' willingness to consider costs when prescribing. Although doctors are not necessarily averse to considering costs, other criteria such as clinical benefit, personal experience or opinion are more valued (Denig and Haaijer-Ruskamp, 1995).

Clinical practice guidelines –specific criteria for how and when particular tests and treatments should be used – have also been employed in an attempt to standardise both physician variation to management of diseases, as well as control spending. While there is often no mechanism for monitoring or enforcement after dissemination of the guidelines, their introduction may be complemented with financial incentives (or disincentives) and educational efforts. Clinical practice guidelines appeal to policy-makers as well as clinicians because their objectives are to improve, not simply ration care. Sometimes these guidelines are used in utilisation reviews (at times used to penalise doctors or hospitals) or to determine coverage policy, which makes them less acceptable to some healthcare professionals. In France, prescribing guidelines were poorly followed because of the volume of guidelines, lack of information systems and limited capacity for monitoring and physicians concern that following the guidelines could negatively affect the quality of care being delivered (Durieux, et al., 2000).

Studies on the effectiveness of clinical guidelines have been conflicting (Gundersen, 2000). Some show little effect of clinical guidelines on physician prescribing behaviour (Hetlevik, et al., 2000), while others suggest that evidence-based guidelines, if designed well and implemented consistently, can help to deliver "best practice" (Garfield and Garfield 2000; Perleth, et al., 2001; Richmond and Lancaster, 2000).

In general, adherence to evidence based guidelines would be expected to improve the quality, efficiency, and equity of care, but might increase or decrease total expenditure depending on previous practice – where patients were undertreated, increases in total expenditure are likely. Guidelines written with the explicit objective of cost-containment are unlikely to be acceptable because of serious ethical and legal implications (Carter, et al., 1995; Cheah, 1998). Guideline development and implementation is expensive and like any other health technology must prove its value (Gandjour and Lauterbach, 2001; Mason, et al., 2001).

Another approach to influence physician prescribing is educational (Soumerai and Avorn, 1990). There can be many forms of educational interventions, ranging from the simple distribution of educational bulletins or pamphlets, lectures or seminars in all of which the prescriber can be a passive recipient. More participatory approaches to prescriber education include audit and feedback, and academic detailing. In general, there has been no good evidence showing effectiveness of the simpler, more passive measures such as circulation of educational materials, or even auditing and feedback (Freemantle, 2000). These do however improve knowledge and while not securing change in themselves, may prepare the ground for more direct approaches, such as academic detailing.

Academic detailing, where a trained individual meets with a physician in their practice setting in order to modify their performance, can change practice (Avorn and Soumerai, 1983), but is expensive. More recent studies in the UK show a useful effect in general practices with small numbers of doctors, but less effect in larger practices with more doctors, where securing the "buy in" to change practice from all the doctors is more difficult (Freemantle, et al., 2002). An alternative method to directly assist in clinical decision-making is the use of computerized decision support systems (CDSS) that use software to generate patient-specific assessments or recommendations. These two educational methods – academic detailing and computerised decision support – can be expected to bring about a 15% change toward the desired behaviour by professionals (Freemantle, 2000). Here, an important qualification to academic detailing is that the people chosen to educate professional not be

seen as biased health managers. In the UK, for example, one problem with prescribing advisors in the early 1990s was that they were seen as agents of the government and thus received with some antagonism by doctors. Finally, other methods such as socialisation and instilling certain norms of behaviour for physicians have been attempted, but with much less success (Robinson, 2001).

3.5. The Changing Doctor-Patient Relationship

Recently, the doctor-patient relationship has changed as patients become more involved in choice of treatment, and can easily access an abundance of detailed medical information through books, the media, and the internet. Many patients seem less trusting of physicians. Furthermore, in an environment geared at containing healthcare spending, patients have an increased responsibility in paying for their medicines and may be encouraged to care for minor ailments with over-the-counter (OTC) remedies, paid for out-of-pocket.

Research on doctor-patient relationships and medicine-taking has revealed that patients have complicated agendas during GP consultations (Barry, et al., 2000). Patients are ambivalent and often averse to taking medicines and do not fully express these feelings to the GPs. At the same time, some patients want prescriptions that may not be medically indicated. These behaviours create communication difficulties between the doctor and patient that can lead to poor consultation outcomes, incorrect use of medicines, and non-adherence with medicines taking. Exacerbating this situation is the fact that patients are often poorly educated by their doctors regarding the correct usage of their medication, expected duration of treatment, possible side effects, available alternatives (medical and non-medical), and indications to return.

Furthermore, national and regional populations differ in how they regard disease, thus influencing how illnesses are managed. Culture is defined as the socially transmitted beliefs, norms, values, religion, civilization, and all other products of human work and thought of a population. Just as healthcare utilisation differs between cultures and nations, so does the use of medicines. The influence of culture on pharmaceutical prescription and consumption must be considered in the context of the respective healthcare system structure and economy (Payer, 1988). Rates of prescription differ enormously across Europe (Table 3.6).

Table 3.6. Prescriptions Dispensed Per Capita Per Year in European Countries, Circa 1995

Country	Number of Rx per cap
Austria	11.5
Belgium	9.5
Denmark	7.1
Finland (1994)	5.7
France	52.2
Germany	12.0
Iceland	16.0
Ireland	11.0
Italy	5.2
Luxembourg	26.0
The Netherlands	11.0
Norway (1994)	6.9
Portugal	21.0
Sweden	6.1
Switzerland	8.0
United Kingdom	10.0

Source: Yuen, 1999.

The use of drugs in a society goes far beyond the chemical properties of a drug and considers the cultural definitions of disease, attitudes towards health and pain, and the perceived effects of the drug on the individual. The ritualistic nature of medicines is deeply embedded in the ethos of a group. Cross-national differences have been observed regarding the acceptance of generics, the sharing of medicines, patient compliance, self-medication, and information seeking. In some societies, the very act of a physician prescribing a medicine may convey the message to a patient that the consultation is complete and the illness is in fact real. Thus, patients need to be educated about the benefits and limitations of specific pharmaceuticals by physicians in a clear, understandable and timely fashion.

Patient compliance is an important area for policy, since its implications are wide. Poor patient compliance can have adverse effects on the public health (e.g. low rates of childhood vaccination in parts of the UK) (Meulemans, et al., 2002). One of the reasons behind non-compliance may be a growing mistrust of the healthcare industry (Robertson, 1985). Another may be that what patients view as a worthwhile personal benefit may not be same as what the health professional considers useful. Better understandings of non-

compliance and its consequences can lead to more effective strategies for improved concordance between doctors and patients and better adherence to medicines (Dardano, 2000). Some non-compliance is not just due to misinformation or individual irresponsibility, but also to external factors outside the patient's control, such as poverty or other logistical problems (Fletcher, 1989). Monitoring patient compliance may also be important to ensure that the potential therapeutic benefits are not wasted (Kaveh, 2001). Financial incentives (cash, vouchers, lottery tickets, or gifts) have also been used successfully in the United States in improving patient adherence (Giuffrida and Torgerson, 1997). Recent initiatives in the UK show anecdotal evidence that patients can manage some of their own health conditions much more effectively than by simply depending on healthcare professionals (Donaldson, 2002). In all cases, an ethos where patients begin to take more responsibility for their health has the potential to improve doctor-patient relationships and health gains.

The media can have a positive influence on healthcare issues through public health education campaigns, or a negative impact when exaggerating the benefits of break-through drugs or the disasters of adverse effects. The news, television, and more recently the internet can manipulate public beliefs, attitudes and behaviours pertaining to healthcare and medicines. Information from particular sources (such as the internet) can often be misleading or wrong, and can contribute to mistrust between doctor and patient. Incomplete information given by pharmaceutical companies, especially about the limits of clinical benefit, is a major concern (Woloshin, et al., 2001).

Since 1997, Direct to Consumer (DTC) advertising of prescription drugs has been allowed in the US, thus influencing medicines consumption by raising public awareness. DTC for prescription only medicines is illegal in Europe and opposition to it generally remains widespread, both among health professionals and by patient and consumer groups. Such opposition stems from uncertainty about any benefits of DTC, and its well documented problems. The industry points to advantages in 'empowering the consumer through information' resulting in more autonomy and speedier access to medicines. This is to be weighed against the often-dubious nature of the information provided. This is apparent from evidence that, in the United States, even over-the-counter advertisements – which the FDA regulates – often make inaccurate statements and neglect to mention potential side-effects (Sansgiry, et al., 1999). The dividing-line between information and advertising is therefore slender.

Evidence from the United States (and to some degree New Zealand) suggests that DTC actually triggers, rather than simply reflects, consumer needs (Hoffman and Wilkes, 1999). DTC has thus been seen as an industry tool, not for the promotion of information, but rather to make further profit. While industries hoping to receive DTC rights in Europe claim that they desire only to share accurate and scientifically-based information with consumers to help patients become more involved in their own healthcare, strident opponents say that, as the goal of providing this information would be to increase sales, it is inevitable that the benefits are discussed more than the risks (Jones, 2003; Garlick, 2003). These are all issues that any future liberalisation of the DTC rules in Europe will have to accommodate.

Pharmaceutical companies can promote themselves in many other ways: in addition to indirect financial support to physicians, such as sponsoring drug lunches or dinners, giving industry gifts, or paying for travel and expenses to educational conferences (Moynihan, 2003a), companies will use ostensibly neutral and independent sources (whether individuals, patients' groups, or medical journals) (Smith, 2003; Wager, 2003) to promote new drugs. Another traditional route is through medical journals, which often depend on the large-volume reprint requests and advertisements of drug companies, and where editorial lines can be influenced. A new approach is to patients' organisations, which gain financial support from drug companies. Yet the unequal 'partnership' can allow pharmaceutical companies to misrepresent their own agendas or distort those of patient organisations (Herxheimer, 2003).

Such potential conflicts of interest should be made more explicit (Burton and Rowell, 2003). There are also recent movements in the United States and the United Kingdom from medical students, professional associations, and other groups who oppose intimate ties with pharmaceutical companies (Moynihan, 2003b). "Good publication practice" (GPP), where drug companies are encouraged to publish negative results, would ameliorate the problem of publication bias (Singh, 2003). Another idea is that of a "blind trust", where pharmaceutical companies could contribute to a national pool of funding, to be allocated to educational providers (Moynihan, 2003c).

The implications of these changes –where patients armed with increasing information of varying quality, as well as more alternatives in obtaining medications– are that new ways of engaging patients with health professionals must be found and encouraged in order to protect patients and prevent abuse of more convenient ways of finding treatment.

3.6. Financial Incentives and Prescribing

Prescribing budgets can be used at the level of the individual doctor, practice, or region to limit the resources available for providing medicines. Hard budgets use penalties or rewards to motivate doctors to meet budgetary goals, while target budgets do not impose an immediate penalty but allow useful record keeping of the costs incurred by the agent concerned. There may be rewards or fines for meeting or failing to meet treatment guidelines or quality targets, or staying within cash-limited prescribing budgets schemes.

Prescribing budgets have generated financial and ethical concerns. They risk reducing patients' confidence in their doctors, as they increasingly become aware of the financial incentives linked with prescribing behaviour. There is a risk that the quality of prescribing may deteriorate if the financial incentive becomes the driving force behind the prescribing decision. Should doctors be especially rewarded for doing a professional job, or perhaps depriving the patients of the medicines they want? The use of cheaper medicines to meet budgetary constraints may not necessarily be cost-effective. Additionally, prescribing economies might be only short-term. Perverse incentives may cause cost shifting to other health services (e.g., improper use of the emergency room) thus decreasing prescribing spend but increasing overall healthcare costs. Moreover, there may be problems of 'cream-skimming' associated with physicians referring severe and expensive patients to hospitals (Goodwin, 1998) (or at least making patients with chronic illnesses less of a priority) and the possibility of doctors denying appropriate but expensive treatments to patients. This suggests that extreme care should be taken in the design and implementation of these incentives.

The conflict doctors face between giving the best treatment to each patient along with being responsible stewards of the healthcare system are felt more keenly with these new arrangements. Awareness of these risks and possible solutions (e.g., compensating physicians not only through financial incentives to decrease utilisation but also through rewards for quality and productivity, providing regular information on approved ways of managing particular conditions) is crucial for policymakers hoping to design incentive systems that align interests of patients, providers, and payers.

Although some suggest that drug budgets may not be necessary for containing costs, and that better data on cost-effectiveness would empower prescribers to make rational decisions regarding treatments (Levy and Gagnon, 2002; Laupacis, et al., 2002), others argue that budget constraint is essential to contain costs (Brougham, et al., 2002). Others still

contend that containing costs without budgets and exclusively depending on prescribers to make their own rational decisions based on evidence not yet been collected is impractical (Fernandes, 2002).

Financial incentives can be effective, but mostly in choice of drug as opposed to volume of prescribing. In other words, whether a doctor prescribes medication is difficult to change; the type of drug chosen, however, is negotiable. Even so, these changes in prescribing (often simple shifts to generic medications) are usually one–off and cannot be repeated although their benefits can be maintained. Punitive disincentives placed on physicians (as until recently in Germany and in France) seem less acceptable as well as more difficult to enforce and thus, less successful. At the same time, weaker schemes that appeal to professionalism but hold no real positive or negative incentives have been shown (at least in the UK) to be relatively ineffective at changing behaviour. The types of incentives employed should be chosen according to particular circumstances, such as current practice patterns and levels of provision. Few studies have determined whether health outcomes are changed due to financial incentives. Most evidence does, however, imply that physicians prefer that their autonomy be protected (as in UK fundholding) and, when combined with simple and transparent appropriate incentives, can save money with no loss of quality. Drawing on less visible yet still persuasive forms of regulation such as peer pressure through professional associations, as well as these other measures, may also be important in changing the culture of prescribing. In the end, while the effects of financial incentives may be more visible in the short-term, they may also be less professionally and ethically acceptable and, in the long-run, less effective at containing costs.

3.7. Regulating Pharmaceutical (Wholesale and Retail) Distribution, and Hospital Pharmacy

3.7.1. Overall Dynamics

The distribution of pharmaceuticals in the EU is governed by both supranational and national regulations in conjunction with professional bodies, health service providers, and healthcare payers. The principal objective of regulating distribution is to protect the public's interest in safety and access to medicines; secondary objectives include ensuring the financial viability and integrity of wholesalers and pharmacies, promoting quality services, limiting overall drug costs, and encouraging increased consumer choice. The specific details of regulation differ between Member States.

The distinction between manufacturers, wholesalers and community pharmacies is becoming increasingly vague with more vertical integration (when permissible) that allows for consolidation of the distribution channel and increased margins for wholesalers. In addition, competition is growing with the introduction of mail-order and online pharmacies. Yet the evolution and further deregulation of the pharmaceutical supply chain in Europe may face countervailing trends: the continued demand for face-to-face pharmaceutical advice and care; divergent and deeply rooted regional histories of pharmacy services; the strength of the professional lobby of pharmacists; and lack of consistent public pressure and sound political vision for the future of the industry. As a result, the likely future of pharmacy service regulation may be one characterised by slow evolution rather than radical change. One radically new role for pharmacists in the UK will be as prescribers, taking on responsibility for dose adjustment and monitoring in a range of chronic conditions where a doctor has made the diagnosis.

3.7.2. The Retail Market Dynamics

In the past, the role of the community pharmacist was to dispense prescription medicines and sell over-the-counter (OTC) products. This is now evolving throughout Europe because of rising awareness of their extensive knowledge related to the appropriate use of medicines and their potential as independent providers of healthcare. Pharmacists are highly educated professionals and in some countries will have a more integrated clinical role in the future. In addition, the pharmacist can be instrumental in controlling pharmaceutical expenditure when given the freedom to engage in generic and therapeutic substitution, and when economical dispensing practices are promoted through financial incentives. There is much variation between the regulatory patterns related to pharmacists in EU Member States. These include controlling community pharmacy ownership and location, setting allowable profit margins, and influencing drug distribution patterns and product selection through different incentives and remuneration methods.

Community pharmacies supply in the order of 80% by volume and value of all pharmaceuticals used in European countries. The number of pharmacies as well as the average population served by each pharmacy in different countries (Table 3.7) varies significantly and is a function of several parameters. For instance, the number of inhabitants per pharmacy ranges from 1,139 in Greece to 18,571 in Denmark (Figure 3.7). In most European countries, community pharmacists outnumber their hospital counterparts by between 12 (Belgium, Denmark) and 25 to one (Spain, Germany). But in the Netherlands and

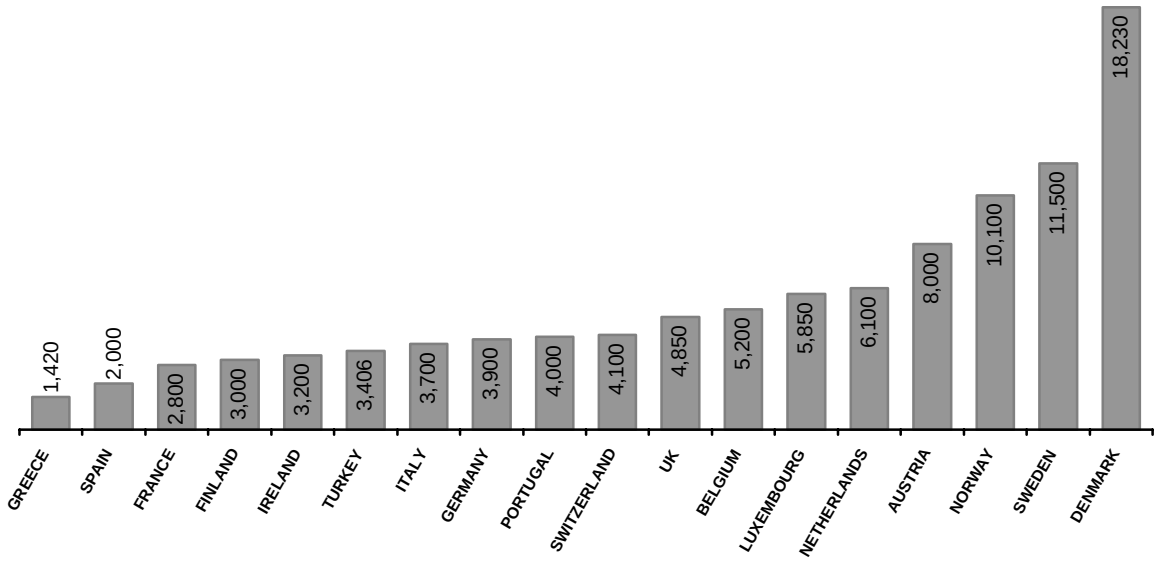
the UK this ratio is about 6 to 1. In population-per-pharmacy terms, southern European nations have more pharmacies than those of the north, although in Denmark, Sweden and Norway the figures normally quoted do not include branch pharmacies and other prescription distribution points. The location of pharmacies may be geographically restricted through licensing or contractual arrangements with healthcare payers. These differences lead to significant differences in the average turnover of individual pharmacies.

Table 3.7. Number of Pharmacies Per Country

Country	Number of Pharmacies
Austria	2,110
Belgium	5,480
Denmark	335
Finland	794
France	22,689
Germany	21,590
Ireland	1,210
Italy	16,541
Netherlands	1,571
Norway	346
Sweden	981
Switzerland	1,654
UK	12,505
Turkey (2002)	20,848

Source: Gehe, 2001 (Turkey; IEIS, 2003).

Figure 3.7. Population Served by an Average Community Pharmacy in European Nations, 2001



Source: Macarthur and Grubert, 2002. Turkey data calculated from MoH Statistics.

Although still sometimes seen as 'merely retailers' outside hospital settings, pharmacists have extensive knowledge relating to the appropriate use of medicines. Community pharmacists can play an important role in fields such as detecting drug interactions and side-effects, and facilitating appropriate medicines use (Chamba, Bauguil and Gallezot, 1999).

Further developments in areas such as the treatment of minor illnesses and pharmacist management of repeat medication dispensing and prescribing may significantly extend their contribution to healthcare delivery in the coming decade (Watson, et al., 2002; Cabinet Office, 2002). There is evidence that services provided by pharmacists can improve outcomes in a range of contexts (Narhi, et al., 2001; Bernsten, et al., 2001; Kansanaho, et al., 2002; Anderson, 2000). Although the debate over extending their clinical role goes beyond the scope of this report, it is relevant to understanding the significance of regulatory provisions such as those controlling the ownership and locations of community pharmacies.

3.7.2.1.Pharmacy Licensing and Location

The objective of pharmacist and pharmacy licensing is to ensure the health and safety of patients in the delivery of pharmaceutical care. All European countries require pharmacists and pharmacies to be licensed. To become a licensed pharmacist, all countries require

pharmacists to undertake specialist university training and in addition, most require the passing of a national board examination. In some countries, the licensing of pharmacists, pharmacies, or both is at the national level, while in other countries licensing is at the regional level. Even when licensing is a regional responsibility requirements are fairly uniform between the regions.

A common trend is the rising number of pharmacy technicians or assistants to counter a shortage of pharmacists being faced by many European countries. In the Scandinavian countries and the Netherlands qualified pharmacy staff other than pharmacists plays a more important role in dispensing OTC and prescription medicines than that currently permitted elsewhere in the EU. They work with greater autonomy, which permits pharmacists to delegate more work and may, for example, allow them to leave their premises to undertake other tasks while medicines are being dispensed.

In France, geographical restrictions are placed on licenses to secure set pharmacy-to-population ratios. This "numerus clausus" (quota) is intended to ensure a balanced geographical distribution of dispensaries, where approximately one third of them are currently in rural areas. The representative of the State in each department takes into account the needs and circumstances of the district when allowing a license to establish a new pharmacy, which restricts its location. The licence is specific to the stipulated 'place of business' and may specify a minimum distance between a proposed and existing pharmacy, or lay down in which neighbourhood it must locate to ensure optimal service coverage for the population residing within proximity of new pharmacy. The licence must be returned to the authorities should the place of business close down.

In the Dutch market, although the number of pharmacies is not regulated, the structure of the market and the relationship between key actors can impede the entry of new pharmacies. To establish a new pharmacy in the Netherlands, the new venture must meet the condition that it is financially sound (i.e. having a market of at least 8,000 patients per pharmacy). This patient-to-pharmacy ratio is dependent on a pharmacy having a contract with a health insurer because the contractual arrangement between a pharmacy and an insurer affects the ability of a pharmacy to attract patients. Furthermore, patient loyalty cards that link pharmacies to insurers has made entry for new pharmacies very limited.

In the Netherlands, because pharmacies are now considered economic undertakings contracting with a health insurer must now comply with competition regulation. Moreover,

since loans to open a new pharmacy are often tied to this condition it can serve as a significant barrier to entry for new pharmacies. It has been argued that this financial condition serves only to limit competition and does not ensure the public interest regarding the quality of the services provided (Philipsen and Faure, 2002). Also established pharmacies in the Netherlands tend to co-ordinate night/weekend services and exchange information on patients with neighbouring pharmacies often informally, which may further obstruct entry of new pharmacies. The Netherlands is a relative outlier when considering the population-to-pharmacist ratio. In addition, this is likely occurring because other health professionals, including chemists and pharmacy assistants, are involved in the dispensing of OTC medicines.

In the UK, "geographical indicators" place restrictions on how and where contracts to dispense NHS prescriptions are awarded. These 'control of entry regulations' (as they are more commonly referred to) were introduced in the UK in 1987. The OFT (2003) reported that prior to the introduction of these restrictions, the net annual average increase in contractor pharmacies was 130 per year in 1985 that later decreased to 4 per year between 1990 and 2000. The study also estimated that 80% of business in a community pharmacy is accounted for by NHS dispensing in the UK, and only a little over 1% of these dispense without such a contract. Restricting the number of pharmacies that can be located in a specific geographical area has protected smaller independent pharmacies from competition with larger chains. Although national pharmacy chains and supermarkets did increase their market share since 1990, only one new major chain (Superdrug) entered the market.

3.7.2.2.Pharmacy Ownership

In terms of pharmacy ownership, two restrictions are observed: i) pharmacy ownership may be restricted to pharmacists and ii) there may be restrictions on the number of pharmacies that can be owned, thus limiting the chaining of pharmacies. The Netherlands, Norway, and the UK allow non-pharmacists to own pharmacies and permit pharmacy owners to own more than one pharmacy. In the Netherlands, a general practitioner (GP) can own a pharmacy. In both France and Germany, pharmacy ownership is restricted to one or more registered pharmacists or a company constituted solely of pharmacists.

Legislation in France also stipulates how many pharmacists must be employed in each pharmacy according to its size as measured by its annual revenue (one pharmacist for every increment of 823,000 Euros in annual revenue). In 2001, France had 29.06% of community pharmacies with one permanent pharmacist, 45.75% with two pharmacists and 25.19% with

at least three pharmacists. Additionally, France and Germany also restrict pharmacists to owning only one pharmacy. This prevents the chaining of pharmacies and restricts competition between pharmacies. An exception may be made to this single-pharmacy-ownership rule in rural areas of Germany where a pharmacist owner is allowed to own a second pharmacy in a remote, less profitable and designated location. Interestingly, France and Germany collectively had just over 40% of all pharmacies in Europe in 2001 (Luckenbach, 2001). Given the regulations, the majority of these are 'small' community pharmacies.

Vertical integration of wholesaling and retail pharmacy business is a common cost-saving strategy for pharmacy chains, and forms an important part of the market in the other countries as well. Two of the largest vertically integrated chains in Europe are Boots and Lloyds in the UK. A chain is generally considered to be five or more stores under single ownership and includes banners (i.e. independent pharmacies affiliated with a central office and paying fees for the right to use a recognized name) and franchises. A pharmacy chain would be assumed to be more productive than an independent pharmacy as they can benefit from economies of scale and scope. In England and Wales, and the Netherlands the share of the pharmacy market accounted for by chains was estimated in 2001 to be 48% and 50% respectively (Table 3.8).

Table 3.8. Share of Retail Pharmacies in Chains or Public Ownership, 2001

Country	Pharmacies in Chains (%)
Sweden[1]	100.0
Norway	85.7
Netherlands	50.0
England & Wales	48.0
Belgium[2]	10.8
Italy[1]	9.8
Switzerland	3.0

[1] Mostly Publicly Owned
[2] Mostly Co-ops

Source: James Dudley Management 2002; Mossialos and Mrazek, 2003.

3.7.2.3.Pharmacy Remuneration

How pharmacists are paid influences their product selection. Community pharmacists have a potentially important role to play in controlling pharmaceutical expenditures through dispensing (or persuading prescribers to select) the cheapest multi-sourced (generic) medicine available. In many EU countries generic substitution is allowed only if the prescription is written using the generic name of the product. Use of lower cost generic products is a direct requirement in some states, but is more typically promoted through financial incentives. Denmark has a unique approach applying a dispensing budget that introduces a collective incentive to dispense cost consciously. In Germany pharmacists are in appropriate circumstances required to dispense from the lowest-cost one-third of available generic versions.

In the Netherlands and UK, as in Ireland and Sweden, pharmacists are paid a fixed fee per prescription. In the case of the British NHS, pharmacists are additionally reimbursed a fixed amount to meet the ingredient cost of each type of medicine dispensed. This offers them an incentive to demand discounts from wholesalers. A simultaneous scheme operates to 'claw-back' (on an averaged basis) some of the profits which the pharmacists accrue from this, penalising those with relatively high medicine purchasing costs.

The Netherlands also operates a form of profit claw-back on pharmacists' earnings from drug price discounts. But if a cheaper product from a reference price cluster is dispensed the pharmacist can charge the insurance fund one-third of the difference between the reference price and the retail price of the dispensed product, on top of the fixed dispensing fee.

In other EU countries (Austria, Germany, Belgium, Finland, Greece, Italy, Portugal and Spain) pharmacists' profits are normally directly linked to the price of the product dispensed. This makes it attractive to supply more expensive medicines. To the extent that regulatory and linked remuneration schemes give pharmacists and/or other professionals a perverse incentive to use higher cost medicines (or alternatively, as with some reference price schemes, effectively impose 'price floors'– PuigJunoy, 2003) questions exist as to why such arrangements continue to exist in many parts of the EU.

As a consequence of restrictions on ownership and pharmacy numbers, a number of European countries regulate the size of pharmacists' dispensing margins. In these markets where competition has often been limited, government regulation of margins is used to ensure

they are reasonable as distribution margins, another measure of efficiency, are assumed to be smaller in a competitive market. However, differences in margins may reflect the degree of integration between retailers and the distribution chain or the respective power of different players (i.e. manufacturers, retailers, wholesalers, and healthcare payers). Moreover, a low margin or productive pharmacy may not be reflected in the quality of pharmaceutical care that is delivered to patients.

France has since 1990 had a 'smooth declining margin'. The permitted pharmacy mark-up declines for each successive increase in the price of each medicine provided. This partly de-links the level of the pharmacy mark-up from the price of the prescribed drug. French pharmacists have also, from 1998, been entitled to a beneficial margin for dispensing from an official list of substitutable generics. In Germany, pharmacists are also remunerated with digressive margins scaled to price bands that decrease as product price increases. Although these margins are scaled digressively the overall effect is that pharmacists receive a higher margin from dispensing a more expensive medicine. The objective of the regulated pharmacist margins in Germany is to ensure uniform retail prices and margins are estimated to be on average 26.8% of the retail price (VFA, 2002). In France, the average mark-up is close to 26% (Blanchier and Kanavos, 2001); however, mark-ups on some non-prescription drugs that are purchased directly from the manufacturer may be closer to 60% of the retail price (AESGP, 2001).

In Spain in 1997, mark-ups for pharmacies were set at 27.9%; then in 2000, lower-cost medicines were promoted though a decreasing mark-up with product price including a monetary cap (78.34 Euros of ex-factory price). Furthermore, to encourage generic dispensing an additional mark-up of 5.1% was set for generic products.

As insurers in the Netherlands have been able to deny the granting of a contract to a pharmacy since 1992, competitive bidding has been used by several insurers to set up pharmacies. The insurers can negotiate a discount of up to 10% on the official prices that it must pay to the pharmacy for prescription drugs, which is in addition to the clawback instituted by the Dutch government. According to the Ministerie van Volksgezondheid, the current negotiated level is set at 6.82%. Furthermore, pharmacists in the Netherlands are faced with a perverse incentive to dispense smaller pack sizes particularly for repeat prescriptions as they are paid a fee each time a prescription is dispensed. The average gross profit of community pharmacies in 2000 was estimated to be 23% including purchasing rebates

(Stichting Farmaceutische Kengetallen, 2000) or on average 33% of the retail price. Table 3.9 details the payment methods and margins of pharmacists in some EU countries**.**

Table 3.9. Pharmacists' Payment and Margins

Country	**Type of Payment/Margin**
France	Digressive margins Beneficial margin for generic dispensing
Germany	Digressive margins scaled to price bands
Netherlands	Fixed fee per prescription Reimbursement at list price Negotiations with insurer incl. clawback
Norway	Progressive annual fee Subsidies Restrictions on turnover
Spain	Digressive margins Monetary cap Beneficial margin for generic dispensing
United Kingdom	Fixed fee per prescription Reimbursement at list price Clawback

Source: Kanavos, 2005.

3.7.2.4. The Clawback

The clawback is a mechanism whereby health insurance organisations ensure that (part of the) discounts pharmacists receive from wholesalers are being passed back on to them as savings. This system has found application in the Netherlands (since mid-1998) and the United Kingdom (since the mid-1990s), two EU member states where pharmacy margins are not fixed and where pharmacists are allowed and encouraged to source from cost-effective sources, including parallel imported medicines.

In the Netherlands, the system requires pharmacists to return 6.82% (clawback – 6.82%) to the sickness funds, but pharmacies may keep the difference between what they are obliged to send and what the actual discount rate with wholesalers is. Indeed, the clawback has been in operation in the Netherlands since July 1st, 1998. The scheme aims to "compensate" Dutch sickness funds for purchasing economies that pharmacists make by negotiating discounts with wholesalers. As part of the trade-off between accepting a gradually increasing dispensing fee, pharmacists accepted a clawback of 6.82% with a ceiling of €6.80 per prescription.

As a result of a flat clawback rate being set at 6.82%, pharmacists do have an extra incentive to procure from PI sources carrying higher discounts. This extra incentive is the

result of an average discount of 20% pharmacists can achieve in engaging in their purchasing economies, although this applies across the board to single source drugs, parallel imports and generics. Alternatively, the reimbursement price to pharmacists for single source PI drugs is based on the list price of the cheapest supplier per country the drug (form) is originating from, minus 8% (with a maximum per prescription of €9.00).

In the United Kingdom, the 'clawback' (known locally as "discount recovery scale") has the same operational principles as that in the Netherlands. The DoH takes into consideration the "Discount to Pharmacy" given by wholesalers to pharmacists. Chain pharmacies are excluded from the inquiry, despite having a greater leverage in negotiations and achieve higher discounts from wholesalers. The DoH refunds the pharmacist based on the NHS price level minus a "clawback" which currently ranges between 6.51% and 13.2% depending of the number of prescriptions dispensed each month. Most pharmacies are falling into the 10.44% bracket. The exceptions to this case are the "zero discount scheme" products in the drug tariff. This scheme applies to products that have a high cost for wholesalers in terms of storage and distribution. It affects about 500 products including 300 fridge-lines (e.g. vaccines), expensive items such as betaferon and controlled drugs that require extensive record keeping. For these products the wholesalers do not discount the product to the pharmacist and the DoH reimburses the pharmacist at NHS-price level without deducting the clawback.

Every pharmacy in the UK is subject to the Department of Health's clawback. Given the flat fee structure of the clawback relative to the number of prescriptions, pharmacies have an indirect incentive to procure more from parallel importers, or, indeed, obtain the so-called price-equalisation deals from official wholesalers, as they can keep a significant proportion of the overall discount given. As the average clawback currently stands at 10.44%, if pharmacies achieve a higher discount on this, then they can keep the difference. Other than discounts given to pharmacies, PI pharmaceuticals do not have an incentive to be priced lower than the list price. Pricing evidence from the UK suggests that actual discounts for the top 10 products to individual pharmacies range from 1.6% to 24.3% off the NHS list price. Of that, an average 10.44% is the clawback, while pharmacies still benefit by the difference.

3.7.3. The Wholesale Market

Wholesaling developments in the majority of OECD countries have in the past few decades been driven by the pursuit of economies of scale associated with the rationalisation of warehousing facilities, computerisation, and the use of electronic record keeping and data

interchange (EDI) systems for ordering medicines and optimising stocks. This is relevant from a regulatory policy viewpoint because the market power and competencies of the surviving wholesalers has been strengthened, and they are now in a position to take a stronger leadership role in the overall pharmaceutical distribution chain.

Although major wholesalers purchase both generic and branded (including patented) pharmaceuticals throughout the EU and as legally permitted from other sources, relationships between pharmacists and wholesalers are normally conducted within national boundaries. That is, even in the case of trans-national pharmaceutical wholesalers pharmacy customers in any one state are normally supplied via the locally based subsidiary. This is not least because of differing controls on product price mark-ups. With the exception of the Netherlands and Denmark (in Denmark it is illegal for wholesalers to offer discounts to pharmacies, while in the former wholesalers' margins are determined by market forces) all European countries impose limits on drug wholesalers' margins, either via statutorily defined mechanisms or through established practice with the public healthcare sector. Permitted wholesaler margins vary significantly between EU states (LIF, 2002), although differences in discounting to pharmacies (plus local VAT policies) to a degree reduce the apparent disparities. A comparison of wholesalers' margins in different countries can be viewed below in Table 3.10.

Table 3.10. Gross Margins for Wholesalers, 2000

Country	Margin (%)
Finland	4.0
Denmark	6.8
France	7.1
Italy	9.0
Spain	10.0
Austria	11.0
Luxembourg	11.0
Netherlands	11.0
United Kingdom	12.5
Belgium	13.0
Germany	13.0
Switzerland	13.5

Source: LIF, 2002 based on MEGROS data.

3.7.4. Hospital Pharmacies

The role of hospital pharmacies has also dramatically been transformed over the past three decades. Hospital pharmacists are increasingly required to become comfortable with larger roles – not only their traditional responsibilities of drug preparation and verification, but also working as clinical pharmacists at the ward level. The international trend in hospital pharmacies has become providing products to meet individual patient need, thus necessitating increased collaboration between hospital pharmacists and prescribers, nurses, dieticians, biochemists, and laboratory scientist. On an institutional level, hospital pharmacies must support the safe, effective, and economic use of medicines in hospitals in accordance with government rules and budgetary requirements. Carrying out these responsibilities requires medicines information services and clinical pharmacy services within the hospital to service outpatient care. In addition, specialised databases and medicine information services based in hospitals have been developed to facilitate drug treatment decision-making by clinicians (Taggiasco, et al., 1992).

Expanding the roles of hospital and community pharmacies also has the potential of reducing medical errors. In the US, fatalities from prescription errors are claimed to have increased by a 243% increase from 1993 to 1998, outpacing almost any other cause of death, and also progressing faster than the increase in prescriptions (Phillips and Bredder, 2002). In one study, errors in prescribing medications appeared as the most common mistake made among family physicians (Dovey, et al., 2003). Another study in an American teaching hospital reports finding four errors per 1,000 medication orders, 70% of which had the potential to be seriously harmful (Lesar, et al., 1997). Preventable adverse reactions to drugs are claimed to be the single leading cause of hospitalisation in the US, where 2% to 7% of hospitalised patients have avoidable adverse drug events and consequently have hospitals stays 8 to 12 days longer than they should (Kohn, et al., 2002). Studies done in the UK have shown similar results, with one report of a 49% error rate in the administration of intravenous drugs (Taxis and Barber, 2003). Medical errors have been attributed to a number of causes: administrative and investigation failures, simple ignorance, lapses in treatment delivery, miscommunication, complications in payment systems, among many others (Dovey, et al., 2002).

The US Institute of Medicine (IOM) and the Agency for Healthcare Research and Quality have both called for a systematic way of formulating and incorporating safety into the process of care. Drawing on examples outside of healthcare and considering such processes

such as incident reporting, root cause analysis, and simulators, specific recommendations regarding certain clinical practices are mentioned, as well as the issue of how to promote safety practices on an institutional level (Shojania, et al., 2001).

The idea of 'pharmaceutical care' (Cipolle, et al., 1998) has changed the traditional role and function of hospital pharmacists from dealing solely with in-patient care, to involvement in the ambulatory-care setting working closely in treatment delivery; in the patient-care setting regarding hospital risk management strategies; and in the clinical-setting contributing information on adverse side effects to national pharmacovigilance systems. In addition, hospital pharmacists play an important role in combating inaccuracies in transmitting patient drug information between community physicians and hospital specialists. Hospital pharmacists can and do works in conjunction with nurse specialists to improve patient education and in special cases provide follow up visits in the patient's home. Furthermore, pharmacists serve a fundamental role in improving patients' self-management in diabetes and other chronic conditions that can potentially reduce hospital readmission rates and improve patient compliance to drug treatment regimes.

3.8. Influencing Patient Demand Through Co-Payments

In most OECD countries, cost sharing for pharmaceuticals has been introduced to try to control pharmaceutical expenditure and influence the demand for prescription drugs. There are three different forms of cost sharing currently employed. Co-insurance, the most common form, requires the patient to be liable for some percentage of the total cost of a drug; flat-rate payments oblige the patient to pay a fixed fee per item or per prescription; and deductibles involve the individual paying the initial expense up to a specified amount. There is great variation across Western European countries with respect to the implementation of prescription drug charges or co-payments. Although co-payments are not usually linked to reference pricing in Europe as they are in North America, there has been linkage with variable co-payments for drugs on restricted lists in France and Italy, based on the perceived therapeutic value of that drug to the health service.

Advocates of cost sharing argue that it increases efficiency by reducing excessive demand and containing overall health costs. Individuals become price sensitive and will seek what is to them the least expensive treatment. If there is competition between providers, individuals' sensitivity to price may result in lower prices. Introducing the price mechanism in this way may also prevent unnecessary (or even potentially harmful) care since individuals

will select treatments and interventions that are of high value to them. Other supporters of cost sharing maintain that any additional revenue raised could be targeted at low-income people or used to confront inequality in the healthcare system. The ability of cost sharing to raise revenue, however, is limited by the prevalence of widely-applied exemptions and high administrative costs. In many countries, significant groups within the population (based on age, income, and clinical condition) are exempt from cost sharing in an attempt to protect the disadvantaged, satisfy need, and ensure equitable access to drugs. Moreover, the existence of complementary voluntary health insurance in some countries (e.g. France, Croatia, and Slovenia) effectively removes price signals for those who can afford to purchase a medicine and therefore negates the potential for cost sharing to reduce demand.

Critics argue that the theoretical case for using cost sharing as a means of reducing excess utilisation is weak because healthcare markets are characterised by information asymmetry, proxy demand and heterogeneity. Furthermore, since demand for healthcare is largely provider-determined, policy tools that focus on the demand side may not be as effective in controlling demand as those that focus on supply. Cost sharing also has implications for equity in funding health, because it shifts the financial burden towards individuals and households and away from population-based risk sharing arrangements. Equity in access to healthcare is also reduced by cost sharing as those with low incomes (and likely to be in poorest health) are most likely to be discouraged from using health services. This decrease seems to be in not just nonessential but also essential drug therapy (Evans, et al., 1995).

In terms of macro-efficiency, the savings in drug costs may be outweighed by increased utilisation of other healthcare services which may, in fact, increase overall healthcare spending. In addition, the transaction costs of implementing prescription charges and exemption schemes limit the cost saving. Third, in cost sharing for pharmaceuticals, governments impose a risk on individuals for an intervention that is largely beyond their control; that is, where consumption depends on prescription by doctors. In other words, financial (dis)incentives are placed on individuals, who have less power to control drug spending than prescribers and user charges can be seen as punishing the patient for following their doctor's orders. The use of co-payments is a blunt mechanism of controlling costs and must be applied cautiously so as not to be counterproductive to the overall objective of a healthcare system. Careful use of differential co-payments or co-payments with well-defined exemptions may be more acceptable.

3.9. The Off-Patent (Generic) Pharmaceutical Market

Once the patent on a pharmaceutical product has expired, generic equivalents may come on the market so increasing competition. A generic equivalent is a perfect substitute to the original brand and competes in price for market share. The new product must demonstrate bio-availability for the main active ingredient comparable to a brand leader. These virtual copies of the original branded medicine may be branded or un-branded and are also known as off-patent, post-patent, or multi-sourced drugs. Because of their low cost compared to the brand leader, generic drugs potentially offer significant savings that can release funds to pay for innovative, patent-protected products.

The low cost of generics is due to supply-side factors such as market size and the number of suppliers. Equally important are the demand-side incentives that encourage prescribing, dispensing and consumption of generics. Financial incentives to increase generic prescribing may tie into physician budgets or guidelines. The selection of the least expensive multi-sourced drugs by the pharmacist and generic substitution where it is allowed is also motivated more effectively by financial incentives which give pharmacists higher margins or additional payments for dispensing a lower-cost generic medicine.

Differential or lower co-payments for generics over brands also encourage patients to ask for generic substitution, and are extensively used by managed care in the United States as part of reference pricing systems linked to co-payments, as described above. This has yet to take hold in the EU mainly because generic substitution for a branded prescription is not allowed in most EU countries. In the UK, the government's promotion of generic prescribing by doctors has been so successful that generic substitution would actually make little further saving. There are other opposing factors: the extent of use of branded generics and low priced original brands impede the extent of price competition. Although evidence suggests that price competition with the right combination of demand-side incentives does stimulate price competitiveness, many EU governments nevertheless choose to regulate the prices of generics directly (UK) or indirectly through reference price schemes.

Some EU Member States have less explicit financial incentives for generic prescribing but do mandate responsibility to inform patients of cheaper generic alternatives to either physicians (as in Sweden) or pharmacists (as in Denmark). Evidence seems to point to the finding that financial incentives for physicians, pharmacists, and consumers toward demand-side cost-awareness may be more effective than regulating prices of generic products.

3.10. The OTC Market

Medicines that can be obtained without prescription from a medical practitioner are termed over-the-counter (OTC) pharmaceuticals. Already this is the largest sector of medicines use as measured by numbers of patients treated. The sale of OTC products might require pharmacist supervision or they may be for general sale. In the past, re-classifying medicines to OTC status required good reasons, the climate now is the reverse: there must be good reasons not to re-classify medicines as OTCs, such as a need for medical supervision to prevent direct or indirect dangers to health; potential for misuse; lack of thorough scientific investigation; or a need to be parenterally administered. The motivation behind this reallocation is to enhance patient access to medicines; to shift drug distribution costs from governments to individual consumers; and to encourage greater public responsibility in self-medication. Product selection in this market has traditionally been based on experience of benefit and safety reported by customers, personal previous use, advertisements, lay advice, and professional advice from General Practitioners (GPs), nurses and pharmacists.

There remain important economic and equity issues here. Achieving overall cost savings requires that the consumer can both diagnose the condition correctly as well as identify the correct treatment, whether it is an OTC product or not. Available data shows that this may not always be the case (Brass, 2001). Furthermore, the equity dimension is an essential consideration; if deregulation form prescription only to OTC removes a drug from the list reimbursed, then those with low ability to pay or cope with these changes may suffer adversely and again, cost the system overall more than intended.

Industry is often keen to promote OTC switches at a late stage of a product's life cycle: it expands the market, especially at a time when a drug is coming off-patent and facing generic competition, and allows direct to consumer (DTC) advertising, perhaps reinforcing brand loyalty. This may increase pressure on general practitioners and other prescribers from patients as consumers demanding certain products – especially if the cost of a prescription charge is less than the price of the OTC product, or if the patient were exempt from the prescription charge. The impact of newly deregulated products has been observed in early health economics research to generate significant government savings in some but not all drug-associated costs (Berndt, et al., 2000). Generally, patients have been receptive to deregulation of medicines to OTC status, even though one of the objectives in deregulation has been to, in fact, increase their financial burden. Doctors, too, seem amenable to this idea, especially in the area of medicines for "social" decisions, such as emergency contraception or

smoking cessation, although in other areas (e.g. dyspepsia treatments) deregulation has made little difference to prescribed drug use.

In some countries, the OTC market has extended the role of the pharmacist. For products requiring 'pharmacist supervision', community pharmacists must ensure compliance with the licensed indications of the OTC products, assessing the potential for drug interactions, and avoiding sales to patients with contra-indications. Difficulties arise when patients are not aware of this role for the pharmacists and are resistant to their professional advice. This may be exacerbated in cases where the patient wants a medication for a purpose outside the OTC licence (e.g. hydrocortisone 1% is often purchased to be used on the face although this is outside the OTC licence). In addition, at least theoretically, the risk of adverse events is shifted onto the pharmacist, who now becomes liable instead of the GP.

Pharmaceutical products are under perpetual monitoring even when fully deregulated to OTC status through the use of spontaneous reporting, event monitoring, and specific surveillance. In spite of these measures, pharmacovigilance monitoring for OTC products is especially difficult because of the lack of detailed records on product users and the rationale for use.

In the majority of EU Member States, OTC drugs are not reimbursed (see Table 3.11), although some exceptions exist, when an OTC product is prescribed by a physician. In many cases, health insurance funds include some OTCs in their positive lists (e.g. paracetamol, aspirin, some vitamins, etc), but their number is limited.

Table 3.11. OTC Regulations in Selected EU Member States, 2002

Austria
- Prices of all medicines, whether they are reimbursed or not, must be approved by the Pricing Commission within the MoH.

Italy
- OTCs are freely priced and are not reimbursed by the NHS.
- OTCs can be sold only in pharmacies and not any other outlets.

Portugal
- OTCs have free pricing and distribution margins
- OTC products are not reimbursed and can be sold only through pharmacies.
- OTC products are not reimbursable, except in exceptional circumstances justifiable on grounds of public health reasons.
- Some works continue to set the principles to be applied in the technical and scientific evaluation of the products applications to be switched from prescription-only status to OTC.

Ireland
- OTCs can be priced freely.
- Pharmacists charge customers a 50% mark-up on their own purchase price, plus a dispensing fee if the product is supplied on prescription.
- OTCs that are intended for self medication and are advertised to the public are not reimbursed.

Netherlands
- OTC prices are not controlled.
- Pharmacists receive two separate lists of OTC drugs, which, in effect, determine their current reimbursement status, as follows:
  - Products considered to be self-care for short-term use only and totally excluded from reimbursement including Anti-virals such as acyclovir and penciclovir and Antifungals, such as clotrimazole, econazole and sulconazole
  - Products which can be reimbursed if for "chronic use" including Paracetamol-based painkillers, Antihistamines, Calcium preparations for osteoporosis
- Previously, all OTCs were fully reimbursed provided that a patient obtained a doctor's prescription. Now- only patients with a doctor's note confirming "chronic use" (CG) can seek reimbursement for products in list 2. Additional conditions are that the drug is used for at least 3 months of the year and the patient has paid for the first 15 days of treatment.
- OTCs are sold in medicinal product stores. Other stores like supermarkets can have a medicinal products store department, subject to the same regulations as the pharmacy stores.
- Decisions about switching from prescription-only status to OTC are made by the Medicines Evaluation Board and, normally, at the request of the producer. The criterion is safety under normal use. The change from OTC to prescription-only medicinal product is made by the Medicines Evaluation Board when side effects give reason to do so. Following several delays in implementation and in the face of widespread opposition from pharmacists, industry and GPs, the Government went ahead with its planned de-listing of OTCs from 1 September 1999 yielding significant savings to health insurance.

Denmark
- Do not enforce price control on the OTC market.
- OTCs may be admitted to the list of reimbursable products. In such cases, the reimbursement is only granted to pensioners and patients suffering from chronic disease, and only if a prescription has been issued for the medicinal products in question.
- OTCs are sold in pharmacies.

Sweden
- OTCs can be reimbursed when they are deemed necessary for the treatment of chronic illnesses, i.e. when continuous treatment for at least a year, or when repeated treatments of at least 3-month durations are needed. In this case, products like antacids, bulk laxatives, vitamins, skin moistents and expectorants can be reimbursed, provided that a reimbursement price has been granted.
- OTCs can only be sold in pharmacies and not in other outlets.
- The Swedish Medical Products Agency is responsible for OTC switch policies.

Norway
- OTC sales account for some 13% of total pharmaceutical expenditure. At present, all medicines are sold through pharmacies.
- Applications for OTC switch in Norway are evaluated on a case-by-case basis.

Czech Republic
- No special "OTC switch" action is proposed, but some drug group considerations are being made, especially with paracetamol and acetylsalisilycacid.
- Policy-makers are afraid of switching from these cheap products to relatively more expensive products containing NSAI agents that will bring no benefit to patients and will increase the amount of money from insurance funds.
- A switch was made 5 years ago when cheap anti-cough drugs were exempted from reimbursement (doctors switched to mucolytics, which are three times more expensive).
- There are 195 defined medicinal (OTCs) products which might be sold outside pharmacies (MoH Decree 21/1998). This decree also defines the conditions at which the distribution outside the pharmacy can be made.

Hungary
- OTC prices are not regulated.
- OTC products are not reimbursed, unless they are included into the special list of drugs, which are available free of charge for low-income groups (Közgyogy list).
- OTC products can be sold in licensed pharmacies only.

Slovenia
- Most OTCs are sold in pharmacies.
- Pharmacies also sell medical aids, hygienic products and cosmetic products.
- OTC switching is possible, but not common.

Source: Kanavos, 2002.

3.11. Concluding Remarks

There are many different approaches to regulating pharmaceuticals that affect public policy objectives to control costs while improving efficiency, quality of care and equity. International comparisons may contribute to a better understanding of how different measures and policies are implemented. However, there are significant limitations to the relevance and transferability of lessons and policies across countries. Contextual factors such as the social, economic, medical, healthcare and political environment as well as constraints of history and institutional frameworks play a major role in how policies are developed and implemented in practice. This is particularly important in the EU because of not only national regulation but also supranational regulations. A policy adopted in one country therefore may not necessarily

work, or at least not to the same degree, in another and may need to be modified to the new context. As described before, it is often difficult to be clear on which component of a diverse range of measures undertaken was most successful. Given these two factors, deriving any sense of which of the many possible interventions is most effective is difficult. A further complication is that governments must consider those policies already in place and their effects before new policies are adopted. Trade-offs between competing policy objectives (health versus industrial) or the needs of different stake-holders (patients, health professionals, and industry) are inevitable.

Governments in OECD countries are all faced with rising pharmaceutical expenditures but have taken widely divergent approaches to tackling these. Some government policies that enhance quality of care or efficiency or access may decrease the ability to contain expenditures. Rising expenditures of themselves may not be a problem if they are accompanied by health gain or by a similar rise in government revenues. In practice, the added health gain for added expenditure is often unclear, and the rate of rise of expenditure often exceeds revenue, so governments are forced to act. At the same time, they must aim not just to contain costs but to improve the efficiency and quality of the health service, and preserve or enhance equity. Any approach to cost containment therefore has to be evaluated in terms of its effects in these four dimensions.

From the review presented here, it is clear that no single policy approach acts without a trade-off on the impact along these four dimensions, in addition to competing trade-offs between the objectives of the policies themselves. Therefore a policy maker needs to be clear what primary impact is desired, but conscious of where a subsequent negative impact of any policy may arise in other dimensions; if the impact of the trade-off along the other evaluative areas out-weighs the gains in the primary indicator, a policy must be reconsidered.

Considering these four dimensions, it is clear that most of the measures intended to contain costs do have an impact; however, the extent of any cost-savings or their sustainability over the longer term is variable, e.g. GP fundholding and associated incentives in the UK, or reference pricing in Germany. In fact, in most cases the cost savings generated by any one policy are either limited or short term. The most effective approaches work best when combined with other policy measures. For instance, price controls alone have a limited effect, but are more successful when policy measures are applied to the volume-side of the expenditure equation as well.

In general, few of the measures demonstrate a clear efficiency gain, in part due to a lack of rigorous studies. This is often however a key aim of government polices – containing costs without any diminution in quality. One that does succeed in this regard is generic prescribing or substitution. Academic detailing might increase quality, equity and effectiveness by encouraging the application of evidence based medicine. It might increase costs by encouraging appropriate treatment where previously there was under-treatment, or decrease costs where there was over-treatment or waste. Of the interventions considered here, it is probably the most professionally acceptable. The use of economic evaluation or wider health technology assessment may improve efficiency, but usually with increased overall costs, as in the case of the National Institute for Clinical Excellence in the UK, most of whose guidance increase NHS costs. Some policies might inadvertently seriously decrease efficiency – e.g. if saving money on drugs led to more hospital admissions, as has been clearly seen in the United States (Soumerai, 1991) and as allegedly happened in Germany in the early 1990s in response to GP budgets. This illustrates the need to consider the broader effects, including efficiency, in evaluating any intervention.

Polices aimed solely at cost containment might reduce equity, but if the aim of cost containment is to reduce unnecessary expenditure (e.g. generics again) so as to allow access to other therapies, then cost containment would increase equity. In general, policies for the rational use of medicines would be expected to result in improvements in equity at an aggregate level. Policies such as reference pricing and prescription co-payments may reduce equity, unless there are exemptions to protect more vulnerable patients: used carefully these interventions can increase efficiency and decrease cost, without damaging quality and with minimal disruption to equity.

The quality of care dimension is usually raised as a primary objective of some measures that target the rational use of medicines. In these, cost is secondary and in fact some measures may be cost increasing. This raises the difficult balance faced by policy makers in this sector to secure quality, maintain equity and improve efficiency, but yet contain costs.

It is clear that there is no perfect solution to balancing these four dimensions in the pharmaceutical sector. Even if one is sure where the balance should lie, no one policy or policy combination is right for all countries. Different countries will need to meet their own objectives and needs through policy approaches that reflect their particular environment.

Nevertheless, there are some general principles of best practice that policy makers should keep in mind. First, the objective of the policy must be clear from the outset, and consideration given to its possible impact on all of the evaluative dimensions of efficiency, equity, quality and cost. Rigorous price control schemes seem to have an impact on controlling prices, but controlling price alone, if this can be achieved, does not necessarily improve efficiency, nor does it necessarily control total expenditures. Attention to the demand-side and the promotion of rational drug use is vital if efficiency, equity and quality are also to be improved. New drugs and changes in product mix will certainly drive drug expenditure in the future. The policy community at large needs to consider how we define and reward clinically valuable innovation, so that drug expenditure reflects the value of the drug's benefits for society. The future will require a greater partnership between all stakeholders if the solidarity of socialised pharmaceutical care is to be maintained despite greater needs and constrained resources.

4. Drug Policy in Turkey Revisited: Caveats

The previous sections have presented and discussed pharmaceutical policy elements in Turkey and a number of countries in the OECD region. The purpose was to first of all understand the process and conduct of drug policy in Turkey and, secondly, to summarise drug policies, policy tools and their uptake in different OECD countries and use these as possible benchmarks to current and prospective Turkish drug policy.

In this section we bring together some of the key features of the Turkish regulatory, pricing and reimbursement regime for pharmaceuticals with a view to highlighting the problems that decision-makers would need to address in the foreseeable future. We also use the international evidence to emphasize the differences between Turkey and some of the comparator countries, but do not argue for Turkey to adopt policies prevailing elsewhere without due consideration to its own institutional context. In this section, we consider (a) drug approval issues; (b) marketing authorisation; (c) intellectual property rights protection; (d) pricing of pharmaceutical products; (e) treatment of generic products; (f) principles of pharmaceutical reimbursement; (g) criteria for reimbursement; (h) measures to control physician behaviour; (i) pharmacy remuneration; (j) generic promotion and substitution; (k) the OTC sector; (l) industrial policy; and (m) the role of information in assisting reimbursement.

4.1. Drug Approval

In the majority of OECD countries, drug regulatory agencies are independent of the Ministry of Health authorities (Table 4.1), although the relevant agencies are usually established within the broad structure of the Ministry of Health. Independence implies that there is no direct or indirect government intervention in the function of the agency and also avoidance of clientelistic relations between regulator (agency) and regulatee (industry).

Table 4.1. How Independent or Integrated is the Drug Regulatory Agency?

Feature	FDA	MHRA (UK)	AFFSAPS (France)	Canada	Japan	Turkey
Independent agency	+	+	+	+	+	
Agency integrated within MoH						+

In Turkey, the drug regulatory agency is currently integrated within the MoH structure instead of being an independent organisation under the broad MoH structure as other

regulatory agencies are in benchmark countries. Independence of a drug regulatory agency is associated with transparency and non-bias, and, although necessary as a brokerage organisation between regulators and regulates, it is not a sufficient condition for other issues related to its function, for instance regulatory capture.

Over the long-term and as part of EU accession, Turkey will need to establish an independent drug agency within the Ministry of Health. We are aware of the fact that legislation is under preparation to set the operational framework of an autonomous agency within the Ministry of Health, which will be (partly) funded by user fees, and believe that this is a very positive development in principle.

4.2. Marketing Authorisation: Regulatory Authority Competences

The role of the drug regulatory agency is to examine whether a new product (branded or generic) meets the criteria of safety, efficacy and quality, thereby safeguarding public health and ensuring that new products offer benefit to patients (Table 4.2). It is on the basis of these criteria that marketing authorisation is granted. Pricing of pharmaceuticals is subsequently examined by other competent authorities within the MoH, or indeed, the processes of pricing and reimbursement of pharmaceuticals are often fused. Consequently, the drug regulator has no competence over pricing of pharmaceutical products (or reimbursement for that matter), as it is purely responsible for providing scientific opinion on new drugs.

Table 4.2. Marketing Authorisation Criteria for Pharmaceutical Products in Selected OECD Countries and Turkey

Feature	EMEA zone	FDA (USA)	Canada	Japan	Turkey
Safety	+	+	+	+	+
Efficacy	+	+	+	+	+
Quality	+	+	+	+	+
Reasonable price	No competence				+

In Turkey, the drug regulatory agency, which is an integral part of the Ministry of Health, is also responsible for pricing of pharmaceuticals, in accordance with the policy that prevails at the time. Planned legislation delegates responsibility for pricing to another committee within the Ministry of Health. This will relieve the new Drug Agency and will strengthen its remit, which is primarily to safeguard public health rather than set prices for medicinal products.

4.3. Intellectual Property Rights Protection

Two key aspects of intellectual property rights protection (IPRP) relate to (a) the patent term and (b) market exclusivity (Table 4.3). TRIPs as well as regional agreements (e.g. the marketing exclusivity term within the recently amended EU pharmaceutical legislation) provide a framework of implementation for countries involved. Both elements are needed for effective protection of intellectual property rights.

Table 4.3. Intellectual Property Rights Protection: Patent Term and Marketing Exclusivity in Selected OECD Countries and Turkey

Feature	EU-25	USA	Japan	Canada	Australia	Turkey
Patent term	+	+	+	+	+	+
Market exclusivity	+	+	+	+	+	+

Implementing intellectual property rights protection (implementation of a patent term since 1995, but not retro-actively) has been a very positive step. Its impact will, however, start to be felt in a few years at the earliest, once the ratio of new products that have entered the market place since 1995 increases further. In the meantime, products that entered the Turkish market prior to 1995, were not protected by a patent, and where, thus, subjected to competition by generic equivalents.

Market exclusivity, however, is critical for products currently on the market, which do not benefit from product patent protection. It is understood that the non-availability of patent protection prior to 1995 in Turkey has resulted in a large number of therapies not being covered by a patent or any form of exclusive rights. Thus, the phenomenon exists of several innovative products on the market not being by any form of IP covered and being subjected to generic competition through generic/copy products, which under the present circumstances are legal. However, The MoH has recently (January 19, 2005) modified its Registration Regulations where a 6 year of marketing exclusivity under certain conditions is allowed. Accordingly, marketing exclusivity will not be implemented retrospectively and will provide protection only for new molecules registered in Turkey after 1 January 2005 where the protection term will effectively begin from the first registration date in any of the EU Customs Union Zone countries. This protection term is limited with the patent term of the concerned molecule, and as prescribed in the Regulations, is also applicable to molecules registered from 1 January 2001 if only there was no generic in the marketplace in Turkey or

no generic application as of 31 December 2004 for these molecules. These conditions are still under debate among stakeholders.

4.4. Pharmaceutical Pricing

A wide variety of regulatory measures and methodologies for the pricing of medicinal products exist in most OECD countries. At the same time, in the majority of OECD countries, the process of setting pharmaceutical prices is kept separate from the process of negotiating reimbursement. At the stage of setting prices, different criteria usually apply, including assessing the medical value of the product, its conditions of use, examining comparator prices and sales volumes, among others (Table 4.4).

Table 4.4. Pricing Criteria for Originator Products in Selected OECD Countries and Turkey

Feature	UK	GER	FRA	ITA	SPA	DEN	POL	NET	TUR
Medical value			+			+		+	
Comparator prices			+					+	
Cross country comparisons			+	+	+		+	+	+
Sales volumes			+						
Conditions of use	+	+	+	+	+	+	+	+	
Price freedom	+	+	+			+			

Turkey relies on international price comparisons to determine the price of a pharmaceutical product. Five EU countries are considered for this purpose and the lowest among them is selected.

Pricing remains a procedural and documents-based issue in Turkey. No other criteria, such as prices of comparator products or comparative efficacy, medical value, etc. are considered. This would probably be problematic, if the process of reimbursement was not being kept separate.

While there are pros and cons associated with international comparisons (pros: administrative simplicity; potentially beneficial pricing regime towards industry, given Turkey's per capita income; and cons: no consideration of volume or therapeutic benefit), one major problem, is that the prices of originator products are used as basis for generics. This

[13] Notable exceptions are those countries, where drug prices are allowed to be set free or with minimal intervention (e.g. USA; UK [subject to profit control]; Germany, Denmark [for innovative products]).

may result in higher prices for generics than is otherwise justified by production costs in Turkey.

4.5. Treatment of Generic Products: Pricing

With few exceptions[14], in the majority of OECD countries, prices of generic products are either directly or indirectly controlled by the relevant competent authorities. Direct controls include price ceilings or price averages (Table 4.5). Price ceilings are administratively set and usually are a proportion of the price of the branded product. Typically, generic prices are set at 70-80% of the branded product in countries such as France, Italy, Spain or Greece. In theory, prices cannot exceed this ceiling. Averages involved an average being obtained from a basket of generics belonging to the same product/molecular class (e.g. the UK). Prices of generics are also controlled indirectly, through upper reimbursement ceilings (reference prices) based on generic prices at large. In this case, regulators set reimbursement at the lowest available generic or some kind of average. In practice, reimbursed prices cannot be higher than the administratively set level, but, of course, can be lower.

Table 4.5. Pricing/Reimbursement Criteria for Generics

Feature	UK	GER	FRA	ITA	SPA	DEN	POL	NET	TUR
Reference pricing		+	+	+	+		+	+	+
Upper ceiling for generic price	+		+	+	+				+
Cross country comparisons			+	+	+	+	+	+	+
Price freedom	+	+	+						

In Turkey, prices of generics are set 20% below those of originator drugs. This does not necessarily always hold, as a recent review of prices of the most sold products in the country revealed. While pricing for originator drugs is currently linked to the lowest EU price from a basket of five countries, generics are also indirectly linked to that process. This may lead to artificially high prices for generics.

In terms of reimbursement, the current rules relating to the use of generics (and copies) present several flaws:

- The reimbursement of “lowest available in the cluster + 30%” may lead to health insurance paying a price for a product (could be a generic or an original), which is

[14] Most notably the USA.

higher than the highest available in the market for that cluster. In particular, if the most widely available generic is priced at 80% of the originator drug, then the "80% + 30%" reimbursement rule would unavoidably result in a reimbursed price for the generic which is higher than that of the original.

- There are no "pure" generics in Turkey and this is a market of "branded" generics; the latter are usually associated with a (significant) price premium.
- There is no incentive for generic drugs to significantly undercut each other, particularly due to the administratively set prices; it should also be borne in mind that all generics are branded, and may be competing on their brand name; as a result, the incentive to compete is less than clear-cut
- Given the structure of the retail market that builds on both officially negotiated and set margins as well as discounts, high and administratively set prices for generics provide generic manufacturers with more flexibility to award significant discounts to pharmacists; these discounts are invisible, although the government is currently trying to claw-back some of these.
- Given the extent of discounts to pharmacy, which provide a potentially significant source of income to pharmacists (in addition to their margins), the latter may have an incentive to substitute for a generic, but it remains doubtful whether cost savings are generated from this process.

4.6. Pharmaceutical Reimbursement Principles

Reimbursement policy typically must satisfy a number of criteria, essentially implying transparency, non-bias, and ensuring access and fairness across insured populations (Table 4.6). These criteria are as follows: first, reimbursement policy must be characterized by transparency; second, it should allow flexibility to ensure that new treatments are effective and are made available to patients within a reasonable amount of time; third, it should be robust in evaluating clinical benefit and assessing the economic impact of treatment; and fourth, it should have common principles across all payers, and, ideally, be a single policy across the range of payers. This latter point is a critical policy objective for the Turkish government and is gradually under implementation.

Table 4.6. Reimbursement Principles for Pharmaceutical Products: An International Perspective

Criteria	EU	USA	Canada	A8[1]
Transparency	+?[2]	+	+	+?[2]
Flexibility to enable inclusion of new medications	+	+	+	+?[3]
Robustness in evaluating clinical benefit	+	+	+	+
Common principles among all payers	+	+	+	+

[1] Refers to the 8 new EU Member States from Eastern Europe (Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Slovakia, Slovenia).
[2] Although there is compliance in principle, this does not necessarily exclude the possibility of non-compliance or violation of transparency as outlined in the EU acquis communautaire.
[3] Flexibility is questionable.

With regards to the first three of the criteria set out above, it is doubtful that the criteria of transparency, flexibility and robustness are met in Turkey. It is also unclear as to who decides on reimbursement, what skills decision makers have, what criteria are used for reimbursement, how well publicized they are, what the procedures are for reimbursement applications, what appeal processes are in place and whether other stakeholders are able to express an opinion about new treatments. It is also not known how frequently lists are reviewed and who reviews them; if products are excluded from reimbursement, the criteria for exclusion (let alone those for inclusion) are not known; finally, the frequency of convening reimbursement committees and examining new applications for reimbursement is not known.

The fragmentation of the health care system is also contributing to differing rules and principles being applied to reimbursement of different products. The recent health care reforms, however, aiming at unifying all health insurance funds under one umbrella, are a move in the right direction and will eventually lead to common principles being applied for reimbursement across all health insurance funds.

4.7. Reimbursement Criteria

A number of criteria apply to decide whether a product can be reimbursed by health insurance organisations (Table 4.7). Typically, across most OECD countries, clinical criteria (i.e. overall efficacy and comparative efficacy) are key in determining whether a product can be seriously considered for reimbursement. Further considerations include clinical cost effectiveness, budget impact analysis and overall projected sales volume. Finally, foreign prices assist reimbursement agencies in determining reimbursement rates in their jurisdictions. OTC products are typically excluded from reimbursement (bar a few) as they

can be acquired by consumers without a prescription and at modest to moderate cost. A key tool in deciding on reimbursement is the inclusion or not into the reimbursement or positive list.

Table 4.7. Criteria for Pharmaceutical Reimbursement

Criteria	UK	GER	FRA	SPA	NET	POL	ITA	CAN	TUR
Clinical	+	+	+	+	+	+	+	+	+
Budgetary	+	+	+	+	+	+	+	+	+
CEA	+	+[1]	+[2]		+		+	+	
Industrial policy	+	+	+	+				+	
Defining who benefits most	+	+	+	+	+	+	+	+	+?[4]
Volume	+	+	+	+	+	+	+	+	
Foreign prices	+	+	+	+	+	+	+	+	
OTC exclusion	+	+	+	+	+		+	+	
Tender	+[3]	+[3]	+[3]	+[3]	+[3]	+[3]	+[3]	+[3]	+

[1] Will be a formal requirement for new treatments shortly.
[2] Not a formal requirement, but is usually requested by reimbursement agencies.
[3] Hospitals only.
[4] Although there seems to be a definition of who benefits most on the basis of a number of clinical practice guidelines, it is unknown whether these are actively used in reaching reimbursement decisions.

In general, the criteria for admitting products into the positive list include, among others:

(a) The seriousness of the condition and whether there are existing treatments

- Providing significant additional therapeutic benefit
- Providing established therapeutic benefit
- Providing greater effectiveness than placebo
- Having modest or marginal efficacy
- Having unproven effectiveness

(b) In terms of disease evaluation, the following criteria are suggested

- Serious diseases
- Non-serious diseases
- Those involving deterioration of physical performance

(c) Disease frequency

(d) Exclude most OTCs from reimbursement

It is very unclear what role the above criteria play in Turkey. Our meetings with decision-makers have revealed a mixed picture, but also the overwhelming lack towards a rational reimbursement policy with adherence to the (clinical) evidence base. One important issue is the wide reimbursement of products that are considered as OTC in other countries. There also does not appear to exist a clear policy on de-listing.

4.8. Controlling Physician Behaviour

Physician behaviour is typically controlled in several countries, as physicians generate demand for services, including prescription drugs (Table 4.8). In terms of policy towards physicians, the main directions from an international perspective are:

(a) Influencing prescribing behaviour

- Prescription monitoring & evaluation;
- Cost-effective prescribing;
- Physician education, training, information

(b) Promoting rational drug use

- Role of evidence-based prescribing
- Reporting Adverse Drug Reactions (ADRs)
- Information systems

(c) Assisting in the establishment and dissemination of clinical guidelines and best evidence (for instance, starting with the most expensive health problems in Turkey)

Table 4.8. Policies on the Proxy-Demand: Physicians

Criteria	UK	GER	FRA	ITA	SPA	DEN	POL	NET	TUR
Monitoring Rx	+	+	+	+	+	+		+	+
Audit Rx	+	+	+	+		+		+	
CE Rx	+		+	+	+	+	+	+	
EBM Rx	+	+	+	+	+	+	+[1]	+	+[1]
Budgets	+	+	+					+	
Financial incentives	+	+	+						

[1] Although there are evidence based guidelines, it is questionable whether prescribing is strictly linked to these guidelines.

In Turkey, our meetings with decision makers have revealed a number of issues, which would merit attention. Among them are the following:

- Although there are published guidelines, no-one adheres to them so far and neither is there some kind of enforcement
- Insurance funds have allegedly developed databases that potentially allow them to monitor physician prescribing and physician authorising behaviour in general, these are not used to shape policy; we are also unclear about the extent to which these databases are used at all.
- There are no drug utilisation reviews.
- Physicians operating in hospitals may have an incentive to over-prescribe (not only medicines, but also other services and diagnostics), because the additional revenue contributes to the revolving fund, which forms part of physician payment.
- According to 2 small scale studies, nearly half of all prescribing is inappropriate; yet no guidelines are enforced and, apparently, there is little follow-up, let alone physician audit.

4.9. Pharmacy Remuneration

In the majority of OECD countries, pharmacy remuneration comprises an officially negotiated set of margins, increasingly on a regressive basis, in order to encourage generic dispensing and substitution (where the latter is allowed) (Table 4.9). To that end, pharmacies receive a fixed income on the basis of their overall prescription business, which is supplemented through the sale of OTC and other health care products or/and cosmetics. In these countries, discounts to pharmacy are typically not allowed, but do occur albeit on a small scale. In other countries (notably the UK, the Netherlands, but, also the US), pharmacy remuneration is less regulated and pharmacies do not rely on fixed margins; rather, pharmacy income derives mostly from wholesaler discounts and there is usually a small fixed dispensing fee per prescription filled, the latter usually being the responsibility of insurance funds/companies.

The co-existence of a dual payment system, where pharmacy margins co-exist with extensive discounts is not practiced; such a system would create perverse incentives to pharmacy and can neutralise official policies to promote certain types of products (e.g. generics). In effect, the availability of discounts could render any attempt to promote

substitution or generic dispensing ineffective, depending on generic pricing policy and overall drug pricing policies. This is precisely the situation in Turkey, where pharmacy remuneration is on the basis of regressive margins and co-exists with (what is thought to be substantial discounts) from wholesalers.

Table 4.9. Pharmacy Remuneration in EU Countries

Countries	Method of remuneration
Greece, Italy, Spain	Percentage margin
Belgium	Percentage margin up to a maximum
France, Germany	Regressive margin
UK, The Netherlands	Fixed fee; discounts to pharmacy combined with differential clawback

4.10. Generic Promotion and Substitution

Clearly, there are variable approaches to generic substitution in different EU Member States. Substitution may be allowed (a) in emergencies only, or (b) with doctors' agreement only, or (c) pharmacists may have wider substitution rights provided physicians have indicated on the prescription they are not against it (Table 4.10). The latest trend among EU Member States, as shown in Table 4.10, is to move towards wider substitution rights, recognising that this may generate wider use of generics and (significant) savings to health care systems.

Table 4.10. Promoting Generics in EU Countries

Country	Promoting Generics?			Generic Substitution		
	Strongly	Yes	No	Limited form	If doctor agrees	Emergencies
Belgium			+		+	
Denmark	+				+	
France		+		+		
Germany	+			+		
Italy		+		+		
Netherlands	+			+		
Spain		+		+		
Ireland		+			+	
Greece			+			+
Portugal		+			+	
Luxemburg		+				+
UK	+				+	

Source: Kanavos, Gemmill, 2005.

In Turkey, the fact that substitution is allowed does not necessarily mean that the cheapest available generic will be dispensed. This depends on the incentive structure particularly the discounts and the number of free goods (samples) received from (generic) manufacturers. The structure of the regressive margin is an additional incentive, although a rather weak one in the presence of the other two.

One of the weaknesses of the substitution system is that there is no sufficient data to understand the dynamics affecting the dispensing patterns of pharmacists and to throw light on the interactions among them. Therefore, the quality of the decision support system is another area to be improved.

With regard to discounts, originator companies seem to act at relatively rigid terms with well defined and limited discounts whereas the branded generic companies are much more flexible in this regard. It is strongly believed that such companies enjoy the advantage of the drug pricing system in Turkey, which gives them the opportunity to price their branded generic products up to 80% of the original drug. They transfer this advantage to marketing power through a spectrum of promotional activities including the distribution of free goods and other forms of extreme commercial and financial incentives for the pharmacists. The magnitude of such marketing practice is believed to approach such amounts that often exceed the threshold of fair competition. It is clear that the abovementioned pricing ceiling for generics (the 80% rule) easily leaves room for a marketing budget of considerable size for such companies allowing them to allocate for promotional activities that transfer this money to the units along the distribution channel, ending up with competition of questionable fairness.

4.11. The OTC Sector

Over the counter (OTC) drugs are typically available without a prescription and at the consumers' own (out-of-pocket) expense. This segment of the pharmaceutical market is very significant in value terms and may account for up to a third of the total pharmaceutical market in value terms, although, usually, it accounts for less (Table 4.11). Many countries view de-listing (i.e. allowing prescription only medicines – POMs to be available OTC), as a means of relieving some of the pressure on pharmaceutical budgets, as patients will be responsible for 100% of the relevant expenditure and the product will not be reimbursed. OTC products are meant for minor ailments.

OTCs are in general non-reimbursed products, although some cough-and-cold preparations, vitamins and some painkillers are often included in reimbursement (positive) lists, as low cost alternatives minor ailments. Other de-listed (and, therefore, OTC) products require pharmacy attendance in order to be dispensed. In some OECD countries, treatments for minor ailments are usually (fully) reimbursed, therefore, they cannot be classified as OTC in these countries. Indeed, the definition of what is an OTC varies by country and so do the requirements for de-listing.

Prices of OTCs have been liberalised in the majority of OECD countries, although they are still controlled if reimbursed by health insurance. OTCs are usually available at pharmacies or drugstores, although in recent years, other retail outlets (e.g. supermarkets) have been allowed to sell these products.

In Turkey, several hundred products that would otherwise be considered to be OTC elsewhere are fully reimbursed; these also include dietary supplements, such as ginkgo biloba. The expenditure implications of reimbursing these products (as opposed to a fraction of them and for defined segments of the patient population only) are quite significant for the Turkish health care system. De-listing legislation does not appear to exist in Turkey at the moment.

Table 4.11. Share of OTC Markets in Total Pharmaceutical Expenditure in Selected European Countries, 1988-2002

Country	1980	1990	1995	2000	2002
Germany	36	36	35	34	33
France	35	35	37	34	35
UK	22	22	20	19	18
Italy	11	10	10	10	9
Spain	13	13	14	13	16
Belgium	29	30	30	29	25
Netherlands	9	11	11	12	11
Portugal	na	na	na	5	4.5

4.12. Industrial Policy

Several countries within the OECD region provide incentives to the pharmaceutical industry to invest and locate within their territory. There are incentives relevant to manufacturing activities (e.g. reduced corporate taxation), but also specific incentives to promote the location and conduct of R&D activities, as shown on Table 4.12.

Table 4.12. Research and Development Tax Incentives in Selected Countries

Country	R&D tax credits	Other subsidies
Netherlands		Special allowance for R&D capital and labour
Spain	15% of R&D 30% of R&D equipment	
Sweden	30% incremental	Special allowance for R&D salaries
USA	20% incremental on R&D 20% incremental on university-based R&D 50% of clinical orphan drug R&D	
UK		Deduction of R&D facilities and machinery; significant R&D allowance (25%)
Belgium		Special deductions for R&D personnel Exemptions from tax of distributed profits
Canada	20% incremental	
France	50% incremental	R&D grants in selected industries
Germany	Tax credits on R&D equipment	Tax grants on capital investment
Ireland		Tax exemption for royalty income from patent R&D done in Ireland
Japan	20% incremental	Trade policies beneficial to R&D equipment R&D grants for selected technologies

Source: Kanavos, 2003.

The promotion of indigenous industry, which is mostly focusing on generics, may be subject to implicit criteria. In the case of Turkey, but also other European countries, price fixing for generics and, in particular, linking prices to branded medicines, may act as a significant incentive to produce generics and indirectly support local industries.

4.13. Ensuring Access to Medical/Pharmaceutical Treatments

There are several aspects affecting access to pharmaceuticals. The first relates to the geographical distribution of pharmacies and/or dispensaries and the second relates to the insurance status of the Turkish population.

With regards to the first aspect, all stakeholders have stressed that access to drugs is not a problem from the geographical standpoint for the nationwide distribution of pharmacies in Turkey is sufficient to allow for such access with ease. Furthermore, the legislation authorizing practicing physicians to dispense drugs in cases where no retail pharmacy exists (the "drug cabinet" system) guarantees wider physical access to drugs.

Recent reforms in the pharmaceutical sector have also meant that access to drugs by different types of insurees is also enhanced. This concerns, first, the SSK-insured population and second, the Green Card holders. SSK insurees are now able to obtain outpatient drugs through all retail pharmacies rather than SSK pharmacies only, as was previously the case. In a similar fashion, Green Card holders are now able to have their out-patiently filled prescriptions reimbursed, rather than only prescriptions filled in-patiently.

Whereas geographical coverage is deemed sufficient and significant steps have been taken in recent months to guarantee equitable access to all insurees, certain aspects of the drug distribution system and the ethics surrounding it, may limit this. This relates to the issues of:

a. Access to physicians and the likelihood of informal payments being offered in exchange for speedy access that would expedite treatment, including pharmaceuticals. There is some evidence that this may be happening from a recent study (Tatar, et al., 2003).

b. The phenomenon of muvazaa, which is widely practiced, implies that pharmacy may not be in a position to properly serve its customers.

c. The possibility that some pharmacies, particularly in rural areas or some inner city areas, may not be as well stocked as pharmacies elsewhere.

4.14. Concluding Remarks

The weaknesses/caveats in the Turkish drug reimbursement system include among others:

- The system has been centralized but fragmented; current policy initiatives aim at reducing fragmentation. Arguably, health care reform and the introduction of a generalised health insurance cover will address this problem in the medium- to long-term, in the short-term (significant) costs of adjustment may be expected.
- One of the major bottlenecks is the insufficiency of the human resources profile, both quantitatively and qualitatively.

- No systemic approach is followed for strategic priority-setting at systemic level.
- The present underlying philosophy of the drug reimbursement system focuses on minimizing drug expenditure rather than promoting cost-effectiveness.
- The roles and responsibilities of the drug reimbursement decision bodies are not clearly defined.
- Evidence that drug reimbursement decisions are based on evidence, whether clinical or cost-effectiveness is rather patchy.
- The drug reimbursement criteria are not sensitive to innovative drugs.
- The drug reimbursement system does not take into account the optimization of public health needs and the pharmaceutical sector strategic expectations with special emphasis on the research-based stakeholders.
- The clinical guidelines and clinical algorithms do not have any enforcing power at all. In fact, enforcement of legislation appears to be a more generalised problem within the context of health policy in Turkey.
- The reference pricing system is far from being dynamic and flexible enough to satisfy the needs of the drug reimbursement stakeholders.
- A knowledge management system selective and sensitive enough to monitor, evaluate, and analyse the intended and adverse effects of the drug reimbursement instruments is not in place.
- The “policy - implementation - policy research” cycle does not exist, making it almost impossible to feed-in the lessons learned.
- The drug reimbursement system is not based on governance philosophy and social dialogue practice.
- The benchmarking approach is far from depicting the external drug reimbursement practices in detail to enable the policy makers understand the models as a whole and predict the long-term effects of the interactions among the contextual dynamics.
- There is no in-depth analysis of the current situation, making it difficult to understand the impact of different drug reimbursement interventions on the quality of pharmacotherapy and drug expenditure.
- Fieldwork and meetings with stakeholders suggest that the data collected at prescribing or dispensing level are either non-existent or not used for policy analysis.

5. Initiating and Implementing Drug Sector Reform in Turkey

5.1. Introduction

Drug sector reform inevitably incorporates interventions in the current system regulating supply but also proxy-demand and demand for pharmaceuticals in Turkey. The parameters of such reform must be set within the current fiscal realities of the Turkish economy, as it is making its transition into becoming a fully integrated EU Member State, as well as the overall framework for ongoing health sector reform, which must be governed by interventions in primary, secondary, tertiary and alternative care, alongside the pharmaceutical sector. The sections that follow outline a number of options on the supply- and the demand-side, which fit within these realities. The options are not exhaustive and neither are they the only ones available in the continuum of health care reform.

Together with reform options, this section also considers the operational environment, how changes can be delivered, what infrastructure (both technical but, also, human) may required, what skills are needed, how can efficiency and transparency be improved. In doing so, it focuses primarily on three aspects, namely:

a. Political feasibility, considering the strength of different stakeholders and the current determination by the government as regards reform implementation

b. Managerial requirements, especially the pressures and requirements at systemic level; and

c. Technical requirements, particularly in what concerns information technology and human resources

The timing of all recommendations is also considered, taking into account the current environment in which Turkey operates and the future impact of accession to the EU.

5.2. General Principles

In drafting the recommendations below, we have kept in mind the following principles:

1. **Respecting and implementing the European Acquis Communautaire:** The operational toolbox should be periodically evaluated in the light of the EU acquis communautaire for Turkey will take active part in the process of full membership negotiations in the near future.

2. **Good governance:** The philosophy of good governance needs to be followed throughout the continuous system performance improvement roadmap makes it imperative to actively listen to the voice and choice of the stakeholders. No party should be left out in order to guarantee the sustainable internalization and ownership of the drug reimbursement system transformation efforts.

3. **Generating consensus**: Consensus building platforms should be established and maintained to reach and sustain a strategic consensus among the stakeholders. Drug reimbursement strategies influence the interests of a spectrum of stakeholders from the health and economic standpoint. Therefore, consensus building for and mutual ownership of policies and procedures should be the rule rather than the exception. This philosophy should also include the professional associations as well as consumer groups and patient associations along the lines of good governance at all times. For instance, formal patient (as well as health care professional) involvement in the process of health technology assessment would contribute significantly to such consensus building.

4. **Matrix Functioning**: The organization and management of the drug reimbursement system should allow for 'cross- healthcare level' disease management. In other words, the policies and procedures as well as the structural components, the budgets, and the decision support systems should be orchestrated in such a manner that allows for effective and cost-effective case management cross-cutting the various levels of healthcare.

5. **Allowing for contextual dynamics:** The operational-level recommendations are aimed at tailoring the components of a comprehensive drug reimbursement system to the contextual dynamics of Turkey. The golden standard should be the development of evidence- and consensus- based national drug reimbursement policies and procedures. The dilemma is to contain significant growth in drug expenditure without any clinical and financial adverse consequences. Thus, the drug reimbursement system should be approached from the standpoint of 'expenditure optimization' rather than cost minimization. The whole criteria set of various perspectives should be considered rather than solely focus on the financial aspect. The expectations of the public should be blended with the priorities of the government, the health professionals, and also allowing scope for expansion in the pharmaceutical sector.

6. **A dynamic perspective in drug reimbursement:** Drug reimbursement should be approached in a comprehensive and dynamic manner, taking into account the various independent variables involved. The demographic and socio-economic profile of the population, the burden of disease, the R&D and marketing management and ethical practices of the pharmaceutical industry and the pharmacoeconomic, pharmacoepidemiologic, and pharmaco-anthropologic aspects should be considered.

7. **Monitoring and evaluation infrastructure**: A monitoring and evaluation infrastructure should be always kept in place to allow the lessons learnt to be incorporated in the continuous improvement process. To fill the gap between the financial burden of drug therapy to the individual and the patient's ability to pay in the most effective and efficient manner is of prime importance in terms of national drug reimbursement policy. The continuous learning culture is one of the critical success factors to this end.

8. **Health outcome improvement and cost management**: The rationale for drug reimbursement system design and development should be built on the pillars of health outcomes improvement as well as cost management. In other words, the drug reimbursement system should simultaneously address the clinical and financial performance of pharmacotherapy. Data should be systematically gathered on health status and outcomes. Investment and resource allocation decisions should be evaluated against gains in outcomes/health status. In other words, health insurance should be in a position to perform a disease management function in order to ensure that investments in health are both effective and efficient.

9. **Feasibility**: The realities of the health care system and characteristics of the health care service delivery in Turkey should always be kept in mind to assure the feasibility of replicating the successful drug reimbursement models. For example, the probable adverse effects of the uneven distribution patterns of physicians on the "access to medicines" principle should be thoroughly analysed when demand-side drug reimbursement instruments are considered such as limiting the prescribing authorization.

5.3. Regulatory Issues

Over the long-term and as part of EU accession, Turkey will need to establish an independent drug agency within the MoH. We are aware of the fact that legislation is under preparation to set the operational framework of an autonomous agency within the MoH and believe that this is a very positive development in principle. Despite not being aware of the full text of the draft legislation, we believe that the following issues should be included in this, among others:

(a) GMP provisions

(b) Generic approvals

(c) Pharmacovigilance provisions

(d) GCP guidance

(e) The extent of user fees in determining the financing of the agency

(f) A list of user fees payable

In updating this legislation, Turkey might want to consider implementing the new European drug regulatory framework (www.europa.eu.int).

We are of the view that the remit of the existing arrangements within the Ministry of Health to also determine pricing at the time of examining a dossier for licensing purposes, be re-visited and responsibility for pricing to be given to a different body within the MoH. The role of the Drug Agency should be to exclusively judge the suitability of medicines for human use on the basis of safety, efficacy and quality.

5.4. Intellectual Property Rights Protection (IPRP)

Developments in the area of intellectual property rights protection should focus around three axes:

1. **Market exclusivity** to be implemented in line with TRIPs/EU norms.

   This is an essential step in ensuring basic intellectual property rights protection in areas and products where cover may not be available.

2. **Bolar amendment** to be implemented.

   A targeted approach to allow for generic product development during the patent period of the original molecule (the Bolar provision) could be considered for

well-described and mutually agreed cases and specifically defined indications. No need to say that this initiative should be synchronized with systematic incentives for the reimbursement of innovative drugs. Otherwise, the principle of fair competition would be adversely affected which, in turn, would have a negative effect on the availability and the accessibility of new drugs of proven pharmacoeconomic value.

3. **Supplementary Protection Certificate (SPC)** to be introduced gradually.

This refers to the patent extension term provided by EU legislation to new medicines. Although Turkey is currently under no obligation to introduce SPCs to products whose patents expire now, it will have to do so once, an accession date has been finalised. It is, therefore, certain that the issue of an SPC in pharmaceuticals will arise at some point in accession negotiations.

All the above developments will align intellectual property rights protection in Turkey with EU practices.

5.5. Pharmaceutical Pricing Policy

5.5.1. Pricing of Branded, In-Patent Medicines

The options below allow for the calculation of maximum allowable prices in the Turkish market. Therefore, local producers or importers are allowed to set prices lower than these levels.

According to the current pricing system in the Republic of Turkey prices are calculated on the basis of external referencing of the lowest ex-factory price from a basket of five EU countries until the end of 2005. Turkey is following a pan-European (and international) trend in this respect, and the current system of pricing, imperfect though it may be, appears to be a compromise between government and industry, whilst at the same time ensures that prices of branded, in-patent medicines in Turkey are not higher than most EU countries, also given the country's differences in GDP per capita compared with other EU countries.[15] It should be recognized, however, that external referencing is intrinsically an

[15] It does not necessarily follow, however, that if countries with lower per capita income are used (e.g. Eastern European countries) *in lieu* of the currently used basket, this will result in lower drug prices in Turkey. Evidence from Eastern European countries, for instance, suggests that there is little or no correlation between GDP levels and drug prices (Kanavos, De Joncheere and Eldridge, 2003). The same evidence suggests that, if anything, this correlation may be inverse, and drug price levels may be higher in these countries than in countries with higher income levels. In principle, it may be the case that external referencing might have a negative impact on affordability and, thus, access to medicines, but, as health insurance will underwrite the cost of medicines for the entire population, this impact is likely to be limited, also given the current state of economic growth of the country.

imperfect and, in many cases, inappropriate criterion for setting drug prices, which does not necessarily reflect market and affordability conditions in the country that applies it. In addition, its generalization may lead to downward price spirals across countries with negative implications for access to patients. External referencing may also be cumbersome in a context where prices change due to inflation and currency movements, thus requiring continuous monitoring and adjustment.

While the model of external referencing on the basis of a basket of countries may meet short- to medium-term objectives, the Turkish government might want to consider improving on this model, at least over the **long-term**, by following a strategy that: (a) would require the continued separation of pricing from reimbursement, (b) switches to a system that requires price negotiation taking into consideration several criteria, as opposed to focusing only on one criterion, and (c) by implication is less directly dependent on explicit international comparisons. This strategy is dependent upon new structures being placed at the MoH and would, of course, require adherence to international standards of intellectual property rights protection, among other things.

For new and innovative in-patent products, pricing/reimbursement could be determined on the basis of negotiations between inter-ministerial committees, health insurance and the pharmaceutical industry. Prices could be set using a number of criteria, including:

- The product's medical value, and whether the product:
  - Is innovative, showing significant therapeutic benefit;
  - Has clearly demonstrated and clinically important therapeutic benefit in terms of effectiveness and/or reduction in side effect profile;
  - Offers moderate improvement in terms of effectiveness and/or reduction in side effect profile;
  - Offers minor improvement in terms of effectiveness and/or utility;
  - Offers no improvement but listing is still recommended;
- The prices of comparable medicines in Turkey (i.e. medicines which are in the same or a similar therapeutic class, medicines that enjoy the same IP protection status);

- Manufacturers would need to submit price data (ex-factory) for the same drug from other countries for information; this can be done for the purposes of taking into account these prices formally (as it is done now), on informally, i.e. just for information;
- Conditions in which the product is used;
- Any R&D or other (manufacturing) investment that has been or is being conducted in the Republic of Turkey, although any such incentives should not be explicit, unilateral, or contradict EU regulations.

5.5.2. Pricing of Generic Products

In principle, the objective would be for health insurance to take advantage of competition in the off-patent sector to pay the lowest prices possible in a market characterized by commodities. In principle, it is also unnecessary and counterproductive to regulate prices. It became evident earlier in this report that, in fact, generic manufacturers compete by giving discounts to pharmacies. Consequently, regulated prices become artificial reimbursement levels to pharmacies, at an expense of payers and patients, while actual prices reflect discounting that accrues as profit to pharmacies rather than savings to payers (and, therefore, patients).

The government needs to address two issues in connection with pricing and one related to reimbursement of generics: the first relates to the current maximum ceiling for the pricing of generic products of 80% of the originator price (plus 30% on top of the lowest-priced generic for reimbursement purposes of the reimbursed generic price), and which may lead to high prices for generic products. Second, the non-existence of pure generic (non-branded) products does not necessarily allow for the implementation of a robust generics policy, although, understandably, generics may still need a further vote of confidence by prescribers and patients alike.

In addressing the first issue, the government will need to consider the strength of the local industry. Whatever this may be, the current reimbursement system of paying for the lowest-priced generic plus 30% does not make sense and needs to be reconsidered radically. In a subsequent stage, health insurance can move one step closer to altogether relaxing regulatory rules for pricing, but monitor prices of generics as well as safeguard their quality. Relaxing regulatory pricing rules could mean, for instance, those payers adopt generic referencing and that reference prices would be based on (actual) pharmacy acquisition costs.

From a technical perspective, continuous monitoring of (branded and generic) drug prices is required, as there may be phenomena whereby the reimbursed generic may be costing Turkish health insurance more than the branded product. Prices need to be monitored by health insurance via access to national and international databases (for instance IMS, or the Vienna-based ÖBIG institute) and the relevant adjustments to be made without delay. This would probably necessitate the establishment of a (small) unit within the SSI, exclusively preoccupied with this. This unit would require minimal administrative support, but good technical backing and access to information technology and databases in order to provide essential background support to SSI. Its remit would be to ensure access to prices at EU level and monitoring of price movements across EU countries.

With regards to the second issue, we feel that the government and health insurance continue to pay high prices for products that are available generically. This is because the leading competitor to the originator drug (that usually registers high sales and has a high market share) offers no significant price advantage to the originator branded product, or because the "generic + 30%" rule, frequently inflate reimbursed prices to levels that can potentially exceed the price of the branded product. In addressing these issues, the government would, first of all, need to address concerns that may exist on the front of their intellectual property rights protection and marketing exclusivity policies. Effective patent protection and marketing exclusivity (the latter especially for older products) imply that for the duration of the patent or marketing exclusivity period, no copy products can be available. On the basis of evidence we have seen on the top-selling products in Turkey (in originator and in generic terms, and in actual market share terms), this (IPR) is not expected to have a significant impact on government/SSI outlays at the top end of the market, as prices of originator drugs are subjected to a ceiling. Subsequently, the government needs to re-consider the "lowest (generic) + 30%" rule. From a health insurance perspective, this policy does not necessarily lead to cost containment or efficiency; from an industrial policy, it can only be perceived as a subsidy for lower cost generics, but may represent inefficient resource allocation.

5.6. Pharmaceutical Reimbursement Policy

This section discusses formal reimbursement policy. For products subjected to reimbursement regulations, it is accepted that their (reimbursement) prices will be determined via negotiation and on the basis of multiple criteria in order to determine value and therapeutic benefit. The section below does not discuss products which are not reimbursed,

but are registered in Turkey. It is recommended that the prices for these products should be free (e.g. OTC products, or, even, other products which may be innovative, but fall outside the scope of statutory coverage, for instance, lifestyle drugs).[16] For new and innovative products as well as life-saving medicines, health insurance and industry should make every effort to include in the reimbursement list at an acceptable price to both parties in order to avoid phenomena of having such medicines excluded from the reimbursement system.

5.6.1. The Issues

Although up until recently there was no unified reimbursement system, the government is gradually implementing such a principle, working from bottom upwards. This will eliminate differences across insurance schemes and will increase equity in access by less privileged social groups, i.e. Green Card holders. The downside to this development is the cost, which, according to some estimates may be as low as $800 million (conservative estimate) and as high as $2.5 billion ("pessimistic" estimate). It is unclear at this point whether the unified reimbursement system (as applied by Bağ-Kur) based on haphazard and selective price referencing yields any benefits or is robust to take account of all market dynamics.

It is unknown what principles guide the admission of (new) products into the reimbursement list and how robustly these are followed. There is also little information on the experts involved in reimbursement decisions and their respective contribution. Indeed, the roles and responsibilities of drug reimbursement decision makers not clearly defined.

It appears that several medications, which should in principle be available as over-the-counter, are actually reimbursed by insurance funds. This may lead to waste of scarce resources by health insurance and could be done on a selective basis initially, before being altogether eliminated (with few exceptions) in the long-run.

It also appears that other elements of Turkish reimbursement policy are not robust; for instance, in addition to the positive list and the criteria for inclusion, our interviews suggest that there is little being done on rational drug use, on monitoring physician prescribing, audit, or drug utilisation review.

[16] It should be borne in mind that although some drugs are considered "lifestyle drugs" decisions about their reimbursement status should not be based on their strict definition as "lifestyle drugs", but on setting up "lifestyle indications" for which these drugs should not be reimbursed. Setting up a list of lifestyle indications should be the responsibility of inter-ministerial committees and health insurance, which would also receive assistance from pharmacologists and medical experts.

Consequently, our proposals below are in the spirit of the broad deficiencies we identified during our fieldwork and meetings in Turkey.

5.6.2. Characteristics of Reimbursement Policy

In general, reimbursement policy must:

(a) Be characterised by transparency,

(b) Allow flexibility to ensure that new treatments and effective and are made available to patients within a reasonable amount of time,

(c) Be robust in evaluating clinical benefit and assessing the economic impact of treatment, and

(d) Take into account available evidence and be updated regularly.

Transparency implies that the criteria for reimbursement are known and publicly available to applicants, together with explanatory notes on the actual requirements for submission of applications. Transparency also requires that the process of examining applications and informing applicants of their outcome, is also known to applicants and should take the form of a notification following the submission of the dossier to the reimbursement authorities. In this notification, authorities should state a proposed path for the review of a received application, together with timelines. Also included should be guidelines for appeal, should the application be rejected. The notification should be a standard operating procedure and authorities should work towards producing a document that addresses the above and is included in their correspondence with applicants, following the submission of the dossier.

Flexibility implies that reimbursement authorities must be at the disposal of applicants to discuss not only current submissions, but, indeed, new medical and economic evidence on treatments that has an impact on patient care and be ready to include this evidence in the decision-making process.

Robustness implies that reimbursement authorities take into account all the scientific evidence that is provided to them, but also check that this scientific evidence is comprehensive and robust.

Finally, **evidence-based decision-making** on drug reimbursement issues should be the norm rather than the exception. First of all, ‘evidence’ of defined quality should be present for comparative clinical and economic evaluation. Pharmacoeconomic analysis techniques are of

prime importance to this end. The decision-making body should include health technology assessment structures and its autonomous functioning be immune from external factors other than the scientific facts. It would be advisable for technology assessment to include the views of all main stakeholders including industry, professionals and patients.

5.6.3. Criteria for Reimbursement

Reimbursement policy should be the responsibility of a reimbursement committee, which usually comprises participants from the MoH, all insurance funds, or, in this case, the SSI, and includes experts on pharmacology, pharmacy, medicine, and economists. Participation by patient groups should also be encouraged. In the committee's mind, there should be a list of criteria that should be fulfilled if reimbursement (a) is to be granted and (b) whether the product in question will be fully or partly reimbursed. Reimbursement should be a transparent process conducted within a pre-determined time frame and should be based on negotiation, rather than being a paper-based-only process. The criteria for reimbursement should be publicly available and could include, for instance:

- **Scientific evidence** in terms of proving safety and efficacy (see below Section 5.6.4 on scientific criteria for admission into the positive list);
- **Diagnoses** for which the drug is indicated and prevalence of disease in these diagnoses in order to estimate approximate numbers of patients;
- **Whether price is fair and affordable in principle** (through approved price and possibly also through the submission of prices from a number of other countries);
- **Budget impact analysis** (the total cost of the drug for the health care budget);
- **Commitments on volume sales.** This would require the submission of relevant price/volume data from manufacturers to the relevant pricing committee, in order to assess the potential impact of a new drug on the health care budget. Annual reviews of this system may be held to monitor impact on budgets. Paybacks may be required if a certain budget ceiling per company is exceeded;
- **Cost-effectiveness criteria** (whether the drug is clinically – cost effective vis-à-vis its competitor, whether this is a drug or a procedure);
- In case clustering and the establishment of a reimbursement ceiling (reference price) are maintained, then the **criteria for inclusion into the clusters and the**

way the reference price is calculated must be transparent and publicly available;

- **Industrial policy** (in some cases, regulatory authorities might consider the potential for local manufacturing of R&D – mostly developmental research, only if applicants commit to these activities and submit the relevant information for them).

It is on the basis of the above criteria that reimbursement can be negotiated and consensus reached on a particular product or intervention.

5.6.4. Criteria for Admission into the Positive (Reimbursement) List

A central piece of fusing the above criteria into a single instrument is the development of a reimbursement list or a positive list. The positive list should continue to be a central feature of reimbursement policy in Turkey, and should be monitored and updated on a regular basis. It should also be "cleaned" on a regular basis of old treatments and treatments of questionable efficacy. Understandably, the existence of different insurance funds currently implies that different lists may exist, current reforms aimed at having a uniform reimbursement list governed by similar principles, are in the right direction. The criteria for admitting products into the positive list should in principle be transparent and may include:

- The seriousness of the condition and whether there are existing treatments. In accordance with this, medicines would be classed as:
  i. Providing significant additional therapeutic benefit
  ii. Providing established therapeutic benefit
  iii. Providing greater effectiveness than placebo
  iv. Having modest or marginal efficacy
  v. Of uncertain effectiveness and not established according to current standards.
- Evaluation would be performed on the basis of clinical trial data from the approval dossier, post-marketing studies (if applicable), meta-analyses if applicable), and consensus conferences (if applicable).
- In terms of disease evaluation, the following criteria are suggested:
  i. Serious diseases
  ii. Non-serious diseases

iii. Those involving deterioration of physical performance (e.g. through the ageing process)

iv. 'Inadequate performance', referring to conditions such as impotence, 'heavy leg syndrome', etc.

- Disease frequency, and whether, for instance, the condition is chronic or acute

5.6.5. Setting Cost-Sharing Rates

Following the criteria for the establishment of a positive list, the reimbursement committee would then need to decide on reimbursement rates and cost-sharing policy. The current status suggests that the main insurance funds have a uniform cost-sharing policy of 20% co-insurance for all insurees except for retired (not elderly) patients, where the co-insurance rate is 10%. Various exemptions apply mainly on the basis of disease type (chronic or not). The marginal cost-sharing rate is not known.

In setting cost-sharing rates, the reimbursement committee could grant full reimbursement for very serious conditions, including life-threatening diseases (e.g. diabetes, cancer, AIDS, chronic conditions, etc), and less than full reimbursement for all other classes of products. Patient co-payment could be set on a proportional rate and could eventually contribute to revenue for the health service. This would also depend on ability to pay, but also on the usual criteria of paying the co-payment (age, disease type, income, etc).

5.6.6. Options for Reimbursement Ceilings of Off-Patent Drugs

For the purposes of this section, off-patent drugs are drugs whose patent have expired.

For off-patent, multi-source products there are two alternatives which can be discussed: first, a purely **internal** reference pricing system could continue to operate in the short- to medium-term, based on identical molecule, i.e. on the basis of patent-expired molecules (for instance grouping all “omeprazoles” together in one cluster; grouping all “enalaprils” together in another cluster). The reimbursement ceiling for each intervention should, in principle, be the same across all three major insurance funds, and could, for instance, be determined on the basis of the average of the two lowest-priced generics in the cluster. This assumes that the “generic being 80% of the branded price” rule is no longer carried forward, and that there is some element of competition in the market. It also needs to be determined whether such a suggestion is feasible in the current environment. In order to reduce or minimise (but never eliminate) phenomena of therapeutic switch (moving up one

category), price referencing ought to (a) be comprehensive and (b) be monitored by health insurance.

However, the global application of a reference price system is a fairly sophisticated process involving the definition and determination of different clusters of drugs as well as the statistical determination of the relative price per package. The establishment of a comprehensive internal reference pricing strategy could be viewed as a long-term strategy. As discussed above, clustering should be done on the basis of identical molecules, rather than similar or comparable molecules or drugs. The latter options could have a negative impact on the launch of new medicines and their access by patients. The positive list(s) should be updated on a regular basis and be "cleaned" of the vast majority of OTC products, to make room for new treatments.

The second option, is to carry forward the pricing rule of "**generic being priced 20% below branded**" to the reimbursement stage. This rule is very simple and essentially guarantees that all generics are (at least) 20% cheaper than patent-expired branded products.

There are two caveats with this approach, however: first, it may be the case, that by linking the pricing of generic products to that of branded products, the former may be over-priced, given the low manufacturing costs in Turkey. By doing this, Turkish policy-makers elevate generic drug prices in Turkey to the level of those in Italy, Spain, Portugal, France, or Greece, all of which apply similar pricing rules for generics, but where manufacturing costs are significantly higher. This rule may, thus, need to be re-visited and perhaps re-adjusted downwards, or, in order to avoid the political cost of doing so, be altogether scrapped in favour of first option above. Second, by establishing a fixed rule of 20%, there is little incentive for generic companies to compete in the market, since, in any case, health insurance will reimburse the generic at 80%. The potential for competition in the off-patent sector, therefore, needs to be examined in more depth, in order for this segment of the market to yield sufficient savings to health insurance, which, in turn, can be used to finance newer interventions. This argument also points towards the inefficiency of operating an ad hoc regulatory intervention.

For clarification, it should be pointed out that the proposals above require the implementation of a sound patent protection regime and marketing exclusivity.

5.6.7. Health Economics and Cost Effectiveness

The formulation of the health technology assessment system including health economic (pharmaco-economic) and pharmaco-epidemiologic approach for comparative analysis of alternative drug therapies should be one of the areas of focus to be managed in the short- to medium-term.

Indeed, over the medium- to long-term, the separation of pricing from reimbursement should continue and the distinction between new and innovative products on the one side, and off-patent, multi-source products (generics), on the other, should also continue to hold. With regards to the latter, internal reference pricing could continue to operate. With regards to new products coming onto the market and seeking reimbursement, health economic evaluations could be made to facilitate evidence-based purchasing decisions. The implementation of a system of health economic evaluations in pharmaceutical reimbursement would require an adequate infrastructure and training of all relevant stakeholders, and would also require the drafting of economic evaluation guidelines that suit the Turkish system. It is not recommended to have such a system in place, unless adequate training of decision-makers and prescribers has taken place and before a consensus develops on the drafting of economic evaluation guidelines. Academic training and background in health economics and cost-effectiveness would also be required to ensure that sufficient numbers of specialists are produced by the system, to staff government, health insurance, industry and academia.

The criteria for deciding whether to admit a new drug to the list should include not only cost-effectiveness, but comparative cost-effectiveness in relation to standard treatment of the same problem(s). If the cost-effectiveness is similar, the addition of a new drug would not be justified, unless some other advantage could be clearly demonstrated.

Over the past decade, several countries have introduced cost effectiveness guidelines in order to assist industry in submitting pharmaco-economic (PE) evidence to the decision-making community. Companies will need to demonstrate therapeutic value, costs and possible savings resulting from use of a new product compared with current treatments, with all studies reporting from a health system and a societal perspective. Analysis of the medicine's anticipated effectiveness, as opposed to efficacy, may also be required, with modeling techniques to reach this opinion permitted where effectiveness data is unavailable.

Overall, cost effectiveness analysis can be a useful tool in determining whether a drug is cost-effective relative to its alternatives, as well as highlight the maximum price at which

this is true. Policy makers in Turkey, should, nevertheless, be mindful of the following issues relating to the use of cost-effectiveness analysis in the decision-making process:

(a) It cannot determine the threshold (e.g. cost per QALY) the payer is/should be willing to pay. This is an issue for health insurance to determine.

(b) It cannot determine whether the payer should pay the maximum price at which the drug is cost-effective, given this threshold, or should negotiate a somewhat lower price. This is also for health insurance to decide upon.

(c) Cost-effectiveness is not a panacea and its use in reaching reimbursement decisions should be done with caution because the measure of cost-effectiveness for a specific drug may differ across countries due to differences in comparator products, their prices, the costs of other substitute or complementary resources (e.g. hospital costs, other health care costs), and epidemiological factors that affect outcomes. Typically, Turkey would probably need adaptation studies to take into account the local circumstances. Consequently, Turkey could review cost-effectiveness measures reported to other countries on particular drugs (e.g. NICE in the UK or CCOHTA in Canada), but Turkey should carefully consider how the analysis and conclusions might differ in the context of its relative income and relative medical prices.

(d) If, at a certain point in time, cost-effectiveness is widely and effectively used in reimbursement negotiations, then a separate system based on external referencing would probably become obsolete.[17]

5.6.8. Reimbursing Expensive Products

Special provisions would be appropriate for expensive products, especially those intended and perhaps needed for chronic treatments, cancer, and rare diseases. For these products, provisions must exist so that they can be funded, perhaps through an earmarked budget managed separately from the rest of the drug benefit. It is especially important for such products to be used in accordance with guidelines that specify the indications in detail, and that describe the sort of supervision that the treatment requires, what qualifications are

[17] Cost effectiveness can, in theory, be used to determine whether a drug is cost-effective relative to alternatives at a given price, and to establish the maximum price at which this is true, based on the price of comparator products and any cost-offsets or quality improvements offered by the new drug. But at this maximum price, the seller captures all the social surplus created by the new drug, hence payers may try to negotiate a lower price, since the drug would be even more cost-effective at the lower price. Of course, setting prices too low may erode incentives for innovation, so there is a trade-off that cannot be resolved by cost-effectiveness alone.

required for that supervision, and at what intervals the patient should be reviewed. The use of individual expensive therapies should be monitored in a regular system of clinical audit and central funding might be appropriate for certain classes of medicines in this category, to ensure equity in access.

'Individual reimbursement' could be considered for patients with (i) specific co-morbidities and (ii) for drug therapy regimes that could result in significant drug interactions that necessitate the utilization of drugs that are not included in the general reimbursement scheme. In such cases, the written request of the physician should be sought and the case should be objectively evaluated by health insurance (prior authorisation). In that case, a system must be in place ensuring speedy resolution to obtaining access and reimbursement. Typically, this process should not take more than 24-36 hours.

5.6.9. Drug Utilisation Reviews

The knowledge management system targeted at the monitoring and evaluation of drug reimbursement policies and procedures is of prime importance for the continuous improvement of the system in a context-sensitive manner.

The design of the drug reimbursement decision support system with special emphasis on drug utilization review bullet points should be approached within the short-term initiatives package. Otherwise, it would not be possible to establish the pillars of a cost-effective drug reimbursement system.

When the drug reimbursement decisions are based on DDD (Defined Daily Dose), it should be remembered that this metric is merely an average of the commonly used dose sizes. Therefore, there exists the possibility that there could be no such drug strength marketed to represent the exact DDD. Moreover, deciding which DDD figure would be the standard could be a problematic issue for cases where there is more than one indication for a specific drug product.

Alternatively, health insurance could monitor volumes and expenditure per drug prescribed and per diagnosis for individual patients. By examining patient diagnosis with their utilization patterns for a particular disease, and benchmarking with the relevant clinical practice guidelines for drug use, health insurance can perform and monitor utilization of a particular drug across the insured population. It should also be in a position to identify outliers (e.g. by region, practice, and physician) for potential over- and under-prescribing.

Consequently, the competent authorities (ministries and health insurance) should develop an appropriate methodology for drug utilization review (DUR) that takes into account the above caveats. This should be the subject of an inter-ministerial and health insurance taskforce, assisted by the relevant professionals.

The drug utilization review initiatives in their broadest sense should be based on a sound methodology to ensure the reliability of national and international comparisons. The methodological issues concerning monitoring and evaluation include the metrics of drug consumption and expenditure, the validation of the statistical data, the analysis tool inventory, and the basis for benchmarking. Specific knowledge is needed to understand the impact of the cost containment measures on the size and growth trend of drug expenditure.

The drug utilization review framework should go far beyond the well-known matrix analyses to throw light to the dynamic and flexible drug reimbursement decisions. For example, the effect of 'drug age' (years since approval) on total drug expenditure should be investigated in detail. Another decision support- type research example underlining the importance of the new drug utilization review philosophy would be the analysis of the net clinical and financial benefit of innovative drugs from the perspective of total drug and/or health expenditure.

Drug utilization review should also focus on ATC class-specific trend analysis to understand both the magnitude of the intended impact and the negative consequences of various reimbursement interventions on selected drug clusters over time.

Monitoring and evaluation of the drug reimbursement system is crucial to observe and gauge the intended impact and the potential adverse consequences of the drug reimbursement initiatives. The monitoring and evaluation component should be incorporated through all phases of planning and implementation. Furthermore, the monitoring and evaluation performance also should be monitored and evaluated.

Finally, it should be borne in mind that drug utilization would apply on drug consumption accounted for by health insurance and would not necessarily capture POMs dispensed OTC. For instance, data on drug use by ATC strongly suggest overuse of antibiotics in Turkey, but is unclear whether the excessive antibiotics use reflects excessive physician prescribing or excessive pharmacy dispensing without a Rx. Understanding which of these is occurring is important to design appropriate policies. If physician prescribing of antibiotics is excessive, then it may either reflect or incentives to generate more income. If the

former, then physician training, continuous contact and feedback from health insurance, and guidance (as well its enforcement) could reduce the problem. If the latter, then the nature of these incentives would need to be investigated further and the appropriate responses to be implemented (e.g. introducing an element of fee-for-service and link it with volume of services). If, on the other hand, excessive antibiotic use is occurring in pharmacies without physician prescription, then pharmacy education and penalties for dispensing antibiotics without an Rx could be useful and should be implemented.

5.7. The Proxy-Demand Side

5.7.1. Introduction

5.7.1.1.Physicians

The proxy-demand represents a critical component in pharmaceutical policy-making, since clinical autonomy lies at the heart of prescribing and, consequently, influences expenditure to a considerable degree. Measures on the proxy-demand seek to influence the behaviour of prescribing physicians, the dispensing of community pharmacists, and the building of an interrelationship between physicians and pharmacists that would give them incentives both to prescribe and dispense rationally and cost-effectively. We feel that there is substantial scope to target this side in Turkey in the near future, but need to point out that investment is needed to alter life-long habits of physicians, pharmacists and health insurance.

With regards to policies influencing physician behaviour, we have identified a number of problem areas, affecting quality and appropriateness of care and may also lead to waste of scarce resources. The problems outlined below reflect the situation in physician prescribing and authorising behaviour.

1. Physicians always prescribe by brand name; although pharmacists can substitute for a (theoretically cheaper) generic, the entire system may not necessarily create any savings worthwhile mentioning. This is perpetuated by the absence of a culture for (pure) generics. This will probably take a long time to instigate as it requires changes in education and training;
2. There is a multi-tier system with physicians also practicing privately. The latter effect acts as an incentive to physicians to feed formal practice in hospitals; it also acts as a potential source of informal payments by patients to physicians.

3. Enforcement of available clinical guidelines by clinicians remains non-existent. While this can be perceived as safeguarding clinical freedom, the authorities in principle have little means available to know how physicians prescribe and why.
4. Physicians and other health care professionals working in hospitals and health posts are considered to be civil servants and their productivity is thought to be low. Coupled with the fact that they are also allowed to practice privately, this effect re-enforces the "low productivity in the public sector" argument.
5. At the other end of the spectrum, an increase in "productivity" is thought to occur through physicians' supplementary payments. Physician authorising behaviour in hospitals is explicitly linked with the size of the hospital revolving fund, from which physicians draw a significant proportion of their salary; there is, therefore, an explicit occurrence of supplier-induced demand, which may lead to a waste of scarce resources because of the financial incentives to physicians from this practice. While policy-makers believe that the Turkish population is potentially under-using the (publicly provided) health care system and encourage utilisation, this practice could have potentially disastrous effects in the long-run.
6. In terms of human resources, there are urgent needs in having more practicing physicians in the country on the basis of (a) increasing patterns of utilisation; (b) increases in population; (c) small number of general practitioners; and (d) physicians who retire.
7. There are great challenges in terms of management team training in hospitals to run the reforms; there are currently very few, if any, hospital managers and most hospitals are run by lead physicians.

5.7.1.2.Pharmacists

With regards to pharmacy dispensing, a number of problem areas were also identified, that may negatively affect the ability of pharmacies to dispense optimally, as follows:

1. Those who dispense medicines may not necessarily be qualified pharmacists, not even trainee pharmacists, but, simply pharmacy employees. Given that a significant proportion of dispensing, including several prescription-only-medicines may be dispensed over the counter and without a prescription, this automatically generates safety concerns.

2. The “muvazaa” practice and the lack of skills among “dispensers” undervalues the contribution of the pharmacy profession and its role as providing, among others, proper counseling to patients.
3. A further “devaluation” of the pharmacy profession is underwritten by the near complete absence of any regulation regarding pharmacy location, geographical distribution and the total number of pharmacies in the country. While this policy was probably important up until this point in order to enable more pharmacies to offer services to patients, policy makers would probably need to address the problem from now on.
4. Pharmacists are paid on a regressive margin basis from health insurance funds, but they also receive discounts and free goods from manufacturers (its extent is not known but thought to be significant). Health insurance is not aware of the extent of such discounts and free goods. An evaluation of pharmacy income as well as target income for the official dispensing (Rx) business has never taken place. On aggregate, it seems that pharmacies receive dual payment; intuitively, the effect of discounts should work in the opposite way to the effect of regressive margins, with the net effect being unknown. The fact remains that, as it stands, the decision-making community cannot use dispensing as a policy-making tool because of this dual effect.

5.7.2. Policies Towards Physicians

Physician prescribing behaviour is key in determining demand for pharmaceutical products and, ultimately, in contributing to overall pharmaceutical expenditure. It is our understanding that in Turkey the central government has targeted prescription volumes as part of its cost-containment policy in recent years. Measures have included reimbursement delisting of certain expensive drugs through a negative list; restrictions in prescribing certain products or classes of products have also been introduced. Computerised systems designed to rationalise dispensing have been introduced by some of the insurance funds, but, overall, the performance of these measures in terms of improving efficiency, equity or containing cost, is unknown.

Overall, prescribing behaviour can be shaped by information policies, influenced by (positive or negative) incentives, and controlled through monitoring and audit policies. Consequently, given the wide range of patient needs, policies towards physicians are multi-faceted and can focus on a number of policy areas:

(a) Influencing physician prescribing behaviour,

(b) Promoting rational drug use,

(c) Assisting in the establishment and dissemination of clinical guidelines and best evidence, and

(d) Potentially providing incentives to prescribing physicians either through their method of payment or through budgetary means.

These help promote more cost-effective prescribing as well as contribute to the objective of overall macroeconomic efficiency. Each of these options is explored below.

5.7.2.1.Influencing Physician Prescribing Behaviour

This section focuses on doctors' prescribing behaviour, and analyses a number of alternatives that may be established in the Republic of Turkey that would lead to effective monitoring of physician prescribing behaviour. Currently, it is felt that little is done to monitor and evaluate prescribing. Educating physicians should be one of the priorities of the drug reimbursement system improvement agenda. Familiarizing them with economic and financial aspects of clinical practice is of pivotal importance in terms of drug expenditure optimisation. The preparation and updating of national and regional drug formularies including comparative evaluation and assessment of drugs in the light of therapeutic and economic performance indicators is a must to this end. A number of priorities are considered below and a series of recommendations are made that touch upon physician prescribing behaviour.

(i) Clinical guidance

It is important for clinical practice guidelines to be fully developed and also enforced. Their development rests with the professional association (Turkish Medical Association - TMA) in collaboration with health insurance, but it would be very important for prescribing physicians to be educated to prescribe in accordance with these guidelines. Clinical guidelines should indicate the appropriate course of action for a particular diagnosis. The existing compilation of clinical practice guidelines should be extended using international evidence on best practice (e.g. consulting the UK and/or US clinical guidance) and adopted by health insurance. Ultimately, reimbursement should be linked with appropriate use of these guidelines. Updating the guidelines should be the responsibility of health insurance and the relevant professional association and should occur on the basis of diagnosis and whenever there are developments in clinical practice.

(ii) Prescription monitoring & evaluation

We feel that an integrated system of monitoring and evaluation needs to be put in place, that would provide accurate information on prescribing patterns and dispensing and would guarantee a continuous flow of information between prescribers, dispensers and health insurance. This would build on current efforts by Bağ-Kur and Emekli Sandığı. Health insurance should be able to;

- Scrutinise pricing and payments to contractors for the dispensing of prescriptions;
- Provide prescribing and dispensing information to the entire health service;
- Manage the Health Insurance's income availability; and
- Prevent prescribing and dispensing fraud within the health service.

In order to achieve the above objectives, an integrated national information system is needed linking prescribers, dispensers and Health Insurance, and providing detailed information on diagnosis, prescribing and consumption. This prescribing information system would eventually be available at the national level and would provide GPs with reliable and regular information on their prescribing and costs. The purpose of providing such data is to facilitate the promotion of high quality, cost-effective prescribing, particularly since patterns of prescribing vary widely not only amongst countries, but also within countries. Such an information system, apart from providing reliable, up-to-date information, could increase GPs' awareness of costs, leading to more rational prescribing.

In order to achieve its objectives a body/unit of this kind, would have to be adequately staffed and trained on a frequent basis. An initiative of this kind is essential for the monitoring of prescribing and dispensing and should be established in the short- to medium-term, drawing (and not necessarily based) upon other international experiments in this area, (one of several examples could be that of the UK Prescription Pricing Authority).

(iii) Cost-effective prescribing

It is often the case that effective new treatment methods take a long time to be adopted in practice. Furthermore, physicians do not have the time or expertise to evaluate for themselves the possibilities of these new interventions. The expected increase in market availability of new technologies would necessitate such a mechanism for evaluating interventions and informing practitioners and the public. In the section on pricing we recommended the adoption of health economic evaluations over the longer term, as one of the

tools on which to base rational decisions on the adoption of new medical technologies. This can be achieved either through explicit adoption of cost effectiveness guidelines in the reimbursement process and/or their use by clinicians as guidance for cost-effective prescribing. The drafting of guidelines c/would be a key focal point in the process of evaluating the clinical cost effectiveness of new technologies and the extent to which the most recent innovations do provide therapeutic benefit at a reasonable cost.

(iv) Physician education, training, information

While it is important to understand the principles of (cost-) effective prescribing, these principles must be reinforced through adequate continuing education schemes for prescribers as well as timely information on new technologies and rational prescribing. This role could be played by the body responsible for cost-effective prescribing and may be resource intensive.

More precisely, its additional remit would be to facilitate and support the promotion of high quality, cost-effective prescribing through a co-ordinated programme of activities for health authorities, medical and pharmaceutical advisers, and GPs. Its objectives would be to develop a co-ordinated programme of activities covering the following five main areas of work:

- **Training and education:** to deliver a co-ordinated program of activities with the aim of supporting health authorities and their advisers in their role to improve prescribing and medicine use.
- **Information:** to provide and help co-ordinate the provision of effective information on medicines and prescribing related issues.
- **Good practice:** to ensure health authorities, GPs, and advisers have accurate and correct information on clinical effectiveness and evidence based care.
- **Information technology:** to help design & develop a prescribing information system, and to assess new technologies.
- **Research**: to help inform national research and development initiatives on prescribing.

Relevant information could also be available, though broader dissemination of systematic reviews of the effects of healthcare interventions. This can be achieved through the Cochrane Collaboration, an international organisation that aims to help people make well-

informed decisions about interventions in healthcare by preparing, maintaining and promoting the accessibility of systematic reviews.

5.7.2.2.Promoting Rational Drug Use

Rational drug use encompasses a set of policy actions targeting mainly prescribers, but, also, consumers/patients. Policies on rational drug use have a long-term horizon, combined with an element of continuity. They comprise changes in national education curricula of medical, dental and pharmacy students, improved and objective sources of information for prescribers, continuing education for practitioners, monitoring and evaluation of prescribing patterns at the national level and promoting consumer/patient awareness of public health issues.

(i) Human resource development

Medical students should be able to analyse critically the enormous number of information concerning various aspects of drug use. Learning of foreign languages should be stimulated and all possibilities for exchange of young people with other EU Member States used. The EU would, most frequently, support these activities. This is true also for education of pharmaceutical inspectors and other professions needed for constant supervision of all events of the drug field. Basic and intermediate health economics should also be introduced in the curriculum of medical students as they are in other countries, and similar principles should govern continuing education of physicians.

(ii) Drug use

Evidence-based prescribing must be taught much more than may be the case now - in Turkish medical schools and the Schools of pharmacy. At the postgraduate level and continuing medical education drug use must get a more important place.

(iii) Adverse drug reactions

Reporting of ADR is also one way of increasing knowledge about drugs. The current system of reporting ADRs called TADMER (Turkish Center for Monitoring and Evaluation of Adverse Drug Effects) has been in place. The work is underway to reform the system for a more effective functioning through the establishment of a new body called TUFAM (Turkish Pharmaco-vigilance Center).

(iv) Monitoring the implementation of policies on rational drug use

It is our perception that, currently, there is no systematic monitoring of various parameters of the function of the drug sector. This can be done through the use of integrated information systems, as outlined previously. Several countries have implemented such systems and monitor prescribing as well as dispensing patterns. This essentially allows sickness funds or the health service to monitor performance, to benchmark prescribing rates, to determine whether there is appropriate prescribing, over-prescribing, or under-prescribing in some areas, and to monitor overall quality of care delivered compared with practice guidelines. Health insurance organisations can perform drug utilisation reviews and discuss with over-prescribing physicians the reasons for over-prescribing compared with their peers, among other things. Available data can also be utilised for pharmaco-epidemiology research, monitoring of outcomes, observational studies, ex-post cost effectiveness analysis for re-granting reimbursement status, etc. Various databases exist enabling this process (see Appendix 2 for this purpose, describing the UK PPA, and the General Practice Research Database [GPRD], among other things).

(v) Consumer/patient education

This is a rather complex area which would probably take a long time to give fruits. Consumers/patients need to know basic facts on prevention focusing mostly on lifestyles, but also on the treatment process of different conditions, particularly those of chronic nature. The Ministry of Health (MoH) and health insurance funds could contribute to this improvement in awareness (which is also part of a prevention strategy) amongst the general population, by designing and distributing leaflets free of charge. Doctors' surgeries would be the obvious place to start with.

(vi) Self-medication

Although significant steps have taken place in Turkey in recent years to assist the development of OTC drugs, the creation of an explicit OTC classification remains at large, but, if established, could generate significant cost-savings to the government. This must be crafted carefully, however, so as not to harm the income sources of pharmacies. To start with, the government needs to improve legislation in the area of OTCs and allow de-listing of products with the assistance of relevant experts on pharmacology.

5.7.2.3.Prescribing Guidelines

Prescribing guidelines are a means of indirectly controlling prescribing patterns, through recommended action by physicians. They can be either positive or negative. Positive prescribing guidelines recommend a course of action (or a series of courses of action, depending on the severity of a given condition) to the prescribing physician. Negative prescribing guidelines describe what is not recommended for a given condition.

Regardless of whether prescribing guidelines are positive or negative, the agents that participate in setting them up are paramount for their subsequent implementation and compliance by the medical profession. It is therefore recommended that the Turkish Medical Association should be actively involved in their drafting. This would ensure that current medical practice is incorporated in the guidelines and would also contribute to increasing compliance by prescribing physicians during the guidelines' implementation.

Priorities for draft guidelines could be given to conditions where prescribing, and therefore spending, is highest. According to the WHO HFA (Health for All) database, from an epidemiological perspective, the most expensive problems in Turkey include

(a) cardiovascular diseases

(b) infections

(c) gastrointestinal disorders

(d) psychotic disorders

(e) hypertension

(f) musculo-skeletal diseases

(g) diabetes

(h) asthma

(i) tumors

Health Insurance and the medical chamber/association could focus their attention to drafting guidelines for the above conditions. A body could be formed which would establish working groups to build such guidelines (or even adapt existing ones from other settings to the Turkish setting), as well as monitor developments and update guidelines in each clinical area. Such guidelines could either be in paper format and disseminated to all contracted

prescribing physicians, or could, at a later stage, also be offered electronically, as part of the monitoring system discussed earlier.

Monitoring is important and might involve physicians marking patients' records and prescriptions with either a "G" if a guideline has been followed, or a "NG" if the treatment pursued falls outside the scope of guidelines. Random checks should be established by Health Insurance Funds and provisions could also be made for penalties in case of continuous breach of guidelines, to the extent this is possible.

It is not known whether prior authorisation obtained by physicians from insurance funds exists for certain (usually expensive) treatments, but, if not, then it should be required before doctors are allowed to prescribe particularly expensive products, or products that are subject to specific restrictions. Exceptional products, innovative and very expensive, could be prescribed on special forms and could also be subject to particular checks. This is another area, where guidelines are needed (area (i) in the above list).

5.7.2.4.Incentives

Physician fixed budgets, relevant for Primary Care physicians, provide an explicit incentive to contain unnecessary costs and improve efficiency. The incentives may be structured to reward physicians who underspend, or penalise those that overspend, or both. Prescribing budgets might be set on a historical basis and taking into account the population mix that each practice serves.

They could also be fixed and subject to penalties if exceeded. Prior to the implementation of this measure, some training may be necessary. Practice allowances could be introduced particularly if physicians undertake the responsibility of offering further services, such as a 24-hour service. Additional services, such as physiotherapy or health checks, could be offered on a fee-for-service basis, payable by the consumer/patient.

Evidence exists from a comparison, within the UK, of General Practitioners (GPs) limited by a spending budget (fundholders) and GPs without this restriction. Any savings that fundholders made could be reinvested in the practice. GP fundholding, while it was in place, led to (modest) increases in generic prescribing. Others have also studied the effect of using financial incentives to change generic prescribing behaviour of non-fundholding GPs and found that the incentives increased generic prescribing and resulted in the achievement of target savings, albeit modest. One potential confounder, however, is the fact that fundholding GPs were partly inhibited by the threat of having their future budgets reduced. Budgets for

physicians have also been present for a long time in Germany, up until they were formally abolished in 2001-2002. There, financial penalties were in operation for prescriptions exceeding the budget for pharmaceuticals. The 1993 Public Health Reform Law set a global GP pharmaceutical budget of US$15 billion. The amount spent above this limit would be paid from physician's remuneration budgets. After the introduction of this policy, surveys showed that in West Germany, 55% of doctors responded by increasing their prescribing of generic medicines. An unwanted side-effect of the policy, however, was an increase in the in number of patients transferred to hospitals, to save on GP's budgets. The problem with budgets in Germany was that the penalties envisaged in the legislation were never enforced. As a result, adherence to the limits imposed was poor and budgets were eventually abolished only to be reintroduced in 1998 and to be re-abolished in 2001-2002 once again. One important policy conclusion, therefore, relates to enforcement of the actual legislation. In this particular case, failure to enforce it led to its eventual abolition.

Within the Turkish setting, the fragmentation of health insurance coverage, makes the process of establishing budgets and monitoring these effectively, rather cumbersome. Alternatives might need to be considered in this case.

5.7.3. Pharmacists

Generic substitution rights and pharmacy reimbursement incentives through regressive margins are two different facets of the same policy that would promote generic use more widely.

5.7.3.1.Generic Substitution

Prescribing should occur by INN, with brands only when requested for an explicit reason. Generic substitution should be encouraged and practiced by pharmacists wherever possible. This has become mandatory in Turkey particularly after the introduction of reference pricing policy for products priced over the reference price levels with the exception of cases where patients prefer to pay the additional co-pays. However, generic substitution is not mandatory for products below the reference price levels. Yet, utilization of evidence-based equivalent generic drug products (branded or not) is one of the most effective and efficient measures for the optimization of the drug expenditure profile.

Through generic substitution a pharmacist is authorised to dispense the generic version of a medicine even when a GP has prescribed it by brand name. There are various levels of generic substitution. Pharmacists may have wide substitution rights, in other words they can substitute freely for a generic, but their rights may also be limited, which may mean

that they need to obtain authorisation to dispense a generic or be allowed to dispense a generic in emergencies only. Generic substitution is potentially a significant policy tool in increasing the market share of generic medicines and is allowed in some form in Canada, Denmark, Germany, the Netherlands and the US. Typically the physician is given some control to prevent substitution where a particular situation warrants this. A flat fee differentiation approach as the co-payment system favouring off-patent drugs could be considered. Of course, generic drug substitution should be coupled with initiatives to change the prescribing and dispensing behaviour towards generics.

Patients usually respond positively in generic substitution, especially when they are presented with the option to purchase, and contribute towards the cost of, a more expensive branded product by means of a higher (tiered) co-payment. A UK study found evidence that patients do not object to being changed from originator to generic medicines. This, of course, is dependent on generics' quality being perceived as equally high as that of branded products. Of 1,917 patients who had their original prescriptions changed from an originator to a generic drug, 90.5% were still taking the generic drug six months later.

At the other end of the spectrum, policy makers should be aware that the introduction of generic substitution complicates the establishment of liability for adverse drug reactions. With generic substitution, the doctor transfers some of his or her professional authority to the pharmacist, and with it the blame for prescribing a cheaper drug if anything goes wrong.

For substitution to work in practice, the system of incentives as well as pharmacy payment schemes must be geared in a particular way. While pharmacy payment schemes are addressed below, the system of incentives relates to the discounts that pharmacists receive from manufacturers. Pharmacy discounts are critical in creating drugs of choice, because pharmacists will have an incentive to procure from and stock the drug that carries the highest discount to them. This may not be the cheapest possible (generic) product, in which case, health insurance may have to reimburse a more expensive option that might otherwise be the case.

Of course, the substitution system could be improved through initiatives targeted at the prescribing habits of physicians, such as prescribing by the INN name as well as measures to radically influence the dispensing behaviour of the pharmacists like approaches encouraging generic substitution.

5.7.3.2.Pharmacy Remuneration Policy

If generic prescribing and substitution policies are to work in practice, then an integrated generic policy is required that encompasses prescribing physicians and dispensing pharmacists. With regard to the latter, the method of paying pharmacists is crucial. Regressive margins rather than a flat fee per prescription or a progressive margin are, in principle, an optimal way of encouraging generic consumption; however, attention should be paid that regressive margins do compensate for the loss of income from dispensing a cheaper product. In that case, a fixed dispensing fee would be the optimal policy. Turkey has a system of regressive margins in place, combined with a system of (informal?) discounts to pharmacies. While the regressive margin system is in principle the right policy direction, it is not clear whether this yields any significant benefit to pharmacists. No studies exist (at least to our knowledge) examining their effect, therefore, it is impossible to say with certainty whether regressive margins are the optimal policy measure or not. As discussed elsewhere company discounts and regressive margins work in opposite directions with the incentive being stronger on the discounts' side, thus rendering regressive margins potentially ineffective as a policy tool.

5.7.3.3. The Clawback[18]

A clawback system, along the lines it operates in the UK or the Netherlands, might also be a useful policy in the Turkish context, where pharmacies receive both margins (regressive) from government per dispensed prescription and discounts from wholesalers. In these cases discounts may in principle be operating at the margin of legality, and may be impossible to account for. Such discounts, whether formal or informal, result in directly benefiting pharmacies with no additional benefit to statutory health insurance organisations unless there is a clawback system in place. For such a system to be in place and to yield significant pecuniary benefits to health insurance, the SSI will need to have a perspective of the extent of discounts to individual products and then, perhaps, apply a fixed rate, which will be retained once pharmacists submit a reimbursement claim. The extent of discounts can be ascertained by SSI inquiries into dispensing. An additional reason where a clawback could be useful is in ensuring that pharmacies do not retain all the discounts they receive from dispensing drugs without a prescription. Although this is outside the scope of health insurance, it could contribute towards the rationalization of pharmacy dispensing.

[18] Of course, if health insurance radically reconsiders its policy on generics, setting reimbursement rates on the basis of a reference price based on the lowest generic, without compromising quality or optimal market function, and abolishes the rule of lowest generic plus 30%, then the little scope for a clawback in the off-patent segment declines in principle.

5.7.3.4. An Enhanced Community Role for Pharmacists

The dispensing phase of rational drug use is another significant element of the roadmap for the cost-effective utilization of public reimbursement funds and the reduction of any waste. An extra dispensing fee per drug item or per prescription could be considered in case the pharmacist provides well-defined and well-monitored information and counseling services along the lines of Good Pharmacy Practice. This 'cognitive fee' for the professional contribution of the pharmacists of the judgmental type to cost-effective drug therapy should be based on a field-tested and standardized template to assure the patient-centred philosophy and the uniformity of the service provided. The monitoring and evaluation of the added value of such dispensing should be a shared authority and responsibility between the governmental bodies and the professional organizations. This would nevertheless imply changes in the ways pharmacies are run, managed, and staffed on a day-to-day basis. It also certainly means moving away from or modifying current practices, which may be to the detriment rather than the benefit of patients (e.g. muvazaa).

Overall, the government should perhaps altogether re-consider the way(s) pharmacists are remunerated in Turkey and provide an integrated way of remunerating them. The policy options that could be considered in this respect are as follows:

1. The elimination of the muvazaa. Pharmacy associations agree this is completely illegal and should be scrapped. Its abolition should be enforced robustly by the authorities with sanctions against those who continue to practice this phenomenon.
2. Reimburse pharmacists either on the basis of a regressive margin (perhaps with the addition of a dispensing fee per item), or on the basis of discounts, but not both. Regressive margins and discounts together work in opposite directions and their effects cancel out, at the expense of health insurance.
3. If discounts are chosen, then health insurance is entitled to implement a clawback in order to retrieve part of the discount given to pharmacists.
4. Enforce the presence of a pharmacist or a qualified dispensary at each pharmacy at all times; enforcement should carry penalties for non-compliance.
5. Substitution is a policy that could yield results (cost savings) in the future on condition that some of the dispensing incentives mentioned above have been scrapped and once there are clear price advantages for different types of drugs (branded vs. generic).

5.8. The Demand Side

Addressing the behaviour of patients that are the ultimate consumers of pharmaceutical products, has two particular facets: (i) cost-sharing, (ii) self-medication.

5.8.1. Co-payments

We are of the view that the public should continue to be partly aware of the cost of medicines, particularly for short-term, acute conditions. This should continue to be the case through co-insurance. The level of co-insurance could vary depending on the condition and could be higher for short-term, acute conditions (see Section 5.6 on reimbursement policy above) and lower or zero for chronic conditions.

Fully reimbursed products would be those that are life-saving and those that treat patients with chronic conditions, and, particularly among them, those who are elderly citizens. All other drugs would need to be classified in categories and, depending on the level of necessity, the level of co-insurance would be determined. Two such categories could be specified. The levels of co-insurance could also be determined by the level of target revenue to the government and the extent of exemptions. Exemptions from paying co-payments might have to be reviewed and further tightened, without compromising access to essential medications. OTCs, with a few exemptions, should cease to be included in the positive list and be de-listed immediately. An evidence-based and transparent procedure for moving certain drugs and/or indications to lower reimbursement categories with a higher co-payment percentage could also be considered. On the other hand, criteria and procedure for 'upgrading' a drug to a higher level of reimbursement should also be subject to a similar approach.

The available cost-sharing options are manifold, each obeying to different policy imperatives, as follows:

(a) ***Fixed fee per prescription***: this can be a flat fee determined by SSI per prescription or, even, related to pack size; this is typically a hypothecated tax on patients. Patients are not aware of the cost of medicines if a flat fee is implemented.

(b) ***Co-insurance***: a fixed proportion of the cost of the drugs; typically, different types of drugs attract different co-insurance rates, depending on whether they are meant for acute or chronic conditions. Typically, drugs for defined chronic conditions are fully reimbursed, therefore the co-insurance rate is zero. The co-insurance rates should be determined by the SSI in collaboration with other stakeholders.

(c) ***Deductible***: a lump sum that all patients will have to pay, before health insurance kicks in. This might include paying the lump sum even if a prescription for a chronic condition is filled. Once patients pay the lump sum, then alternative arrangements apply (e.g. co-insurance). A universally applied deductible has important (and negative) equity implications as all patients have to contribute to it. Setting its level is also a function of fiscal and equity objectives and their trade-off.

(d) ***Differential co-payment***: applying different cost-sharing options for branded and generic products

(e) ***Ceilings of patient cost-sharing***: whatever policy is adopted, setting an upper ceiling for patient cost-sharing contributions may be desirable, beyond which health insurance will cover the entire cost of medicines.

(f) ***Combination of the above***: typically, a combination of the above can be implemented, for instance, a fixed fee with co-insurance, or a deductible with co-insurance.

In setting the levels of cost-sharing, the SSI should, therefore, consider and study the following issues:

1. Co-payments' revenue raising capacity and the extent to which co-payments should contribute to the health care budget: All cost-sharing options reviewed previously can contribute significantly to the health care budget. That depends on the level at which they are set.
2. Raising awareness among consumers/patients about the cost of medicines: This works particularly in connection with discouraging frivolous drug use among patients.
3. Choice of cost-sharing policy/-ies from the above options, maintaining the principle of equity.
4. Maintaining equity and ensuring that vulnerable social classes and the chronically ill are (partially) relieved.

Section 2.8. "Out of Pocket and Informal Payments by Turkish Patients" of this report also highlighted the problem of informal payments. Typically, informal payments that patients are required to pay can greatly increase actual co-payments above levels intended by

the insurance structure. These informal payments might be serving a potentially useful market function, by encouraging providers to supply more services than they would otherwise. Nevertheless, this might be better addressed by shifting both hospital and physician reimbursement to some form of payment related to output. Health insurance, when setting payment and reimbursement policy would need to consider this, as with some form of output-based provider reimbursement, providers' demand for informal payments might decrease, and it would then become more politically feasible to ban such payments and gradually[19] eliminate them.

5.8.2. Over The Counter (OTC) Medicines

We are of the view that self-medication should be encouraged. The role of the pharmacist in this is quite important in terms of advising the consumer. High co-payments (or indeed full payment) for specific classes of drugs (those classed as non-essential) could also contribute to expanding the extent and scope of self-medication, without compromising patient access to essential medicines. Such policy actions would yield significant savings to the Turkish health care system, which could be invested elsewhere to include and reimburse novel treatments. Current data presented earlier in this report, suggest that there may be significant overuse of several product categories that are potentially OTCs and that delisting those from reimbursement is an obvious and important approach to reducing patient incentives for overuse.

In order to establish an integrated policy towards OTCs, government action is needed on four fronts:

- First, to update (or initiate) legislation on self-medication, defining what OTC products are and how they should be treated,
- Second, to review the body of evidence from Turkey or/and other countries indicating that certain medicines are safe and effective under patient self-medication (which includes cough and cold medications, most analgesics, etc).
- Third, to educate the public about the benefits as well as the related risks of self-medication, thus increasing consumer awareness, and,
- Fourth, to promote a positive environment for de-listing, particularly old products, and may require legislative action to establish the criteria for switch from

[19] Understanding, of course, that informal payments are frequently a cultural issue and a significant shift in mentality needs to take place for these to be eliminated altogether.

prescription-only-medicines (POM) to OTC. Switching from POM to OTC would require continual action by the drug committee that decides on reimbursement as well as close monitoring of the products on the list.

The current situation in Turkey is that a large number of products are reimbursed when prescribed, compared with the international trend where such drugs are not reimbursed. This also includes dietary supplements (vitamins and Ginkgo Biloba), which do not have proven clinical or therapeutic benefit. This is a policy area where Turkey could realize significant savings by improved policy design. While it may be essential to retain a few OTC products in the positive list and reimburse these when needed (and when prescribed by a physician), our view is that the vast majority of these products should gradually be de-listed.

Understandably, from a cultural perspective, it may be difficult to do a big-bang de-listing of all OTCs, but this can take place over a period of years. In the interim, health insurance should set low reimbursement – high co-payment (e.g. 50 or even 75% co-payment) rules for products that could be designated as "of limited efficacy", or "comfort products" and which, in the medium- to long-term would be designated as OTC and be delisted altogether.

Finally, and assuming an OTC regulatory framework is in place, similar to what prevails in other countries, three additional policy measures could be implemented:

- First, for products that are designated as OTC, price controls are unnecessary and usually have the effect of raising rather than reducing prices to consumers. Bearing in mind that OTCs are (in their vast majority) off-patent drugs, competition should be feasible and should occur if prices are de-regulated. Of course, if some OTCs remain in the reimbursement list, their prices should continue to be regulated for the segment that is prescribed by a physician.
- Second, if all pharmacies in Turkey were attended by pharmacists at all times, it would make sense to have a third category of "behind the counter" drugs that are available from a pharmacy without a physician prescription, but which must be dispensed by a pharmacist only since OTC drugs must only be dispensed by a pharmacist. At present, granting this authority to others than pharmacists is not desirable on the grounds of patient safety.
- Third, the government must decide whether OTCs (excluding the "behind-the-counter-OTCs") should be available from pharmacies only, or whether should be

made more widely available, e.g. supermarkets, thus completely de-regulating their status.

5.9. Hospital Pharmacy and Procurement

The Hospital Formulary system should be approached as the backbone of the hospital-level drug reimbursement initiatives. Infrastructural issues for the institutionalization and the sustainability of the Pharmacy and Therapeutic Committee type decision platforms should be handled within the quality management framework.

A well-designed and periodically updated formulary which is binding for a specific hospital or a hospital cluster is a powerful tool for rationalizing drug selection and procurement procedures as well as optimising the other components of the drug utilization framework with regard to in-patient pharmacotherapy. Provisions should also exist for the inclusion of expensive medications within a hospital setting, for example, monoclonal antibodies, which could be available on the basis of authorisation by a clinician and patient numbers be monitored closely.

5.10. Industrial Policy

The pharmaceutical industry is an asset for all countries where it operates, including the Republic of Turkey. It is a high-tech industry providing employment, contributing to manufacturing value added, and linking the clinical side with the commercial sector, through clinical trials. We are of the view that this asset should be preserved and, if possible, enhanced further, especially in light of the country's strong indigenous industry. To that end, policy-makers might wish to consider having a balance between health policy and industrial policy. Such policy, however, should not favour one segment of the industry versus another, but should be uniform in nature.

Industrial policy should focus on the type of activities that the industry is pursuing in the country, supporting particularly any R&D conducted in the country as well as manufacturing activities (although not discriminating in favour of these). An indirect way of recognising the importance of these activities might be reflected in the price of pharmaceutical products as we suggest in Section 5.5. “Pharmaceutical Pricing Policy” and in the way the entire sector is viewed upon, without directly or indirectly favouring one segment of the industry over another. The latter practice is against EU law within the context of an integrated internal market.

Encouraging pharmaceutical investment in Turkey is desirable but it is also a function of several parameters, because of the nature of pharmaceutical business, one of which is the distinction between generics and innovative drugs. Clearly, there are different requirements for each of these groups of products.

Generic investment requires good facilities, GMP and, since it is chiefly cost-based, the government may want to consider offering tax and other relief to generic manufacturers in return for more cost-effective pricing.

However, European law forbids discrimination between different industries or, indeed, segments of the same industry. In other words, it is not possible to offer these incentives to generic manufacturers and not to research-based manufacturers. Similarly, authorities should not favour one product versus another, when negotiating reimbursement. Although this is not an issue to be addressed at the moment, it is more than likely that it will be raised once accession negotiations begin in earnest.

Encouraging inward pharmaceutical investment is probably more complex since it requires a confluence and coordination of policies between various government ministries (Ministries such as Health, Social Security, Industry and Trade, Finance, and National Education; the Undersecretariats of Treasury and Foreign Trade; as well as TÜBİTAK –The Scientific and Technical Research Council of Turkey– and YÖK –Higher Educational Council–). In terms of encouraging manufacturing, it is important to see whether there are significant cost advantages, which, combined with the current small size of the Turkish market, can not only yield sales for the domestic market, but also significant exports. Tax advantages or breaks and, indeed, special manufacturing facilities are important in this respect. But, as discussed above, such incentives cannot be offered only to pharmaceuticals.

In terms of supporting R&D, it is important to distinguish between discovery and developmental research. Whereas discovery research takes place in only a handful of locations worldwide and requires excellent science base, university-industry collaboration and government funding of research, among others, developmental research does not necessarily require such culture and infrastructure. Instead, it requires the availability of good scientific base and the ability and willingness to conduct collaborative research. Significant incentives can be offered in this respect to multinational manufacturers to conduct part of their regional R&D in Turkey, because the latter has the scientific potential, for example, to conduct clinical trials, and can do these at a significantly lower cost.

5.11. Operational Requirements

The timing for reforms is ideal at this juncture as the government has embarked on extensive changes in pharmaceutical reimbursement. There are, however, managerial issues, IT issues, human resource issues and other infrastructure issues that need to be addressed within this context.

5.11.1. Managerial Requirements

Within the SSI, a sustainable quality management framework should be set up to assure the continuous improvement of the drug reimbursement system-related structures and processes. The following are the minimum requirements for this approach:

- Priority setting and strategy formulation, within the context of overall reimbursement policy and as part of the remit of the reimbursement committee.
- Defining the clinical and financial outcomes in quantifiable terms. This should be the remit of the IT unit that monitors prescribing patterns and overall consumption of medicines in the country.
- Criteria and standards formulation that allow for internal and external benchmarking.
- Developing structure, process and output indicators reliable enough in terms of clarity, measurability and utility value.
- Designing a continuous auditing system for the uninterrupted measuring of intended and unintended consequences of the drug reimbursement instruments.
- A dynamic matrix of interacting cost containment interventions approach should be modeled and implemented in a systemic manner.
- Furthermore, alternative models should be comparatively evaluated to throw light on: a) Favouring and opposing factors evaluation (Force Field Analysis) for the feasibility of their implementation in Turkey, and b) The benefit, risk, and cost positioning of each model.

5.11.2. Ensuring the Sustainability of the System

1. Human resources both at the policy level and other roles should be empowered enough to make rational decisions and to translate these into operational level activities. Expert panel opinion platforms, e-discussion fora, and facilitated case analysis sessions could be given as methodological examples to realize this. New skills may need to be developed in health services, health services management,

and health economics. Graduates with these skills will be essential in running health units in the future as well as advising the Ministry of Health and SSI on decisions regarding pricing and reimbursement of medicines.

2. A national database should be established that would monitor, evaluate and audit prescribing patterns, drug use, and overall drug policy in Turkey. There are several examples of how this can be done (and what parameters it could or should include); one of them is the General Practice Research Database (GPRD) in the UK.

3. A smooth transition should be accomplished throughout the continuous drug system improvement which almost always would be of the revolutionary-type change when the traditional character of the drug reimbursement management systems in Turkey are considered. Otherwise, the stakeholders would not find enough time to adapt to the proposed drug reimbursement system reforms such as decision process reengineering. Social marketing techniques should be utilized as change management tools to let the interested parties exhibit the needed buy-in behaviour.

4. An 'expert committee' should be operationalized to formulate the code of conduct for 'GDRP' (Good Drug Reimbursement Practice).[20]

5. A 'drug reimbursement clearinghouse' should be considered for collecting, analyzing, evaluating, storing, formatting, and disseminating the scientific literature findings and professional reports on drug reimbursement to the interested parties. This should also assist the monitoring, evaluation and formulation of recommendations on drug reimbursement issues.

6. A methodological framework for the transferability of pilot success stories to other drug reimbursement issues and institutions should be designed to enable them to build up 'drug reimbursement system development know-how' through benchmarking.

7. Virtual platforms like e-forum sessions should be considered to catalyze the continuous coordination and cooperation both among the team members and the teams. This approach will further the consensus building and allow for the research and development of system designs realistic enough to be implemented.

[20] Good Drug Reimbursement Practice (GDRP) is a term coined in this study.

8. The legislative infrastructure of the improved drug reimbursement system framework should be reformed through social dialogue among the stakeholders to realize the abovementioned pillars of institutionalization and sustainability.

5.11.3. System Development Infrastructure

1. A series of task forces should be considered for situation ("as-is") analysis and fact finding. Task forces on EU drug management issues, Delphi technique, SWOT analysis, benchmarking, social marketing methodology, and system feasibility should be operationalized within this framework.
2. A steering committee should be established to facilitate the pipelining of the meeting management flows of these task forces in an orchestrated and synergistic manner.
3. A "drug reimbursement glossary" should be developed to build a common base concerning the definitions of the strategic keywords (e.g. 'equivalence') and to draw the affinity diagrams among them. This glossary would also help to manage misunderstandings that might surface by furnishing the rationale behind the agreed upon definition for each keyword.

5.11.4. Legislation Enforcement

A key general problem in Turkey is the enforcement of legislation; this is thought to lead to the continuation of old and persisting problems on the demand-side but also the supply-side. These phenomena relate to prescribing, dispensing, as well as the existence of informal payments, as discussed in previous sections.

A key task for the present government will be to enforce legislation, if reforms are to succeed, despite the political cost this may imply.

6. Conclusion and Policy Directions

The timing of the reforms is ideal since the government is going through an intensive transformation process in pharmaceutical reimbursement policy. To date a number of significant changes have already been made (e.g. pricing decree, efforts towards adopting a common reimbursement policy for the public sector, and draft legislation on regulatory, pricing and reimbursement issues). It appears that the process of restructuring of the sector will continue. Political determination is the most significant signal to this end.

Successful completion and sustainability of this process are dependent upon implementation of a series of radical transformations, specified below, as a whole. The main headings of this transformation are infrastructural elements in management and organization, information management, and human resources.

6.1. Management and Organization Infrastructure

The priority issue is the "governance" approach. In other words, the priority is to follow a management concept based on participation and interaction. In this framework, "consultation culture", "transparency" and "accountability" come to the fore.

In order to determine operational procedures of "Good Drug Reimbursement Practice" a "steering committee" should be established.

When designing the structures required by the system, elasticity and dynamism should always be taken into consideration. Within this framework, human resource quality will be a determining factor. Therefore, a sufficient pool of human resources which is conducive to the envisaged transformation process needs to be developed. Realization of this would in turn call for detailed analyses of decision and work flow processes and clear job descriptions. Human resources should be adequately strengthened and continuously developed.

The need to develop the capacity for evaluating comparative cost-effectiveness of new/innovative drugs needs to be emphasized. Thus, it will be possible to implement the health technology assessment approach. This can be medium or long-term policy goal. However, it should be kept in mind that it is necessary to undertake preparatory work to this end in the short- term.

A "drug reimbursement clearinghouse" should be devised for collecting, analyzing, assessing, storing, shaping and distributing to the related parties of the findings of scientific

literature and professional reports on drug reimbursement. This should also provide support for monitoring, evaluating and shaping the recommendations on drug reimbursement.

When judged from a strategic point of view, the "transformation programme" underway is in essence a "change" project. That is why, it should be handled in the light of principles and methods of change management and through a holistic manner.

6.2. Critical Success Processes

Continuous improvement steps in drug reimbursement system are of the nature which could deeply affect the future of Turkish health sector. Therefore, the issue should be viewed from a strategic perspective. In other words, each issue should be handled with a long-term perspective and a holistic manner. In this context, harmonization with the EU acquis communautaire is an important factor that requires further attention.

In order to transfer successful pilot studies to other drug reimbursement issues and reimbursement institutions, a methodological framework should be developed allowing know-how accumulation through benchmarking.

The success of the system is dependent on the development of a decision making mechanism not based on convictions but on evidence. This would require an information management/decision support system infrastructure that ensures data quality. In this context, developing sub-systems especially for drug management is important. A national database should be established in Turkey which would enable monitoring, evaluation and financial audit of prescribing behaviours, drug utilization and general drug policy. There are several international examples on how to achieve this.

Benchmarking should be conducted for continuous improvement of the drug reimbursement system. International comparisons will facilitate adaptation of other country experiences in rational methods of improving drug financing. On the other hand, this will ensure the transfer of lessons learned to continuous development activities.

In order to ensure the continuous improvement of the structures and processes related to the drug reimbursement system, a continuous quality management framework should be established within the Social Security Institution (SGK). The following are the minimum requirements of such an approach:

- Priority setting and strategy development concerning the entire reimbursement policy as part of the tasks of the reimbursement committee.

- Statement of clinical and financial results quantitatively. This should be the mission of information technology unit which monitors prescribing behaviours and general drug consumption.
- Development of performance indicators for process, outcome and a structure which is reliable enough in terms of transparency, measurability and utility.
- Development of a continuous financial audit system for continuous measurement of foreseen and unforeseen outcomes of drug reimbursement measures.
- Establishing criteria and standards for internal and external benchmarking.

Transformation project in drug reimbursement system by its nature requires collaboration and cooperation of various stakeholders. These include private sector and nongovernmental organizations alongside the public sector institutions. Coordination mechanisms need to be planned and implemented for effective and productive interaction of these parties. Social marketing techniques should be used so as to allow time to the related parties for adopting and internalizing the recommendations.

Infrastructure factors, primarily preparing legislations and their effective implementation, should be handled with care in order to institutionalize and sustain the transformation of drug reimbursement system.

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