



MINISTRY OF
HUMAN RESOURCES



World Health
Organization

REGIONAL OFFICE FOR **Europe**



ANALYSIS AND
RECOMMENDATIONS

IMPROVED EFFECTIVENESS OF GENERIC MEDICINE MARKETS IN HUNGARY

Edited by **Gergely Németh,**
Szabolcs Szigeti
and **Zsófia Pusztai**

**IMPROVED EFFECTIVENESS OF GENERIC
MEDICINE MARKETS IN HUNGARY**

ANALYSIS AND RECOMMENDATIONS

Edited by:

GERGELY NÉMETH
SZABOLCS SZIGETI
ZSÓFIA PUSZTAI

ABSTRACT

This publication summarizes the findings of a series of technical reports by many experts involved in assessing the effectiveness of pharmaceutical policy on generic essential medicines markets in the context of the Hungarian health system. Within the framework of certain agreements, WHO provided technical advice in collaboration with local experts and with involvement from international consultants. The primary objective of this report is to provide an overview of the development of incentives to use generics in the Hungarian health system up to the end of 2011, focusing in particular on the reference pricing system and assessing what impact these incentives have had in recent years.

KEYWORDS

EFFECT OF DRUGS

GENERIC DRUGS

HEALTH POLICY

HEALTHCARE FINANCING

INDUSTRY, HEALTHCARE

PRICES

Address requests about publications of the WHO Regional Office for Europe to:

Publications

WHO Regional Office for Europe

UN City, Marmorvej 51

DK-2100 Copenhagen Ø, Denmark

Alternatively, complete an online request form for documentation, health information, or for permission to quote or translate, on the Regional Office web site (<http://www.euro.who.int/pubrequest>).

© World Health Organization 2015

All rights reserved. The Regional Office for Europe of the World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use. The views expressed by authors, editors, or expert groups do not necessarily represent the decisions or the stated policy of the World Health Organization.

CONTENTS

PREFACE	XI
ACKNOWLEDGEMENTS	XIII
LIST OF ABBREVIATIONS	XIV
1. KEY FINDINGS AND RECOMMENDATIONS	
FOR THE IMPROVEMENT OF GENERIC INCENTIVES	1
1.1. Key findings	1
1.2. Key recommendations	6
2. OVERVIEW OF EVOLUTION OF POLICY TOOLS TO INCREASE	
THE EFFICIENCY OF GENERIC MARKETS IN	
THE HUNGARIAN HEALTH SYSTEM CONTEXT	9
3. THEORETICAL APPROACHES TO THE MARKET EFFICIENCY OF	
GENERIC MEDICINES	17
3.1. Explaining price efficiency in the medicines market	17
3.2. Characteristics of the medicines market	18
3.3. Generic price-setting from the point of view of auction theory	22
3.3.1. Achieving price competition.....	22
3.3.2. Ideal situation	23
3.3.3. Who should sell?	23
3.3.4. How should the best prices be set?	24
3.3.5. Summary	25

4. ANALYSIS OF THE USE OF GENERIC REIMBURSEMENT TOOLS	
– FACTORS INFLUENCING MARKET FUNCTIONALITY	27
4.1. Aspects of entering the market	27
4.1.1. Ideal situation	27
4.1.2. Current situation	28
4.1.3. Factors influencing process dynamics	29
4.2. Supply side	32
4.2.1. Ideal situation	32
4.2.2. Current situation	32
4.2.3. Factors influencing process dynamics	33
4.3. Demand side	33
4.3.1. Ideal situation	34
4.3.2. Current situation	34
4.3.3. Factors influencing process dynamics	35
4.4. Interchangeability/homogeneity of products	35
4.4.1. Generic medicines	36
4.4.2. Ideal situation	37
4.4.3. Current situation	37
4.4.4. Factors influencing process dynamics	38
4.5. Information	38
4.5.1. Ideal situation	39
4.5.2. Current situation	39
4.5.3. Factors influencing process dynamics	40
4.6. Agency	40
4.6.1. Ideal situation	41
4.6.2. Current situation	42
4.6.3. Factors influencing process dynamics	42
4.7. Prices	43
4.7.1. Ideal situation	44
4.7.2. Current situation	44
4.7.3. Factors influencing process dynamics	48

5. ANALYSES OF MARKET EVOLUTION OF

SOME SELECTED ACTIVE SUBSTANCES	51
5.1. Analysis of the atorvastatin 40 mg market (January 2005 to July 2012)	51
5.1.1. Development of the statins market in Hungary (January 2009 to July 2012)	51
5.1.2. Development of the atorvastatin 40 mg market in Hungary (April 2007 to June 2012)	52
5.1.3. Development of market shares on the atorvastatin 40 mg market in Hungary (January 2005 to May 2012)	53
5.1.4. Development of prices on the atorvastatin 40 mg market in Hungary (April 2007 to July 2012)	53
5.1.5. Unit prices of atorvastatin 40 mg – an international perspective, 1 July 2012	54
5.1.6. Conclusions on the development of the atorvastatin 40 mg market in Hungary (2005–2012)	55
5.2. Analysis of the levofloxacin 500 mg tablets market (January 2005 to July 2012)	56
5.2.1. Development of the flouroquinolones market in Hungary (January 2009 to July 2012)	56
5.2.2. Development of the levofloxacin 500 mg tablets market in Hungary (April 2007 to July 2012)	57
5.2.3. Development of market shares on the levofloxacin 500 mg tablets market in Hungary (January 2005 to May 2012)	58
5.2.4. Development of prices on the levofloxacin 500 mg tablets market in Hungary (April 2007 to July 2012)	58
5.2.5. Unit prices of levofloxacin 500 mg tablets – an international perspective, 1 July 2012	59
5.2.6. Conclusions on the development of the levofloxacin 500 mg tablets market in Hungary (2005–2012)	59

5.3. Analysis of the losartan 100 mg market (January 2005 to July 2012)	60
5.3.1. Development of the angiotensin receptor blockers (ARBs) market in Hungary (January 2009 to July 2012)	60
5.3.2. Development of the losartan 100 mg market in Hungary (April 2007 to July 2012)	61
5.3.3. Development of market shares on the losartan 100 mg market in Hungary (January 2006 to July 2012)	62
5.3.4. Development of prices on the losartan 100 mg market in Hungary (April 2007 to July 2012)	63
5.3.5. Unit prices of losartan 100 mg – an international perspective, 1 July 2012	64
5.3.6. Conclusions on the development of the losartan 100 mg market in Hungary (2005–2012)	64
5.4. Analysis of the fentanyl 50 mcg/hour market (January 2005 to July 2012)	65
5.4.1. Development of the fentanyl 50 mcg/hour market in Hungary (April 2007 to May 2012)	65
5.4.2. Development of market shares on the fentanyl 50 mcg/hour market in Hungary (January 2005 to May 2012)	66
5.4.3. Development of prices on the fentanyl 50 mcg/hour market in Hungary (April 2007 to July 2012)	66
5.4.4. Unit prices of fentanyl 50 mcg/hour – an international perspective, 1 July 2012	68
5.4.5. Conclusions on the development of the fentanyl 50 mcg/hour market in Hungary (2005–2012)	68
5.5. Analysis of the risperidone 4 mg market (January 2005 to July 2012)	69
5.5.1. Development of the anti-psychotics market in Hungary (January 2009 to July 2012)	69
5.5.2. Development of the risperidone 40 mg market in Hungary (April 2007 to July 2012)	69
5.5.3. Development of market shares on the risperidone 4 mg market in Hungary (January 2005 to May 2012)	70

5.5.4. Development of prices on the risperidone 4 mg market in Hungary (April 2007 to July 2012)	71
5.5.5. Unit prices of risperidone 4 mg – an international perspective, 1 July 2012	72
5.5.6. Conclusions on the development of the risperidone 4 mg market in Hungary (2005–2012)	73
5.6. Analysis of the clopidogrel 75 mg market (January 2005 to July 2012)	74
5.6.1. Development of the B01AC molecules market in Hungary (January 2009 to July 2012)	74
5.6.2. Development of the clopidogrel 75 mg market in Hungary (April 2007 to June 2012)	74
5.6.3. Development of market shares on the clopidogrel 75 mg market in Hungary (January 2005 to May 2012)	75
5.6.4. Development of prices on the clopidogrel 75 mg market in Hungary (April 2007 to July 2012)	75
5.6.5. Unit prices of clopidogrel 75 mg – an international perspective, 1 July 2012	76
5.6.6. Conclusions on the development of the clopidogrel 75 mg market in Hungary (2005–2012)	77
REFERENCES	79

PREFACE

This publication summarizes the findings of a series of technical reports by many experts involved in assessing the effectiveness of pharmaceutical policy on generic essential medicines markets in the context of the Hungarian health system. The WHO Regional Office for Europe and the Government of Hungary signed biennial collaborative agreements for the years 2010–2011 and 2012–2013. Within the framework of these agreements, WHO provided technical advice in collaboration with local experts and with involvement from international consultants. Under the priority goal of supporting the implementation of health financing reform through improved stewardship, the expected result of the collaboration was improved effectiveness of pharmaceutical policy on the generic essential medicines market. In particular, the biennial collaborative agreement identified two principal tasks regarding pharmaceutical policy: (1) assessment of the current incentives for generic substitution and competition in Hungary, and (2) recommendations on further refinement of the pharmaceutical policy in terms of the generics markets.

The primary objective of this report is to provide an overview of the development of incentives to use generics in the Hungarian health system up to the end of 2011, focusing in particular on the reference pricing system and assessing what impact these incentives had on the efficiency of the generics markets, using empirical evidence from selected substance groups. The authors looked at the financing and governance functions of the health system in detail; however, they limited their analysis to the framework of the health system as their intention was not to discuss the wider scope of economic policy or the importance of the local pharmaceutical industry to the national economy. Of course, governments across Europe try to strike a balance between the lowest possible pharmaceutical prices and ensuring the profitability of the pharmaceutical companies (Mrozek & Mossialos, 2004). It cannot be disputed that this factor is very important in shaping the national pharmaceutical policy in some countries, but the nature of

the negotiations and agreements between government and industry makes it very difficult to carry out scientific analysis and impact assessment of the benefits from industry contributions in terms of employment and income, compared with additional costs from extra rewards through the reimbursement system. This analysis can be carried out with close cooperation between experts, the Ministry of National Economy and the Ministry of Human Resources in the future.

It is important to note that the research and consultation process behind this report contributed to local capacity building and political commitment to developing the financial incentives of the Hungarian generics markets during recent years, and part of the formulated recommendations in this report had been taken into account in developing the incentives for generic medicines in parallel with the preparation of this publication.

In 2010 the Ministry of Health (at the time of writing the Ministry for Human Resources) nominated the Semmelweis University Health Services Management Training Centre as national counterparts. Other local experts – mainly from the National Health Insurance Fund Administration – were also invited to collaborate and their work was partly coordinated by the national counterparts and partly by the WHO Regional Office for Europe. The delegated experts of the Hungarian Government worked closely with the WHO Regional Office for Europe on improving the analytic capacity in the country to assess the attainment of policy objectives and measure the impact of health system reforms, in order to better inform policy-makers and to promote transparency and accountability for pharmaceutical policy performance.

ACKNOWLEDGEMENTS

The editors and authors are especially grateful to Beatrix Horváth (Head of Pharmaceutical Department, Ministry of Human Resources) and to Judit Bidló (Head of Pharmaceutical Department, National Health Insurance Fund Administration) for their insightful review and comments. The authors and editors are indebted to Kees de Joncheere, Hanne Bak Pedersen and Nina Sautenkova (WHO Regional Office for Europe) for their support in writing the report, to Rita Kleska (WHO Regional Office for Europe) for her dedication to the project in terms of administrative arrangements, and to Nicole Satterley for editing and Ferenc Lindeisz for copy-editing the text.

LIST OF CONTRIBUTORS

Rudolf Czech, Head of Unit for Analysis and Planning, Department of Reimbursements for Pharmaceuticals and Medical Aids, National Health Insurance Fund Administration, Hungary (Chapters 1, 4, 5)

Gábor Molnár, Analyst, Department of Reimbursements for Pharmaceuticals and Medical Aids, National Health Insurance Fund Administration, Hungary (Chapters 1, 5)

Márk Molnár, Corvinus University of Budapest, Hungary (Chapters 1, 4, 5)

Gergely Németh, Analyst, Department of Reimbursements for Pharmaceuticals and Medical Aids, National Health Insurance Fund Administration, Hungary (Chapters 1–5)

Balázs Szentes, Professor of Economics, London School of Economics, United Kingdom (Chapters 1, 3)

Szabolcs Szigeti, Health Policy and Systems Officer, WHO Regional Office for Europe (Chapters 1–5)

LIST OF ABBREVIATIONS

ACE	angiotensin-converting enzyme
ARB	angiotensin receptor blocker
AUC	area under the curve
c_{\max}	maximum concentration
DM	Decree of the Minister (ld. 14. o.)
DOT	days of treatment
DTC	daily therapeutic cost
DTC-FRP	daily therapeutic cost of fixed reference price
eFt	thousand Hungarian forints
EURIPID	European Integrated Price Information Database
FRP	fixed reference price
GD	Government Decree
HUF	Hungarian forint (currency)
ISO	International Organization for Standardization*
IT	information technology
LOE	loss of (market) exclusivity
MKT(mFt)	market (million HUF)
MKT(mDOT)	market (million days of treatment)
MSD	Merck Sharp & Dohme
NHIFA	National Health Insurance Fund Administration
t_{\max}	time to reach maximum concentration
RP	reference product
RPS	reference pricing system
VCG	Vickrey–Clarke–Goves mechanism

* The country codes used in some of the illustrations in this report refer to the ISO 3166-1 Alpha2 country codes. A full list of these can be found at the ISO website (ISO, 2013).

1. KEY FINDINGS AND RECOMMENDATIONS FOR THE IMPROVEMENT OF GENERIC INCENTIVES

1.1. KEY FINDINGS

- At the beginning of 2007 a quarterly recalculation of internal reference prices was introduced, together with a tightening of the stepped pricing system for generics. This change in the reference pricing system allowed a period of movement towards the more efficient prices;¹ however, in several product groups the effect was only marginal.
- At the end of 2011, more privileges were granted when reference products were used (lower rate of reimbursement for higher priced products, longer reference product status, exclusive eligibility in the reimbursement scheme for people in socioeconomically disadvantageous situations) and the stepped pricing system was tightened. The changes resulted in a breakthrough compared to the previous attempts; however, several elements of the introduced changes are controversial in terms of the theoretical models.
- The Hungarian generics market is traditionally a branded generics market. For companies entering the market for the first time, lack of marketing and sales force² is possibly be one of the most significant barriers to entry. Introduction of a new generic to the market and its withdrawal impose a considerable logistical burden on the distributor, as sales are difficult to plan; competing products and their prices often change.

¹ The efficient price is equal to marginal cost (including normal profit but not extra profit).

² Sales force is the ability to increase sales (taking into account personnel and other factors).

- The analysis of selected substance groups shows great variety in the intensity of price competition among the products. Significant differences can be seen between the selected substance groups in terms of changes in prices, in total sales volumes after patent expiry, and in the penetration of new generics. Until 2011, when the blind bidding system was introduced for reference pricing, strong competition after the patent expiry could be observed only in one group (clopidogrel) of the six selected substance groups analysed.
- In particular between the mid 1990s and the end of the 2000s explicit incentives to pursue price-based competition were missing from the reimbursement scheme. Regulation kept supply price above equilibrium price; hence supply prices were frequently above marginal costs. This meant that there was a potential impact on welfare in the form of unnecessarily high social health insurance expenditure and patient co-payments.
- Empirical evidence from the analysis of the selected substance groups in this report clearly shows that the number of manufacturers actually present on the market in the years before 2011 correlated weakly with the creation of price competition; that is, the number of market participants in itself was not enough to create price-based competition, and consumer culture and environment of competition might have had a stronger impact on market price than the number of participants on the market. In some substance groups (atorvastatin, losartan, levofloxacin) the market sales boosted after the generics entered the market, while the price competition proved sluggish. In a climate lacking in effective incentives for competition, some administrative price regulation measures could have a considerable effect on price levels (such as a stepped pricing system for first generics);³ however, this policy measure alone could not ensure efficient prices.

³ First generic(s) is the term used for the first generic product(s) to enter the market.

- It is clear that the special taxes collected from product sales also effectively moved the market price towards the most efficient price but this type of tax policy intrinsically contradicts the logic of market competition, and it might therefore be difficult to maintain in the long term. Tax policy and incentives for price competition interfere with each other.
- The changes introduced in August 2011 – when the so-called system of blind bidding was introduced to reference pricing – had a considerable effect on prices in some sizeable off-patent markets in which competition had been absent thus far (only administrative measures could decrease the prices in the 100% reimbursement category).
- At the end of 2011 the criteria for eligibility in the reimbursement scheme for people in socioeconomically disadvantaged situations changed, resulting in only reference or cheaper products being reimbursable in this category, comprising around 10% of the total pharmaceutical expenditure in the reimbursable segment. This change also led to a substantial decrease in prices at the second recalculation of reference prices.
- People's lack of knowledge about generic medicines – along with physicians' and pharmacists' mistrust of such medicines – are significant obstacles to creating market balance.
- The current reimbursement scheme is very complex, with diverse and partially overlapping and combinable categories of reimbursement and reimbursement techniques, and with reimbursement prices often (and for patients incomprehensibly) changing. It does not allow patients to make informed, conscious decisions as consumers.
- In the current situation, effective incentives are missing for physicians to provide patients with medicines with the same therapeutic effect

but at lower prices. In many cases, measures intended as incentives are not clear, creating an impenetrable system for physicians.

- Due to the particularities of the reimbursement system, physicians have an interest in cooperating with pharmaceutical companies, rather than achieving the goals of health care policy (for example, switching from a cheaper, off-patent product to a more expensive, patented product).
- Choosing the reference product is based on retrospective conditions, which can cause delays in validating favourable prices. For example, exceeding the 1% market share threshold (which is a prerequisite for being eligible as reference product) can be a serious problem for companies without adequate marketing or sales force. It should be noted that there is a trade-off between two factors: low prices and security of supply. It is unknown how much weight the Hungarian generics policy attributes to each of these factors.
- The regulations of the fixed reimbursement scheme are too complicated and in most cases ambiguous. In addition, they often change and thus create a business environment in which it is difficult to plan.
- In order to understand the dynamics of the generics market and the impacts of the current incentives to increase price competition, the National Health Insurance Fund Administration (NHIFA) developed an effective analytical framework that was used for the analysis in this report.
- National examples showed that focusing on prices is not enough to achieve cost containment with the introduction of generics. Pharmaceutical companies tend to switch patients from cheap generics to more expensive active substances or patented drugs.

- International examples show that there is no single optimal solution to achieve market efficiency for pharmaceuticals. The factors of utmost importance in designing the regulative framework are that the applied measures must be coherent and must not provide any counter-incentives to achieving market efficiency for any stakeholders. Two main approaches have emerged in Europe in terms of assuring efficient prices on the pharmaceuticals market: (1) incentives for pharmacies to buy the cheapest products (Norway, United Kingdom) and (2) tendering systems (Denmark, Sweden, and the Netherlands).
- The Ministry of Human Resources and the NHIFA have the appropriate tools at hand to provide a comprehensive picture of the performance of the various applied policy approaches.
- From the late 2000s, NHIFA experts began to elaborate reporting standards on the most important trends of aggregate volumes and prices, and developed the framework for a transparent monthly report on the basic aggregate indicators of prices and turnover. The report has been regularly published on the website of the NHIFA since 2009. The changes introduced in 2011 further strengthened the existing reporting and evaluation mechanisms between the Ministry of Human Resources and the NHIFA. In light of this, the lack of sound basis for a systematic and regular evaluation process at policy level between the mid 1990s and the late 2000s might have been one of the reasons for which the Government concentrated on systematically increasing the efficiency of the generics market, by focusing on selected elements of the reference pricing system for many years, without measurable impact in the selected substance groups evaluated in this report.

1.2. KEY RECOMMENDATIONS

- The focus of policy measures for improving the efficiency of essential generics markets should not be placed exclusively on prices, but should also encompass the general objectives of national pharmaceuticals policy, in particular patients' access and security of supply.
- Intramural (hospital) use of medicines should also be considered when designing interventions on the pharmaceuticals market. Interface management should be established between in- and outpatient sectors.
- The principles of pharmaceutical market regulation must be kept stable for a longer period, in turn making the business environment understandable to all stakeholders.
- Companies setting efficient prices should be rewarded, while those with inefficient prices should be penalized through the reimbursement system. However, policy-makers should explicitly consider the balance between cheap prices and security of supply. Clear measures and weights should be defined in these terms.
- Prescribing protocols should also be extended to the most common active substances in order to prevent doctors from switching patients from cheaper active substances to more expensive ones with the same or very similar therapeutic benefits.
- The analytical framework should be developed further with the aim of including and assessing more off-patent substance markets, where the use of reference pricing would have an impact on achieving the efficient market price. The reporting mechanism should also be linked to the health system performance assessment framework of the health policy cycle.

- Policy interventions could be considered in order to provide better efficiency gains in terms of governance. Most importantly, more attention should be paid to better linkages between the various important elements of the policy process, especially between monitoring and planning. In addition, a systematic move towards a more balanced approach to applying the policy tools would be beneficial. With these steps, the main generics pharmaceutical policy cycle would be more efficient and would begin to function in a systematic manner. In addition, the comprehensive accountability framework in the health system context could be better defined, in order to clearly describe the responsibilities, targets and incentives for each of the participating stakeholders within the policy cycle.
- Policy-makers should create a coherent policy framework and should be clearly engaged in one of the following prescribing approaches, based on international experiences.
 - Doctors should prescribe the active substance, not the brand;⁴ and pharmacists should be incentivized to dispense the cheapest medicines among those that are substitutable.⁵
 - The platform for price competition should not be the market on which consumers and companies trade. Instead, it should be a centrally designed, optimal mechanism. The introduction of an auction based on the Vickrey–Clarke–Goves (VCG) mechanisms

⁴ It should be noted that active substance-based prescription may not be introduced for all pharmaceuticals.

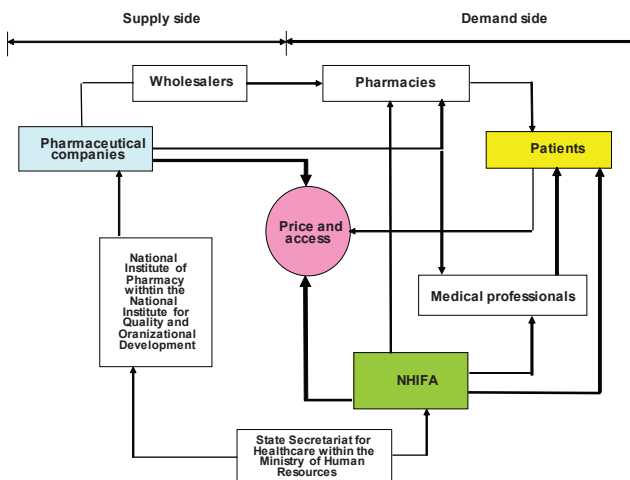
⁵ The Hungarian Government recently introduced a dedicated budget to reward pharmacists for increased generic substitution. It remains to be seen to what extent this incentive has proven useful in achieving a larger market share of cheaper generic medicines. In determining the optimal method of financing pharmacists, applying fixed dispensing fees should also be considered, instead of a proportional mark-up, and pharmaceutical companies and wholesalers should be prohibited from offering non-transparent advantages to wholesalers and pharmacists for the products that are not the cheapest (that is, discounts).

should be considered. According to these mechanisms, the winning price does not depend on the winning bid itself but only on the bids of others. The main advantage of these mechanisms is that they are strategically very simple: the bidders must tell the truth in order to win. Versions of the VCG mechanisms are abundant throughout the world and they are known to generate high efficiency and significant revenue.

2. OVERVIEW OF EVOLUTION OF POLICY TOOLS TO INCREASE THE EFFICIENCY OF GENERIC MARKETS IN THE HUNGARIAN HEALTH SYSTEM CONTEXT

In general, the Hungarian health system has been based on a contracting model since the early 1990s. The stewardship of pharmaceutical policies has been divided between the Ministry of Human Resources and the NHIFA. The Ministry of Human Resources is responsible for assigning, regulating and supervising the responsibilities of the various actors in the system (Fig. 2.1), while the NHIFA finances the services provided, monitors the pharmaceutical use patterns and contractual relationships, and makes proposals for policy interventions to the Ministry of Human Resources.

Fig. 2.1. Overview of the links between different actors in the health system with regard to pharmaceutical policy in Hungary



Since the beginning of the 1990s the Hungarian policy mix has focused on generics markets in which the institutional design of the system promoted the use of reference pricing as the central element for enhancing the market efficiency of off-patent markets. Furthermore, each consecutive government had relied on cost-sharing going back as far as the late 1980s, with the aim not only to contain the rising pharmaceutical expenditure of the NHIFA, but also to use patients' price sensitivity to switch from more expensive pharmaceuticals to less expensive ones. The majority of out-of-pocket payments – which are comparatively high in Hungary (25.3% in 2009 (OECD, 2012)) – are spent on pharmaceuticals.

In the development of the policy approach of the generics markets, four phases can be distinguished between the early 1990s and the present day (Table 2.1). In the first phase, the Hungarian Government introduced the possibility of using the reference price system based on active substance in 1991; then, from 1995, pharmacists were obliged to inform patients of the possibility of purchasing cheaper alternatives; and finally, in 1998, reference pricing based on therapeutic classes was introduced. In the second phase, in the period between 2000 and 2004, policy measures concentrated on developing the criterion of the reference product in detail – sometimes requiring a significant amount of “back and forth”. In addition, the NHIFA applied administrative price-setting, taking experience from other countries as lessons. One example of this is that the first generics must have entered the market at 30% less than the price of the originator (from mid 2004).

The third phase – from 2006 to 2008 – extended the scope of the generics policies to include measures targeting medical professionals and patients; in particular, by influencing prescription patterns through centrally accredited information technology (IT) software and by setting standards alongside targeted monitoring, as well as by raising significant levies on marketing agents working for pharmaceuticals traders. The latter measure aimed to reduce commercial influence on the prescription patterns of medical professionals. The NHIFA also created a website to provide information to patients on the prices of generic products, in order to stimulate generic substitution from the patients' side.

Coupled with these measures, patient co-payments were essentially increased by reducing the reimbursement for pharmaceuticals financed from public sources. Finally, the Government set out more rigorous rules for excluding the expensive products (those exceeding the price of the reference product by more than 20%) from the positive list in generics markets in 2007. The Government later reversed this measure by raising the exclusion criteria from 20% to 30% in 2008.

The most recent phase of the evolution of the policy framework began in 2011. As this report discusses (see Chapter 5), the new approach to increasing market efficiency through a bidding system – introduced in mid 2011 – had resulted in a real breakthrough in terms of increasing competition within the generics markets and successfully decreasing the average price in many substance groups to an extent that had not happened previously.

As far as stewardship function is concerned, while Hungarian health financing is based on a well-designed, comprehensive system of data collection (relating to prices and the dispensing of pharmaceuticals) managed by the NHIFA, the monitoring system could be better linked to the generics pharmaceutical policy cycle. The possible outputs of the monitoring system are not used to their full potential for evaluating policy outcomes. The Ministry of Human Resources and the NHIFA have the appropriate tools at hand to provide a comprehensive picture of the performance of the various policy approaches that are applied. Since the introduction of the blind bidding system in 2011, the NHIFA reports regularly to the Ministry and to the public on the main outcomes of the price competition system.

Most importantly, it would be essential to develop organizational processes to synthesize and review regularly the outputs and outcomes from the different monitoring subsystems. Performance assessment should be implemented in order to provide a systematic analysis and update of the main performance indicators. The sophisticated IT background and data collection systems of the Hungarian health system would make it technically feasible to produce a comprehensive and detailed overview of all important aspects.

Table 2.1. Overview of the evolution of generic pharmaceutical policy in Hungary, 1991–2012

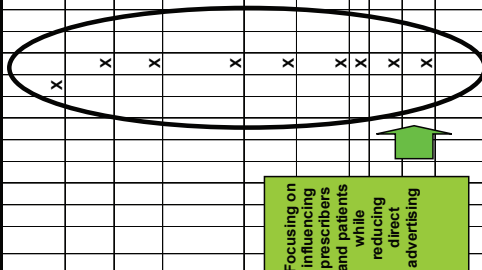
No.	Policy measures	Policy approach	1991	1992	1996	1997	2000	2001	2002	2003	2004	2006	2007	2008	2010	2011	2012	Act	GD	DM
1	Introduction of the RPS based on substance into Hungarian pharmaceutical policy. Reference pricing by active substance can be applied in cases of same substance and same application.	RPS	X																86/1990 MT (9/315) 332/1997 (232) 171/1998 (233) 322/2004. ESc-CSM	
2	Reference pricing by active substance can be applied for medicines if the National Institute of Pharmacy has declared their bioequivalence status. The medicines must have contained the same substance in equivalent form, and their application methods must have been the same. Medicines above the price of the RP could receive a fixed amount of reimbursement, derived from the reimbursement level of the RP.	RPS		X															11/1995 (4)	3/1995 NM (9) 8/1995 NM (1) 37/1997 NM (2) 217/1999 EDM 295/2002 44/2004. ESc-CSM
3	Introduction of pharmacists' obligation to inform patients of cheaper alternatives and of the possibilities regarding the substitution of products.	Generic substitution		X															11/1995 (4) 217/1999 295/2002 44/2004. ESc-CSM	
4	Introduction of therapeutic-based RPS in Hungarian pharmaceutical policy.	RPS				X													217/1997 (24)	
5	Clarification of the RPS rules by therapeutic class to define that the fixed amount of subsidy can be applied to medicines with a comparable therapeutic effect when treating the same indication. These conditions should be defined by the competent authority.	RPS				X													217/1997 (24) 11/2000 (34) 301/2004	322/2004. ESc-CSM
6	Clarification of the conditions for selecting the RP and calculating the reference price. The RP was selected based on the cheapest daily therapeutic cost. The RP must have reached 1% market share in the previous consecutive 6 months. Further clarifications of the reference price definition. The RP had to reach 5% market share and it should be on the market for 6 consecutive months before being selected as a RP. If a generic product was selected as an RP, the bioequivalence should be stated by the National Institute of Pharmacy.	RPS				X													11/2000 (34)	
7	Further amendments to the reference price definition. The RP must have reached 3% market share calculated on the basis of DOT.	RPS				X													77/2001 (27) 217/1997 (7C) 295/2002 (7D) 217/1997 (7C) (18)	
8	The first generic must enter the market at a price 30% lower than the price of the originator product.	RPS				X														322/2004. ESc-CSM (14/D)
9	Further clarification of the rules for reference pricing. Reimbursement in the RPS is calculated based on the daily treatment cost of the RP, which is the product available on the market for at least 6 months with the lowest cost of daily treatment if its market share exceeds 3% of the sales (as expressed in DOT).	RPS				X														322/2004. ESc-CSM (14/D)
10		RPS				X														322/2004. ESc-CSM (14/D)

Moving the RPS forward with the introduction of possibilities for RP and generic substitution

Promoting competition with price-setting

Table 2.1. contd

No.	Policy measures	Policy approach	1991	1992	1995	1996	2000	2001	2003	2004	2006	2007	2008	2009	2010	2011	2012	Act	GD	DM
11	The NHFA must exclude the products from the positive list if the price of the product exceeds price of the RP by more than 20%. Introduction of stepped pricing in reimbursement for those generics that cannot be involved in the RPS (30-10-10%). Generics aiming to apply for reimbursed status must have a set price equal to or below the price of the RP.	RPS									X						2006/98/31 (10/11); 2008/106/35		53/2006 EIM (102-3); 32/2004 (14 (f- g))	
12		RPS									X								53/2006 EIM (102); 32/2004 ESZGM (19)	
13	Lewy significant tax on the sales representatives of the pharmaceutical traders and producers (HUF 5 million per sales representative per year). Introduction of accredited prescribing software to inform doctors about the alternative generics without bias in order to support cost-effective prescription. Currently, accredited prescribing software lists the generic medicines in ascending order according to their daily therapeutic costs (the cheapest marked with green, the more expensive with yellow and the most expensive with red).	Reducing direct advertising to prescribers									X						2006/98/31			
14		Influencing prescribers									X						2006/98/77 (10, 87, 89)	17/2007 (42)	53/2007 EIM	
15	Introducing the recalculation of reference prices 4 times a year. The RP should have 1% DOT market share in 3 consecutive months in the previous 6 months.	Influencing prescribers										X							32/2004 (8-10); 32/2007 (3-4); 32/2005 (2/2)	
16	Introduction of a minimum co-payment in the 100% reimbursement category (HUF 300 - €1).	Cost-sharing																	53/2006 EIM (4)	
17	Reduction of reimbursement levels (50% to 25%; 70% to 55%; 90% to 85%). Creation of a website by the NHFA in order to provide information to patients on the prices of generic products.	Cost-sharing Information to patients										X							53/2006 EIM (2)	
18	Introduction of an online system for the electronic submission of price notifications. All price changes were promptly visible to registered users.	Influencing prescribers										X								
19												X								
20	Exclusion criteria in the RPS were relaxed. The NHFA must exclude the products from the positive list if the price of the product exceeds the RP price by more than 30% (RP based on substance) and by more than 60% (RP based on therapeutic group).	RPS															2006/98/31 (14/1); 2008/106/35			



Focusing on influencing prescribers and patients while reducing direct advertising

Table 2.1 contd

No.	Policy measures	Policy approach	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Act	GD	DM
21	The reimbursement category at 85% in the normative list was reduced to 80%.	Cost-sharing																		X							62/2004 (4/5)
22	The online service for price notification is obligatory for pharmaceutical companies.	RPS																			X						
23	Only those products that exceed the price of the RP by less than 5% can receive reimbursement of the RP. The others can receive reimbursement by 15% less than the reimbursement of the RP.	RPS																				X					47/2011 (NFML, ESCOM, 32/2004 (8/5/a-c), (10A as 10 (1), 10(D) (1), 14 (1)); 201181 (31, 47, 59), 200698 (235-37, 27 (4))
24	Recalculation of reference prices in case of new groups 4 times per year, or in case of older groups, twice per year.	RPS																				X					
25	Relaxation of the criterion for becoming an RP: by decreasing the time required at 1% market share from 3 to 2 consecutive months before the date for setting the reference prices.	RPS																				X					
26	Introduction of the one round blind bidding procedure for selecting reference prices and adding special privileges for the RPs.	RPS																				X					
27	Reduce in the levy on marketing agents from HUF 5 million to 10 million per year per agent.	Reducing direct advertising to prescribers																					X				
28	Pharmacies receive financial incentives in the form of a targeted budget for increasing generic substitution.	Generic substitution																					X				
29	Increase in the levy on marketing agents from HUF 5 million to 10 million per year per agent.	Generic substitution																					X				
30	The stepped pricing system is slightly modified (40-20-10-5-5-5%).	RPS																					X				
31	The DOT market share criterion in the preferential fixed groups was raised from 1% to 3%.	RPS																						X			
32	The exclusion criteria in the active substance-based fixed groups was raised from 30% to 50%.	RPS																						X			
33	The threshold of eligibility for the reimbursement of the RP in the preferential fixed groups was raised from 5% to 10%.	RPS																						X			

Notes: Act: law approved by the Parliament. DM: Decree of the Minister. GD: Government Decree. RP: reference product. RPS: reference pricing system.

From the late 2000s NHIFA experts began to elaborate reporting standards on the most important trends in terms of aggregate volumes and prices, and developed the framework for a transparent monthly report on the basic aggregate indicators of prices and turnover. The report has been regularly published on the website of the NHIFA since 2009. The blind bidding system introduced in 2011 strengthened further the existing reporting and evaluation mechanisms between the Ministry of Human Resources and the NHIFA. In light of this, the lack of a sound basis for a systematic and regular evaluation process at policy level between the mid 1990s and the late 2000s might have been one of the reasons for which the Government concentrated on systematically increasing the efficiency of the generics market, by focusing on selected elements of reference pricing for many years, without measurable impact in the selected substance groups evaluated in this report.

In the current organization the main responsibilities in terms of pharmaceutical policy are regulated in the acts on health and on the services of the compulsory health insurance (Gaál et al., 2011). However, some improvement is needed in the integrated accountability framework, in order to fill the gaps in governance; this could be accomplished in particular by the delegation of responsibilities for evaluation and planning.

Based on the clear commitment among the priority stakeholders at government level, a reliable analytical framework and strategy should be developed to support the application of the different elements of the generics pharmaceutical policy in a balanced manner. Most importantly, more attention should be paid to better linkages among the various important elements of the policy process, especially between monitoring and planning. In light of the promising results of the new approach to reference pricing – experienced in particular since 2011 – setting specific and realistic policy targets would create strong incentives for the specific stakeholders to improve their performance for a more efficient generics market. With these steps, the main generics pharmaceutical policy cycle would be strengthened and would begin to function in a systematic manner. In addition, the comprehensive accountability framework in the health

system context could be more clearly defined, in order to describe in full the responsibilities, targets and incentives for each of the participating stakeholders within the policy cycle.

3. THEORETICAL APPROACHES TO THE MARKET EFFICIENCY OF GENERIC MEDICINES

3.1. EXPLAINING PRICE EFFICIENCY IN THE MEDICINES MARKET

According to patent protection regulations, medicines can be classified into two types: innovative (originator) medicines and generic medicines. The term innovative medicine typically refers to a patent-protected development and can either be a new active substance, or a new or more modern dosage form. The markets of innovative medicines are monopolistic markets in which monopolistic position is granted by patents.

Generic medicines are medicinal products with the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies (Hungarian Ministry of Health, Social and Family Affairs, 2005). Generic medicines markets are competitive.

From an economic perspective, prices are said to be efficient if price is equal to marginal cost. Theoretically, efficient prices can only occur in competitive markets. Monopolistic markets do not have efficient prices as, owing to the monopolist's intention to maximize profit, products are typically sold above marginal cost.

It is common to talk about cost–effectiveness in connection with innovative medicines (medicines in a monopolistic position). From the point of view of economics and health technology assessment (HTA), the interpretation of cost–effectiveness means the determination of the inefficient price that – in the light of therapeutic effectiveness – society considers acceptable, taking

into consideration costs of therapeutic alternatives and willingness to pay for additional quality of life.

It is a great temptation for health care decision-makers to interpret the cost-effectiveness of generics in the same context as that of innovative products. If the tools of HTA are applied in order to measure effectiveness in the case of generic medicines, just as is the case with innovative medicines, then with a simple cost-minimization analysis it is possible to arrive at the conclusion that generic medicines are cost-effective, as they allow for cheaper therapies with the same effectiveness, compared to innovative medicines that were once declared cost-effective. This approach, however, does not consider that the ultimate reason for the use of generic medicines is that they remove welfare loss caused by the monopoly of innovative medicines, by creating price-based competition. It must be emphasized that welfare loss still exists in competitive markets as well; that is, markets cannot be considered efficient until market prices reach efficient prices, with respect to the marginal cost discussed earlier.

Of course, marginal costs are not known, but theoretical considerations and empirical factors can help estimates to be determined, if prices on the generics market are near efficient prices. This report examines whether the requisites for efficient prices on the generics market were present in Hungary and genuinely efficient prices were determined.

The term efficient market covers sustainability as well, in that the market environment should ensure that efficient market prices survive in the long run.

3.2. CHARACTERISTICS OF THE MEDICINES MARKET

It is often said that the health care market and the medicines market within it cannot be viewed as traditional markets. This opinion is confirmed by several economic arguments (for example large-scale information asymmetry, monopolies, and

so on), and often by arguments appealing to the emotions (for example health cannot be a question of money, patients deserve the best treatment regardless of costs, and so on).

It is undoubtedly true that medicines markets differ in many aspects from the theoretic models describing the functioning of perfect markets; however, only very few markets exist that are close to these models – in this sense, medicines markets cannot be regarded as special. Of course, features characteristic of medicines markets make them unique and distinguishable from other markets (for example telecommunications, energy industry, automotive industry). It is necessary to remain aware of these features when studying market functioning or planning government interventions to regulate market functioning.

Self-regulatory market mechanisms do not necessarily lead to optimal outputs. They do not result in efficient markets; thus, on almost every market, governmental interventions influence mechanisms too (such as governmental supervision of financial institutions, food marketing regulations, and so on). Governmental measures in themselves do not guarantee, of course, that markets will function more efficiently; misdirected government regulations can deteriorate market functioning efficiency, while well-planned government interventions can improve it.

When discussing health care markets and medicines markets, it is important to mention that in these markets demand is derivative, which means that patients are not in fact in need of health care or medicines, but health itself. Health care and medicines are only measures through which patients can regain or partially re-establish their health. However, in the re-establishment of health, it is not only medicines that play a part but also lifestyle change and surgical interventions; moreover, certain health damages are even preventable. These other consumer goods can function as substitutes for medicines in certain cases.

Perhaps the most salient difference between medicines markets and markets that are viewed as traditional is that the participants of the market transactions

do not only play the classical roles of seller and buyer. On the supply side there are the pharmaceutical companies and on the demand side, doctors and patients (in the case of prescription-only medicines). Demand and supply are influenced by physicians, pharmacists, health care funds and legislation, and in certain cases by wholesalers and pharmaceutical companies as well. Another peculiarity of this type of market is that behind the buyer's side stands the national health insurance fund (in this case Hungary's NHIFA), which can be in a considerably stronger bargaining position than individual buyers, and can even act as a monopsonist.

Principal-agent relationships exist behind the individual roles of seller and buyer. Physicians, pharmacists and the health care fund also act as assigned agents for patients, while they pursue their own special, sometimes clashing interests.

In the market, balance between demand and supply is created by price. The price of reimbursed medicines is regulated; suppliers cannot change their prices freely. Price regulation should be developed in such a way that prices, determined by regulation, reach the optimal level of price and output that would be determined on a perfect competitive market.

When buying reimbursed medicines, in the majority of cases, patients do not pay the full price but rather a reimbursement price that is usually a fraction of the actual medicine price. The fact that patients do not pay the actual price has an effect on demand. In terms of the features of the Hungarian reimbursement scheme, reimbursement prices of various medicines might reflect price differences among the products of different manufacturers in different ways (for example fixed reimbursement scheme, different percentage of reimbursement, fixed reimbursement price), which might manifest itself in distortions in the demand.

In general, health care markets can be characterized as displaying information asymmetry; that is, buyers are not aware of their choices. Moreover, in many cases, neither are agents; they make decisions on the basis of false assumptions

(prejudices concerning generic medicines). Patients cannot usually make informed decisions regarding efficacy, or safety and quality of medicines.

One of the key factors in the functioning of competitive markets is the interchangeability of products. Interchangeability becomes concretized in consumer decisions, which is why companies in most industries (and the medicine industry is no exception) strive to create the consumer perception that their products are different from those of competitors. In an economic sense, generic medicines are perfect substitutes for originators and for each other: generics are declared substitutes by the authorities on the basis of strict requirements. However, despite the strict regulation, the perception of each actor (patient, physician, pharmacist) concerning interchangeability can differ considerably, not least owing to the product differentiation strategies of pharmaceutical companies. Participants' perceptions regarding interchangeability might influence market functionality on a fundamental level.

The various sectors of the medicines industry might differ from each other in size and in terms of the number of suppliers. In larger sectors, several suppliers might appear on the supply side, while in smaller sectors the number of participants on the demand side may be too low. The supply side might become oligopolic, while on the buyers' side, alongside the large number of consumers (patients), demand is influenced by the monopsonic health insurance fund.

Legal regulation on medicines markets ensures monopoly rights, in order to incentivize innovation. Monopolistic markets do not belong to efficient markets, and monopolistic pricing results in welfare loss. However, society considers that this welfare loss is compensated for by the social gains that are obtainable through innovation. It is the task of generic medicines, following the expiry of the patent, to remove welfare loss resulting from monopolistic pricing.

3.3. GENERIC PRICE-SETTING FROM THE POINT OF VIEW OF AUCTION THEORY

There are two main features of the markets for generic medicines, which are the points of departure in recommending policies. First, the products in the market for generic medicines are (nearly) perfect substitutes. As a consequence, efficiency requires that firms compete on prices (and only on prices) in these markets. Second, the patients are insured and they only pay a fraction of the price. Therefore, the platform for price competition should not be the market in which consumers and firms trade. Instead, it should be a centrally designed optimal mechanism. The policy recommendations below focus on the following issues: regulations that promote price competition, and the mechanism for determining low prices.

An ideal policy should accomplish two principal goals: (1) the cost of the medicine should be kept low, and (2) the medicine should be available to patients. There is a potential trade-off between these two objectives because the market supply curve is likely to be increasing; that is, fewer firms enter these markets if the prices are low. This section discusses optimal policy relative to this trade-off.

3.3.1. Achieving price competition

- Ideally, doctors should only prescribe the substance, not the brand.
- If the above option is not feasible, pharmacies should be able to give the patient the choice to substitute. Pharmacies should be provided with financial incentives to sell the cheapest product.
- Pharmaceutical companies' efforts to influence doctors' choices should be regulated, or perhaps even prohibited.

3.3.2. Ideal situation

In general terms, an auction for some goods is a game in which bidders bid, and the winners – along with the prices of the goods – are determined as a certain function of the bid profile. In the current context, a good is the right to sell a specific product. An auction (run by a government agency) determines the set of firms that can sell a certain medicine, and the price at which they can sell it. There are two features of this environment that differ from standard auctions. First, there can be many winners and the number of goods is a choice variable. The auction itself can determine how many firms are allowed to sell their products on the ex-post market. Second, the government agency does not charge a price and pay a transfer fee to the bidders. The transfers are determined on the ex-post market (after the auction), on which the medicine is traded.

The rest of the discussion focuses on two distinct but related questions: (1) who should sell and (2) at what prices?

3.3.3. Who should sell?

Perhaps the most basic lesson from auction theory is that optimality requires efficient bidders to be rewarded and inefficient ones to be penalized. The larger the gap between the treatment of efficient and inefficient bidders, the fiercer the competition among them, which in turn leads to a higher surplus of the auctioneer. The harshest punishment for inefficient bidders is their exclusion from the group of winners; that is, the objects of the auction should only be rewarded to the efficient bidders. In the current context, the right to sell medicines should only be rewarded to those firms that are willing to sell at low prices. High-price bidders should not be granted the right to sell goods on the ex-post market.

It is important to emphasize that penalizing high-price bidders with lower reimbursement levels is not the optimal solution and can lead to distorted strategic considerations. A firm (even with low marginal production costs) might bid high because the high bid is likely to win and the downside to be considered is only the relatively mild punishment of receiving a lower reimbursement rate. Such strategic considerations might be self-enforcing: if each firm bids relatively high, then bidding high becomes a best-response scenario. Indeed, this argument implies that, provided firms have fixed marginal costs, all but one firm should be excluded from the ex-post market; that is, only the most efficient firm should be allowed to sell at a price determined in the auction.

A potential concern related to this argument is that if there are too few firms able to sell a certain medicine, then there is a significant probability that there will be an insufficient supply of this medicine on the ex-post market; for example, if companies go bankrupt, or realize that their actual costs are higher than their calculations at the time of the auction. If these concerns have any real basis, the auction should determine several companies to sell the medicines and exclude all the others. However, it is not clear whether the auction should penalize companies that are winners but are not the lowest-price bidder. In other words, it is not clear whether it is optimal to give a lower reimbursement rate to a bidder that was granted the right to sell but that bid higher than the reimbursement of the lowest bidder.

3.3.4. How should the best prices be set?

Most auctions identify the most efficient bidders as winners but they vary regarding the determination of prices. An important class of auctions – the VCG mechanisms – has received special attention from both empirical and theoretical economists. According to these mechanisms, the price of a winner does not depend on that (winning) bid but only on the bids of the others. Perhaps the most prominent example of such a mechanism is the so-called

second-price auction, whereby several bidders compete for a single object. The winner is the highest bidder and the price paid is that of the second-highest bid. It is crucial to note that the bid only influences the probability of that bid winning, but not the price paid. It is not hard to see that, as a consequence, each bidder optimally bids its own valuation in such an auction, no matter what the others do. The main advantage of these mechanisms is that they are strategically very simple: the bidders must tell the truth in order to win. Versions of the VCG mechanisms are abundant throughout the world and they are known to generate high efficiency and significant revenue.

In the current context, a VCG approach would work as follows. Bidders would submit bids simultaneously. The winners would be the bidders with the lowest bids and they could all sell at the same price. This price would be the lowest losing bid; that is, the lowest bid from among those that are excluded from the market. It is important to observe that in such a mechanism, it is in the best interest of each firm to bid at their own marginal cost, no matter what others are doing. The only undetermined feature of this mechanism is the number of winners. The optimal number depends on the trade-off mentioned at the beginning of this section. If the number of winners is small then prices are low, but supply might be insufficient.

3.3.5. Summary

It seems optimal to design an auction that is both transparent and simple from the strategic point of view. Such a mechanism penalizes high-price bidders by excluding them from the ex-post market, but treats all the winners in the same way. In particular, the reimbursement of all sellers should be identical.

4. ANALYSIS OF THE USE OF GENERIC REIMBURSEMENT TOOLS – FACTORS INFLUENCING MARKET FUNCTIONALITY

4.1. ASPECTS OF ENTERING THE MARKET

An important requisite for the formation and survival of well-functioning competitive markets is to have no significant obstacles to the exchange of participants in the industry; that is, new participants can enter or existing ones can leave the market.

When discussing aspects of entering the market, it is not the intent to examine the issues surrounding establishing medicine production plants or medicine distribution companies, nor the questions of medicine registration or marketing authorization.

With regard to the market entry of reimbursed medicines, it is important to examine how much time is required for inclusion into the list of reimbursed medicines, as well as the factors that influence the start of distribution and actual market presence.

4.1.1. Ideal situation

Immediately after the expiry of the originator's patent, all authorized generic products can enter the market. A competitive environment makes it possible for products at favourable prices to obtain higher market shares; it is possible to forecast the extent of consumption and to plan logistics. There are no major difficulties in removing products from the market (for example no bulk of stock is left that cannot be sold). Participants entering and leaving the market do not threaten the security of medicine supply.

4.1.2. Current situation

Methods delaying market entry of generics and hindering market share increase may also be present in Hungary, as described in a relevant report on the pharmaceuticals sector inquiry (European Commission, 2012). Such methods include debates over patents, agreements between manufacturers of originator and generic medicines, techniques to prolong the product life cycle, and so on. The Bolar provision is in place in Hungary, owing to which manufacturers can apply for marketing authorization while a patent is still in place and market their generics as soon as the patent expires. According to the regulations and reimbursement list update practices regarding the inclusion of medicines into the positive list, generics can obtain reimbursement approval within 20 but within no longer than 50 days after submitting the application for reimbursement (Hungarian Parliament, 2006; Hungarian Ministry of Health, Social and Family Affairs, 2004).

Due to the specific features of the Hungarian market, some difficulties exist in terms of generics obtaining the necessary market share on the basis of price. The Hungarian market is traditionally a branded market (the pharmaceutical industry produces generic medicines that are mostly branded generics); prescribing and dispensing are typically based on brand names, and generics manufacturers also carry out product promotion activities. For companies entering the market anew, lack of marketing and sales force is possibly one of the most significant barriers to entry. Introduction to the market and withdrawal from it impose a considerable logistical burden on the distributor, as sales are difficult to plan, while competing products and their prices can often change.

4.1.3. Factors influencing process dynamics

4.1.3.1. Factors promoting quick market entry

These include:

- the Bolar provision (European Parliament & European Council, 2001);

- the fact that products can be included in the positive list even before the patent expires;
- the quick approval of reimbursement applications (that is, generic products can obtain reimbursement approval within as few as 20 days of submitting the application).

4.1.3.2. Factors promoting market expansion

- The fixed reimbursement scheme is intended to promote market expansion of generic products in such a way that, compared to the difference in their consumer prices, a disproportionately higher co-payment has to be paid for products that are more expensive than reference products. Only the cheapest products can be prescribed within the framework of the reimbursement scheme for people in disadvantaged socioeconomic situations.
- To promote market expansion of generics, the Hungarian health care administration introduced authorized prescription software in which the cheapest generic medicine should be listed first when prescribing a medicine.
- Physicians and pharmacists are obliged to inform patients about cheaper substitutes.

4.1.3.3. Factors delaying quick market entry

- The attitude/approach of pharmaceutical companies manufacturing innovative medicines can delay market entry of generic products, for example by means of patent-related strategies (creation of an insecure patent environment, debates over patents with the aim of deterring market entry), agreements with manufacturers of generic medicines, and strategies aiming to prolong the life cycle of innovative products (European Commission, 2009).

- The existence of other patents not related to the active substance can delay generic products' entry into the market. For example, in the case of inhaled medicines, the manufacturer of the generic medicine can encounter the problem of the inhalation device being protected by a separate patent. As in the case of inhalation devices, the effect is that local, traditional examinations of bioequivalence in themselves are not sufficient (EMA, 2008).
- Confusing regulations on bioequivalence and interchangeability can also delay market entry of generics. Certain products are bioequivalent but are not interchangeable, due to differences in indications or in usage (Hungarian Ministry of Health, Social and Family Affairs, 2005).

4.1.3.4. Factors hindering market expansion

- Physicians' and patients' aversion to the cheaper products can hinder market expansion; for example, the attitude "if it is cheaper, it is worse" is not uncommon (Himmel et al., 2005).
- Physicians often think in terms of brands rather than active substances or substance groups that appear in their treatment schemes.
- Patients' previous bad experiences with generic medicines (Kjoenniksen, Lindbaek & Granas, 2006) can negatively effect market expansion. Particularly when taking multiple medicines, patients have difficulties in learning which of their medicines is for what, and interchanged bioequivalent medicines can also be insufficient in their effect, if taken for the wrong condition or in the wrong dosage. Such an experience might considerably weaken physicians' and patients' confidence in generic products.
- In the case of products with a narrow therapeutic window, physicians might be averse to prescribing generic medicines that are

pharmacokinetically bioequivalent within $\pm 20\%$. Such medicines include, for example, anti-arrhythmic drugs, and immunosuppressants. However, certain systematic reviews and meta-analyses found no superiority of originators versus generics in treatment outcomes in the case of certain molecules with a narrow therapeutic index (Kesselheim et al., 2008, 2010).

- A switch in therapy can be risky without medical supervision (for example in the case of products containing excipients that are potentially allergenic).
- Strategies of innovative medicines to prolong the product life cycle (for example products of modified pharmaceutical form) can negatively affect market expansion.
- Doubts can arise relating to the use of the generics due to differences in salt format and the wording of indications (Baumgärtel, 2012a, b).

4.2. SUPPLY SIDE

On the medicines market prices are controlled and demand is finite; these two factors fundamentally affect supply.

A key requisite of a market is an adequately large number of sellers competing with each other. In spite of the mergers that have taken place in recent years, the generic medicines industry is still fairly segmented (compared to other industries), featuring a large number of companies.

In those reimbursement schemes in which pricing is regulated (regulations exist regarding the price of generics entering the market), manufacturers typically fulfil only the minimum requirements set for their prices.

4.2.1. Ideal situation

The ideal situation would be a large number of manufacturers providing products of high quality and pursuing price-based competition.

4.2.2. Current situation

At present in Hungary there are a large number of generic medicines manufacturers and a large number of registered generics, and there are still generics manufacturers that have not yet entered the market. For those about to enter the market, one of the most significant entry barriers is that they cannot keep pace with competitors as they are lacking strong marketing techniques and sales force.

It is important to highlight that the number of manufacturers actually present on the market correlates weakly with the creation of price competition; that is, the number of market participants is not enough in itself to create price-based competition. In fact, consumer culture and a competitive environment have a stronger impact on market price.

A marketing-led market is not favourable for companies pursuing price-based competition and lacking in sales force.

4.2.3. Factors influencing process dynamics

4.2.3.1. *Factors that support achieving the ideal state*

- Owing to its size, the Hungarian market is relatively attractive to pharmaceutical companies.

- The launch of generics registered via the European Medicines Agency (EMA)'s centralized procedure is particularly simple.

4.2.3.2. *Factors that hinder achieving the ideal state*

- A marketing-led market creates a barrier to market entry for companies lacking in experience or knowledge of the local market.

4.3. DEMAND SIDE

The ultimate consumer on the demand side is the large group of patients; however, it should be noted that in the case of prescription-only medicines, the influence of prescribers on demand is extremely important, particularly because advertising directly to patients is prohibited in Europe (European Parliament & European Council, 2001), so prescribers are the primary target population for promoting medicines. At the same time the health insurance fund (in the case of Hungary, the NHIFA) also acts as a consumer, since it finances medicine consumption via reimbursement, and it is the role of the fund to decide whether a product can enter the market (inclusion into the reimbursement scheme).

As prices are regulated, demand does not necessarily match health care needs. If co-payments are too high, demand is lower than necessary; if they are too low, an excess of demand can even be created (McPake & Normand, 2008).

4.3.1. **Ideal situation**

In terms of the behaviour of the demand-side participants, the ideal situation would be if the large number of consumers were well informed and unbiased, and/or the monopsonic health care fund were able to act as a real buyer on the market; that is, if prices and reimbursement adjusted demand in order to meet needs.

4.3.2. Current situation

As is the case for most patients in other countries, Hungarian patients are generally underinformed. They are not aware of the relevance of generic medicines and the risks and possibilities associated with substitution, and therefore their demand does not create a market balance. The NHIFA is not allowed the same level of freedom that a health insurance fund (monopsonic purchaser) could have in terms of purchasing generic medicines; consumer decisions of the NHIFA are strictly limited by statutes (Hungarian Ministry of Health, Social and Family Affairs, 2004).

4.3.3. Factors influencing process dynamics

4.3.3.1. *Factors that support achieving the ideal state*

- A flexible scheme exists for determining reimbursement prices.

4.3.3.2. *Factors that hinder achieving the ideal state*

- The NHIFA has a restricted purchasing role.
- Consumers are underinformed.
- Reimbursement prices that are too high or too low hinder progress.

4.4. INTERCHANGEABILITY/HOMOGENEITY OF PRODUCTS

One of the key factors in market competition is the complete interchangeability of competing products from the buyer's point of view. It is a logical ambition for manufacturers to try to maximize profit by following a strategy of product

differentiation; that is, to create a perception on the part of the buyers that their products cannot be substituted with products of other manufacturers – hence, they ask a premium price. The strategy of product differentiation in a medicines market can be met with mistrust of generic medicines and result in product developments that offer minimal therapeutic advantage but still hinder substitution (for example, the introduction of orodispersible tablets into the market after the patent on film-coated tablets expired) (European Commission, 2009).

Governmental regulation of the medicines market also speaks to interchangeability; the interchangeability of medicines is ascertained by the responsible authority, with bioequivalence as a prerequisite in order to become a registered generic medicine (Hungarian Ministry of Health, Social and Family Affairs, 2005).

According to regulation, it is important to differentiate between the interchangeability of traditional generic products and biosimilars; the latter being of biological origin. As little information is available regarding the application of biological products, substitution is contraindicated.

4.4.1. Generic medicines

From the microeconomic point of view, generic medicines are considered to be perfect substitutes for themselves and for originator products, and their quality has been ascertained by the relevant responsible authority.

The definition of the term generics can be found in Directive 2001/83 of the European Union (European Parliament & European Council, 2001):

‘Generic medicinal product’ shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated

by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form.

According to this definition, generic medicines mean considerably more than same active substance: other important requirements are the same qualitative and quantitative composition, the same pharmaceutical form and the demonstration of bioequivalence with the reference medicine by appropriate studies.

During pharmacokinetic studies conducted to demonstrate bioequivalence, area under the curve (AUC), c_{\max} (maximum concentration), and t_{\max} (time to reach maximum concentration) values must be within $\pm 20\%$ compared to the reference product (log scale: 0.8–1.25).

It is important to understand that the bioequivalence of generic products is always examined only in relation to the reference products. Such examinations are not carried out among generic products due to the high number of tests required; for example, even for just four generic products, this would mean 12 detailed examinations.

Parenteral products are bioequivalent by definition, as there is no absorption with these products and the active substance enters the bloodstream directly.

4.4.2. Ideal situation

The ideal situation in terms of substitution would be if generic and biological medicines were considered in consumer decision-making as products that

could be substituted perfectly with each other. In the case of traditional generic medicines, it is possible to switch to the product of another manufacturer during therapy.

4.4.3. Current situation

To the authors' knowledge, no comprehensive research has taken place in Hungary on consumer (patient), physician and pharmacist perceptions of generic medicines. Anecdotal evidence about practices shows that mistrust of switching active substances is quite high, sometimes fuelled by previous failures of substance switches. On the branded Hungarian medicines market, both physicians and pharmacists usually choose products according to their brand name and they tend to stick to the well-known brands.

4.4.4. Factors influencing process dynamics

4.4.4.1. Factors that support achieving the ideal state

- Medicines can only be prescribed using authorized software, which contains all reimbursed medicines without bias and lists them by price (Hungarian Ministry of Health, Social and Family Affairs, 2007b).
- Physicians and pharmacists have a legal obligation to inform patients of cheaper generic medicines that are available (Hungarian Parliament, 2006).
- Since 2012, if the patient opts for a medicine that is more expensive than the reference product, the price difference should be printed on the receipt in the pharmacy (Hungarian Ministry of Health, Social and Family Affairs, 2004).

4.4.4.2. *Factors that hinder achieving the ideal state*

- Patients lack basic knowledge relating to generic medicines.
- Physicians and pharmacists have little confidence in generic and biosimilar medicines.
- Generics are not well or widely promoted.

4.5. INFORMATION

An important prerequisite of markets to function properly is the level of information the participants have about products and their prices. It is widely understood that in health care markets one of the most important factors contributing to competition distortion is information asymmetry. It is outside the scope of this paper to study information asymmetry in detail; the focus here is more specifically on the question of the use of generic medicines in relation to informedness.

Two important factors should be taken into consideration in terms of how information relates to the use of generic medicines. Participants in the medicines market should be: (1) aware of the relevancy of generic medicines and their interchangeability; and (2) informed of what products are available on the market and at what prices.

4.5.1. **Ideal situation**

The ideal situation would be if all actors (patients, physicians, pharmacists) were aware of the relevance of generic medicines and of the risks and advantages of their substitution, and if the choice of substitutes were governed by price.

Other important aspects include the necessity of an easy-to-understand reimbursement scheme and for patients, physicians and pharmacists to be aware of the principles of that reimbursement scheme.

4.5.2. Current situation

While definitive research is lacking, it is clear that Hungarian patients are not adequately informed about the relevance of generic medicines and about possible substitutes for prescribed medicines. The Hungarian medicines market is typically a branded market in which patients, physicians and pharmacists appear to have a high level of brand loyalty, whereby the expansion of products under generic names is slow.

In recent years, efforts have been made to increase physicians' informedness, but the measures introduced resulted in limited success.

The current reimbursement scheme is very complex, with diverse and partially overlapping and combinable categories of reimbursement and reimbursement techniques, as well as reimbursement prices that often (and for patients incomprehensibly) change. It does not allow patients to make informed, conscious decisions as consumers.

4.5.3. Factors influencing process dynamics

4.5.3.1. Factors that support achieving the ideal state

- The regulations on software to be used for prescribing medicines (Hungarian Ministry of Health, Social and Family Affairs, 2007b) require that medicine prescription can only occur via authorized software, which contains all reimbursed medicines without bias and lists them by price.

- Physicians and pharmacists have a legal obligation to inform patients of cheaper generic medicines that are available (Hungarian Parliament, 2006).
- A web application to enhance public informedness about prices is available at the website of the NHIFA (OEP, 2013).
- Current prices are also available on the NHIFA website (OEP, 2013).

4.5.3.2. *Factors that hinder achieving the ideal state*

- Public knowledge relating to generic medicines is limited.
- Physicians and pharmacists lack precise knowledge of generic medicines, and there is a general mistrust associated with prescribing them (Kobayashi et al., 2011).
- Physicians' and pharmacists' obligation to provide information to patients is difficult to fulfil and it is also difficult to monitor compliance.
- The reimbursement scheme is complex.
- Pharmaceutical companies' marketing and medicine promotion policies are a contributing factor.

4.6. AGENCY

Agents are market participants that act on behalf of and in the interest of a principal. The problem of the role of agents in economics is that the interests of principal and agent very rarely coincide completely. In a situation in which agents are compelled to choose between self-interest and the interest of the principal, agents are likely to pursue their own goals at the expense of the principal's

interest. It is a well-known problem in economics; business economics deals with the principal–agent problem extensively.

It is the principal's interest to have an agreement with the agent to minimize conflict of interest between principal and agent and to be able to decide unambiguously whether the agent's decisions are in accordance with the principal's interest.

The most obvious agent role in a medicines market is that of a sales representative. They carry out product promotion on behalf of pharmaceutical companies. Less obvious agent roles are those of physicians and pharmacists; as agents on behalf of sellers (pharmaceutical companies) and as agents on behalf of buyers (patients, but also the health insurance company).

In the case of pharmaceutical sales representatives, the agent–principal relationship is clear, while the principal–agent relationship in the case of physicians and pharmacists is complicated because physicians and pharmacists are agents of several principals (patients, pharmaceutical companies, insurance companies), which also have contradicting interests. Moreover, because of the nature of medicine, it is not possible in health-related decision-making situations to provide definitive answers, but only complicated probability outputs depending on many variables. This makes physicians and pharmacists' decisions difficult to monitor. The situation is made even more complicated for agents by the fact that expectations set by some of their principals are not necessarily clear (for example, to seek to maximize patients'/society's health status or utility) (McPake & Normand, 2008).

4.6.1. Ideal situation

In an ideal situation, the only task of pharmaceutical sales representatives would be to inform physicians and pharmacists about the effects of new innovative products. In the case of generic medicines, a network of sales representatives

is therefore unnecessary and the principal–agent relationship relating to pharmaceutical companies is undesirable.

In this ideal situation physicians and pharmacists would be expected to take into account both the patient’s and society’s health status and utility in making prescribing decisions.

4.6.2. Current situation

In generics markets, the pharmaceutical companies with the highest market share maintain an extensive network of pharmaceutical sales representatives.

In such a situation, there are no concrete incentives for physicians and pharmacists to provide patients with medicines with the same therapeutic effect but lower prices. In many cases, measures intended to be an incentive are not clear, contributing to an impenetrable system for physicians.

Owing to the way the reimbursement system functions, in many cases physicians are more interested in cooperating with pharmaceutical companies than with the health insurance fund. Furthermore, pharmacists – as a result of pharmacy margin regulations – are not explicitly interested in dispensing cheaper medicines.

4.6.3. Factors influencing process dynamics

4.6.3.1. Measures that support achieving the ideal state

- Fees are charged to medical sales representatives (10 million Hungarian forint (HUF) per representative per year) (Hungarian Parliament, 2006).
- Compensation exists for pharmacies for the smaller profit margin on cheaper products.

4.6.3.2. *Factors that hinder achieving the ideal state*

- Clear financial incentives for physicians and pharmacists to prescribe cheaper medicines are missing from the reimbursement scheme.
- Pharmacists are not interested in substituting with cheaper equivalents as selling cheaper products reduces their profit margin (except in the case of very high-priced medicines).
- The system of effective prescribing is complicated and it is not clear what is expected of physicians.
- Administrative incentives (financing protocols, obligation to inform patients) are difficult to monitor.

4.7. PRICES

In a market, supply and demand are balanced by price. In the reimbursed medicines market, however, both supply and demand are controlled and price in itself does not create balance.

In the majority of European countries, the first element of price control from a product life cycle point of view is approval of the price of the innovative medicine. In general, the approved price must fulfil two criteria: the technology must meet the national HTA requirements and the external price referencing criteria.

In many European countries (including Hungary) in which the prices of pharmaceuticals are regulated, the prices of generic medicines are linked to the prices of the originator products (Simoens, 2012).

An important element of price control is the amount of reimbursement provided towards the price, as what consumers actually pay is the full consumer price reduced by the sum of reimbursement (that is, the patient co-payment).

The main principle in the so-called fixed reimbursement scheme – as also introduced in some other European countries – is that the reimbursement of the products in the same therapeutic group is only ever as high as the reference price. The difference between the reference price and the actual price must be paid by the patient; thus, in the case of more expensive products, their patient co-payment is considerably higher than the price difference between products. Consequently, price-sensitive patients tend to buy cheaper products.

4.7.1. Ideal situation

The ideal situation in the field of price regulation would be if prices achieved by means of regulation (that is, not as a result of market mechanisms) were to approach the efficient price under perfect competition conditions; namely, at marginal cost. An important aspect to consider is how fast the prices of products reach the efficient price; in an ideal world, product prices would immediately reach the efficient price following the expiry of the patent.

An important factor in determining patient co-payment levels is to ensure that the price for patients is not so low as to create excess demand but not so high as to restrict access.

4.7.2. Current situation

For applications for reimbursement of innovative medicines, preparation of an HTA report is compulsory and the manufacturer price that is submitted cannot be higher than the lowest European manufacturer price.

After patent expiry, the first generic product can be reimbursed with a 40% price advantage (reduction) compared to the originator product; the second product with an additional 20% price advantage; the third product with an additional 10% and the next three products thereafter with an additional 5–5% price advantage. The regulations do not explicitly deal with the pricing of the products that enter the market thereafter.

If the proposed price of the product is accepted by the NHIFA, the regulation is applied to the wholesale and retail margins in order to calculate the wholesale and the net pharmacy (net retail) prices (Hungarian Ministry of Health, Social and Family Affairs, 2007a) (see Tables 4.1, 4.2, 4.3 and 4.4). Value-added tax (VAT) at 5% is added to the net pharmacy price.

Table 4.1. Calculation of wholesale price up to 1 August 2012

WHOLESALE MARGIN		
MANUFACTURER PRICE (HUF)	% OF THE MANUFACTURER PRICE	HUF
0–150	12	–
151–180	–	18
181–300	10	–
301–333	–	30
334–500	9	–
501–600	–	45
601–1000	7.5	–
1001–1154	–	75
1155–2000	6.5	–
2001–2600	–	130
2601–	5	–

Source: Hungarian Ministry of Health, Social and Family Affairs, 2007a.

Table 4.2. Calculation of wholesale price since 1 August 2012

MANUFACTURER PRICE (HUF)	WHOLESALE MARGIN
0–500	8.0%
501–1000	6.5% BUT MINIMUM HUF 40
1001–2000	5.0% BUT MINIMUM HUF 65
2001–	4.4% BUT MINIMUM HUF 100

Source: Hungarian Ministry of Health, Social and Family Affairs, 2007a.

Table 4.3. Calculation of net retail price up to 1 August 2012

WHOLESALE PRICE (HUF)	MARGIN (% / HUF)
0–500	26%
501–590	HUF 130
591–1500	22%
1501–1737	HUF 330
1738–3500	19%
3501–3911	HUF 665
3912–5000	17%
5001–	HUF 850

Source: Hungarian Ministry of Health, Social and Family Affairs, 2007a.

Table 4.4. Calculation of net retail price since 1 August 2012

WHOLESALE PRICE (HUF)	MARGIN (% / HUF)	NET RETAIL PRICE (HUF)
0–500	27%	0–636
501–590	HUF 136	637–726
591–1500	23%	727–1845
1501–1737	HUF 345	1846–2082
1738–3500	20%	2086–4200
3501–3911	HUF 700	4201–4611
3912–5500	18%	4616–6490
5501–	HUF 990	6491–

Source: Hungarian Ministry of Health, Social and Family Affairs, 2007a.

Manufacturers can decrease product prices freely each month, but increasing prices is a very complex procedure: companies have to justify the increase and the Technology Appraisal Committee has to approve the application. If the request to increase a price is declined, the applicant can either accept the decision or withdraw the product from the reimbursement scheme (or at worst case, from the market).

Beyond this, price competition should be created and ensured by a fixed reimbursement scheme, the core tenet of which is the fact that the reimbursement of products belonging to the same substitution group is adjusted to the reimbursement price of the reference product (that is, the cheapest product among those fulfilling certain criteria regarding market shares). These criteria have changed several times in the period analysed for the purpose of this report. The required length of this period was decreased from three consecutive months to two months in October 2011, and the requirement to reach at least 1% market share was increased to 3% in October 2012. Reference prices were recalculated quarterly until October 2011, when a 6-month recalculation frequency was introduced for those groups in which the recalculation had already occurred at least three times.

In October 2011, so-called preferential reference price ranges were introduced, meaning that in the old (existing for at least one year) reference price groups, those products that are over 5% more expensive than the reference product receive 15% less reimbursement (the range was modified to 10% in October 2012). Only the products within the preferential range can be dispensed to the patients who are eligible for the reimbursement scheme (those in disadvantaged socioeconomic circumstances). An important change was the blinding of the bids, which means that the bids of the companies are published the day after the deadline, so that competitors cannot see the bids of others during the bidding period.

Experience shows, however, that the reimbursement scheme and reference pricing system cannot reduce the price level to the hypothetical equilibrium price in the case of several high-volume and mass-produced generic active substance groups with expired patents (Németh et al., 2009). The basic miscalculation of the fixed reimbursement scheme is that it builds on the assumption that patients are price sensitive. In broad terms, the demand for health care services is price inelastic (McPake & Normand, 2008) and in addition, patients are fundamentally uninformed about substitutes and their prices. The demand-side price inelasticity does not encourage manufacturers to reduce their prices, so ultimately the system does not reach its intended goal.

In trying to establish whether Hungarian pharmaceutical prices are near marginal cost, other European countries' medicine prices can be used as benchmarks. External price referencing is a prevalent practice among European countries, but one that Hungary only applies to innovative medicines.

As the medicines market is global, it makes sense to assume that marginal costs cannot differ from each other across countries; thus, the marginal cost of each medicine cannot be higher than the lowest perceived price. If Hungarian prices differ from this lowest price, the assumption must be that it is the result of dysfunction in the Hungarian market. Practice shows that in the case of high-circulation medicine groups, Hungarian manufacturer prices can be significantly higher than the lowest western European manufacturer prices.

4.7.3. Factors influencing process dynamics

4.7.3.1. Measures that support achieving the ideal state

- Introduction of a fixed reimbursement scheme is a positive factor.
- Price advantages have been in place for using reference products since 2011.

4.7.3.2. *Factors that hinder achieving the ideal state*

- In a fixed reimbursement scheme, determination of reference prices occurs too late following patent expiry (at least six months later); meanwhile, the originator product retains its original price.
- Quarterly cycles of reference product recalculation appear to be too frequent for manufacturers, considering their market development plans and activities in a mature, competitive, multi-product market. This makes logistics planning difficult for companies, it makes patients switch products too often, and it creates a sense of insecurity around the issue of reimbursement prices.
- The fixed reimbursement scheme contains only few explicit privileges for the cheaper/reference products.

For example:

- competing products that are less than 50% more expensive than the reference product can remain reimbursed (prior to 2013, this threshold was at 30%);
- any product competing with the reference product can be prescribed by a physician or dispensed by a pharmacist;
- a price correction opportunity arises every month (competing products have the chance to reduce their prices to the level of the reference product price (or below), thus reaching the co-payment level of the reference product).
- Choosing the reference product is based on retrospective conditions, which can cause as much as a 6-month delay in validating favourable prices; exceeding a 5% market share threshold can be a serious problem for companies without significant marketing or sales force.

- Pharmaceutical companies and wholesalers grant favourable conditions to pharmacies; the majority of pharmacies have a delivery contract with one of the wholesalers.
- Physicians, pharmacists and patients are not made aware of the principles of the reimbursement scheme.
- The regulations of the fixed reimbursement scheme are too complicated and in most cases ambiguous. In addition, they often change and thus create a business environment in which it is difficult to plan.

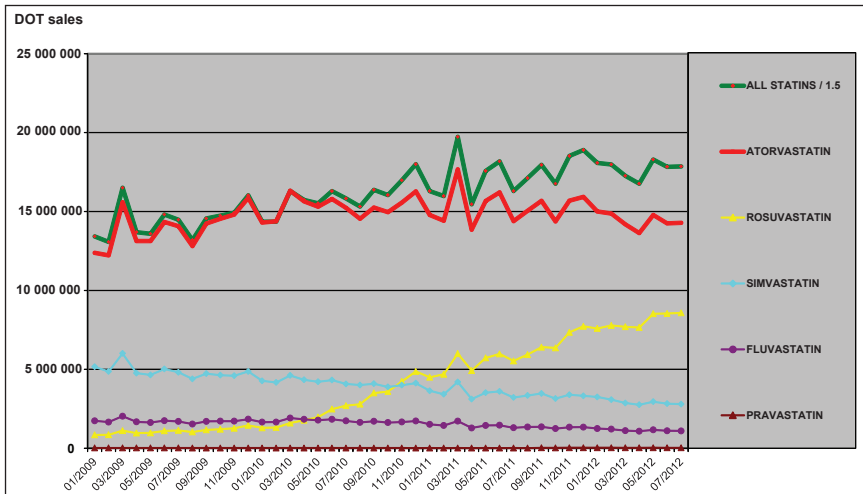
5. ANALYSES OF MARKET EVOLUTION OF SOME SELECTED ACTIVE SUBSTANCES

5.1. ANALYSIS OF THE ATORVASTATIN 40 MG MARKET (JANUARY 2005 TO JULY 2012)

5.1.1. Development of the statins market in Hungary (January 2009 to July 2012)

In the Hungarian statins market, atorvastatin (C10AA055) has been in a market leader position since 2007, reaching a dominant market share (over 50%) in mid 2010. Rosuvastatin has had the highest growth rate in the Hungarian statins market since 2009, with sales of the earlier market leader – simvastatin – continuously declining in the period examined (see Fig. 5.1). The days of treatment (DOT) turnover appears to be saturated since the beginning of 2011.

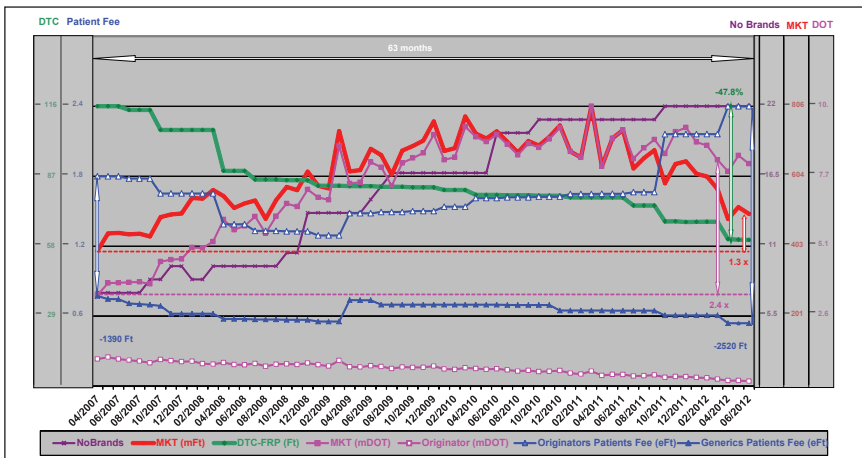
Fig. 5.1. DOT sales of various statins, 2009–2012



5.1.2. Development of the atorvastatin 40 mg market in Hungary (April 2007 to June 2012)

Atorvastatin is indicated for the treatment of hypercholesterinaemia and the primary prevention of stroke, myocardial infarction and other cardiovascular events. Atorvastatin had a 90% reimbursement level until January 2007, when the reimbursement rate was cut to 85%. In April 2009 the reimbursement rate was cut again to 80% (see Fig. 5.2). The originator brand of atorvastatin – Sortis/Lipitor (Pfizer) – is the most sold drug ever, worldwide, and was the best sold brand in Hungary in 2005. Atorvastatin has the highest ATC5 turnover on the Hungarian market since 2005. Generics suppliers existed on the market at the beginning of the period being examined, although the drug is still patented (known as on patent) in some other countries. Despite the drops in the reference price (which is the basis for the reimbursement level in the reference pricing groups), the total sales volume of 40 mg atorvastatin increased until the end of 2009, when the market started to become saturated. The sales value began to decline steeply in parallel with the daily therapeutic cost (DTC) in October 2011 due to the modified reference pricing system (preferential price range) that was implemented.

Fig. 5.2. Market development of 40 mg atorvastatin, 2007–2012

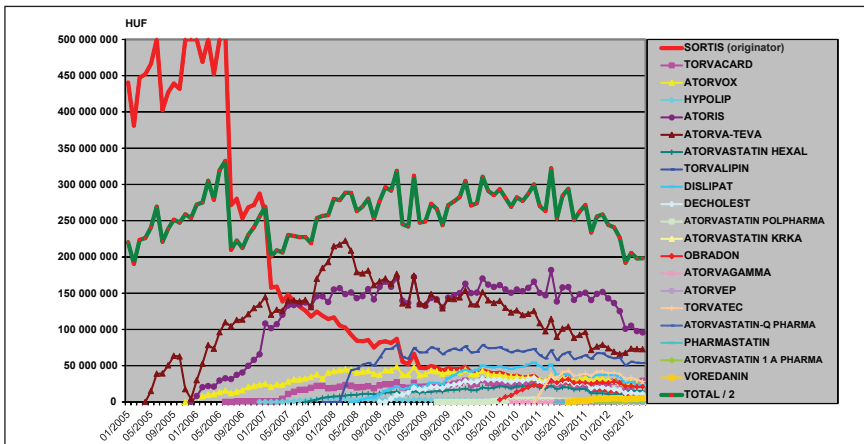


Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF.

5.1.3. Development of market shares on the atorvastatin 40 mg market in Hungary (January 2005 to May 2012)

The originator brand – Sortis (Pfizer) – lost sales dramatically in 2008. The greatest market shares were reached by the first two generics, Atoris (KRKA) and Atorva-Teva. Only one product, Torvalipin (Actavis), which entered the market later, was able to achieve an outstanding market share among the 20 competitors. The total consumption of atorvastatin 40 mg in terms of value (cost) reached saturation level at the end of 2009/start of 2010 and seriously started to decline in October 2011 due to the modified reference pricing system (preferential price range) that was implemented (see Fig. 5.3).

Fig. 5.3. Sales of various 40 mg atorvastatin presentations, 2005–2012

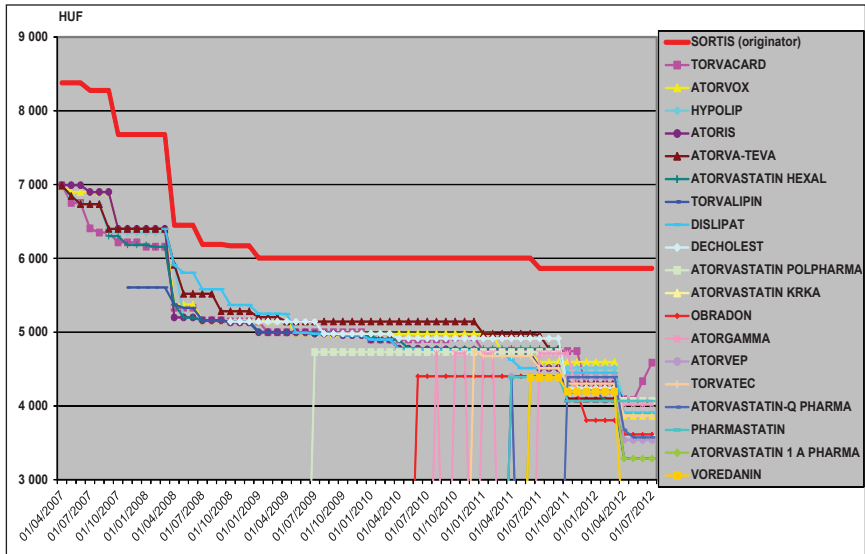


5.1.4. Development of prices on the atorvastatin 40 mg market in Hungary (April 2007 to July 2012)

Fig. 5.4 shows that an increase in the number of suppliers does not lead necessarily to a decrease in unit price (see the period between January 2009 and June 2010). There were considerable drops in the unit price of 40 mg

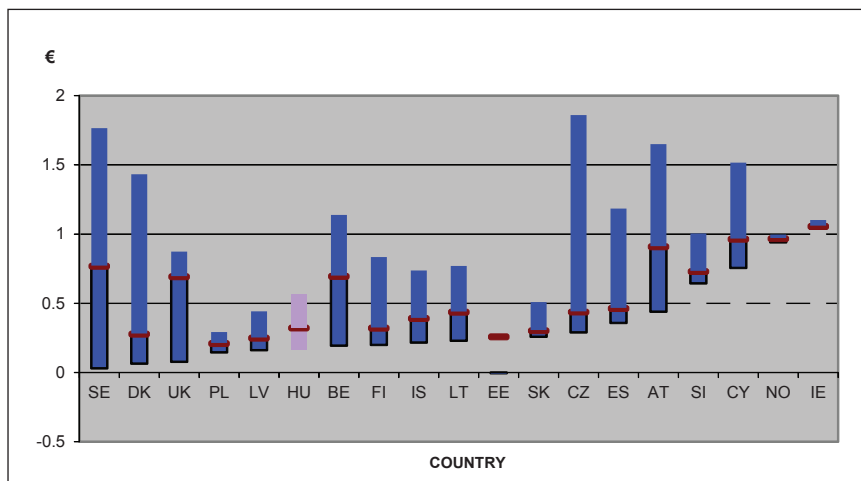
atorvastatin in both October 2007 and in April 2008, with the aim of gaining market share and at the same time avoiding being removed from the reimbursement list (in July 2007 a new regulation was implemented regarding removing from the list any products more expensive than 120% of the reference price). Between April 2008 and October 2011 there were only three minor decreases in unit prices. Between October 2011 and April 2012 there were significant price decreases as a consequence of the modified reference pricing system (preferential price range) that was implemented.

Fig. 5.4. Prices of various 40 mg atorvastatin monthly presentations, 2007–2012



5.1.5. Unit prices of atorvastatin 40 mg – an international perspective, 1 July 2012

The Hungarian unit prices of 40 mg atorvastatin are quite low compared to other European countries (see Fig. 5.5); however, it should be noted that in some countries the minimum prices are significantly lower than in Hungary.

Fig. 5.5. Atorvastatin 40 mg unit prices, international perspective, 1 July 2012

Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

5.1.6. Conclusions on the development of the atorvastatin 40 mg market in Hungary (2005–2012)

Atorvastatin has had the highest DOT turnover since 2005, among the statins. The atorvastatin market became saturated in 2009. While the DOT turnover of simvastatin has been declining since 2008, rosuvastatin has the highest growth rate since 2009.

Despite the existence of 20 generics competitors, for many years the reimbursement system was not able to facilitate a decrease in the unit prices much below the obligatory level for the active substance with the highest turnover.

The most effective measure that was introduced before 2011 was the introduction of the delisting threshold in July 2007.

The relatively higher priced first generics were able to keep their dominant positions on the market, with only one latecomer company reaching the 10% market share level. Marketing is apparently still a strong driving force on the atorvastatin market.

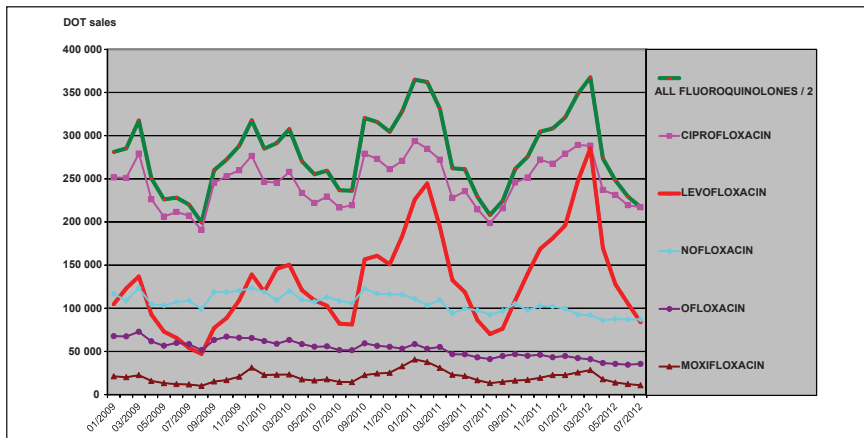
The price of atorvastatin started to decline again after the introduction of the modified reference pricing system with the preferential price range.

5.2. ANALYSIS OF THE LEVOFLOXACIN 500 MG TABLETS MARKET (JANUARY 2005 TO JULY 2012)

5.2.1. Development of the fluoroquinolones market in Hungary (January 2009 to July 2012)

Fluoroquinolones are antibiotics that are indicated for the treatment of a wide range of infections. Sales of levofloxacin showed significant growth in the period 2009–2012 in Hungary (see Fig. 5.6). Due to its market performance in recent years, levofloxacin became the second fluoroquinolone on the market in terms of turnover.

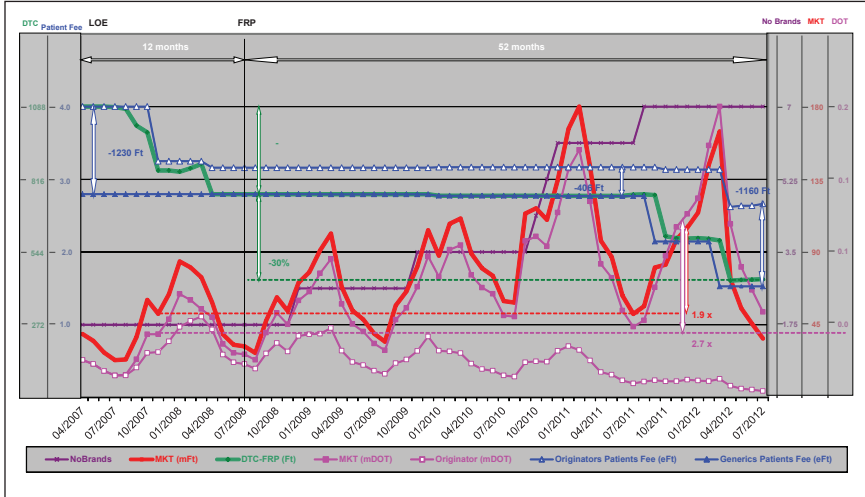
Fig. 5.6. DOT sales of various fluoroquinolones, 2009–2012



5.2.2. Development of the levofloxacin 500 mg tablets market in Hungary (April 2007 to July 2012)

The levofloxacin market is a medium-sized market that shows clear seasonality in line with the seasonality of infectious diseases (with a peak from winter to spring). Levofloxacin was reimbursed by 50% until January 2007, when its reimbursement rate was cut to 25%. The introduction of two new generics in 2010 resulted in an increase in consumption (see Fig. 5.7). As a consequence of the low rate of reimbursement and the relatively uncompetitive environment, DTCs were unchanged – the market share grew in parallel in terms of value and volume (DOT) until the end of 2011. The sales volume seriously started to decline in parallel with the DTC in October 2011, as a result of the modified reference pricing system (preferential price range) that was implemented.

Fig. 5.7. Market development of 500 mg levofloxacin tablets, 2007–2012

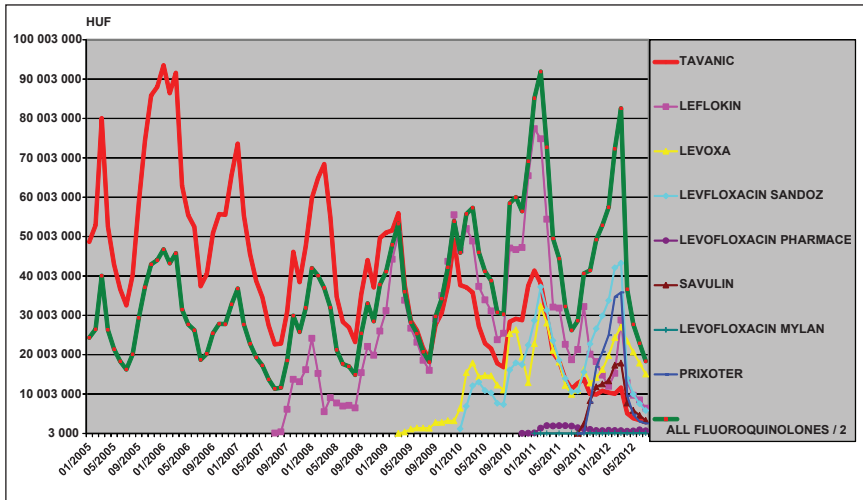


Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF.

5.2.3. Development of market shares on the levofloxacin 500 mg tablets market in Hungary (January 2005 to May 2012)

The original product, Tavanic (Sanofi) suffered a loss of (market) exclusivity (LOE) in April 2007. Only one generic – Leflokin (Teva) – was available for two years. The newcomer generics increased their sales in the period 2011–2012, which was detrimental to the sales of the first two products (see Fig. 5.8). Since the implementation of the modified reference pricing system (preferential price range) in October 2011, the newcomer generics took over as leaders of this market segment.

Fig. 5.8. Sales of various levofloxacin 500 mg tablets presentations, 2005–2012

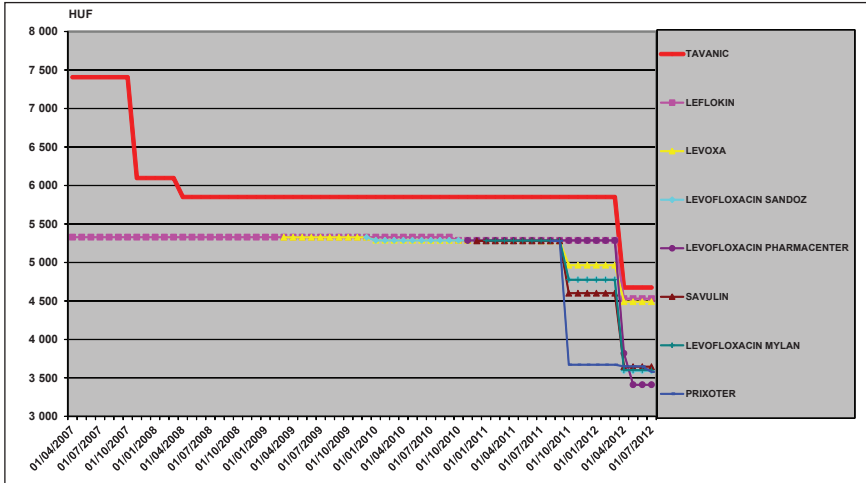


5.2.4. Development of prices on the levofloxacin 500 mg tablets market in Hungary (April 2007 to July 2012)

The unit price of Tavanic (Sanofi) decreased by 30% when the first reference price was introduced (one year after the market entry of the first generic). Unit prices remained constant (see Fig. 5.9) until changes to the internal reference pricing

system took place in October 2011. The price level of levofloxacin fell by more than 40% since early 2012.

Fig. 5.9. Prices of various levofloxacin 500mg tablets weekly presentations, 2007–2012



5.2.5. Unit prices of levofloxacin 500 mg tablets – an international perspective, 1 July 2012

Hungarian unit prices can be classified as mid-range, compared to other European countries (see Fig. 5.10), although the price of the cheapest product is less than its half that in the United Kingdom.

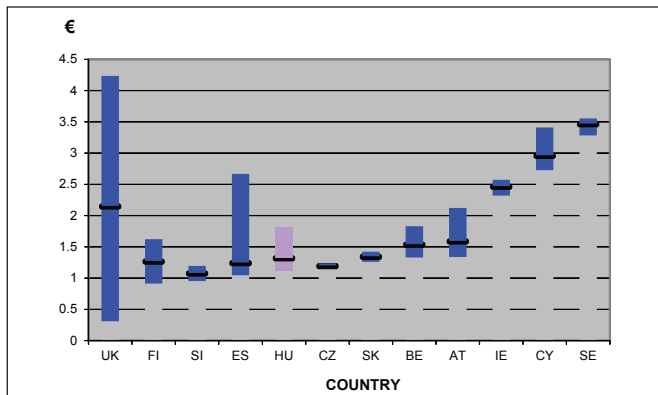
5.2.6. Conclusions on the development of the levofloxacin 500 mg tablets market in Hungary (2005–2012)

The levofloxacin market shows clear seasonality and the reimbursement rate in this group of generics is quite low.

Due to the low reimbursement rate (50%, then later 25%), the effect of the fixed reimbursement scheme on price competition is obviously less than in the case of higher reimbursement rates (for example for clopidogrel, atorvastatin, and losartan).

Market prices were frozen at 30% lower than the price of the originator product until the reference pricing system was changed in October 2011. In addition, the price level for levofloxacin dropped dramatically since early 2012.

Fig. 5.10. Levofloxacin 500 mg tablets unit prices, international perspective, 1 July 2012



Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

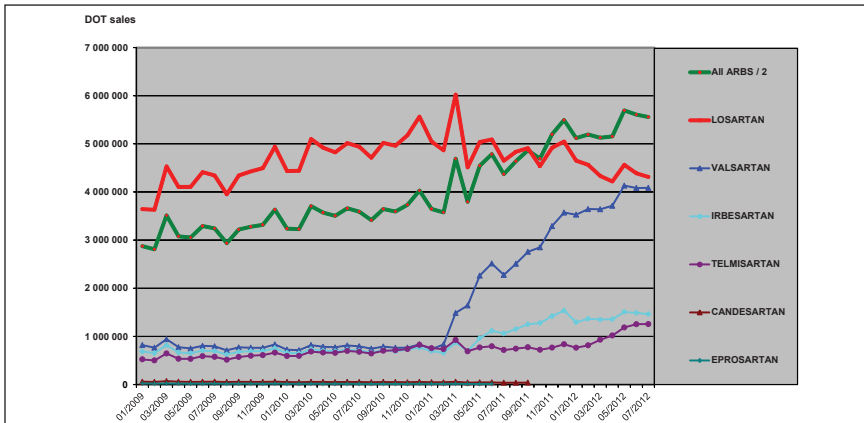
5.3. ANALYSIS OF THE LOSARTAN 100 MG MARKET (JANUARY 2005 TO JULY 2012)

5.3.1. Development of the angiotensin receptor blockers (ARBs) market in Hungary (January 2009 to July 2012)

The main indication of ARBs is the treatment of hypertension, but they are also indicated for stroke risk reduction, to protect the kidneys in patients with type

2 diabetes and for the treatment of heart failure. Losartan became the most-sold sartan (in terms of DOT) after its patent expired. Sales of valsartan also started to grow after the end of its patent protection period (see Fig. 5.11) and its DOT sales reached almost the same performance level as losartan.

Fig. 5.11. DOT sales of various ARBs in Hungary, 2009–2012

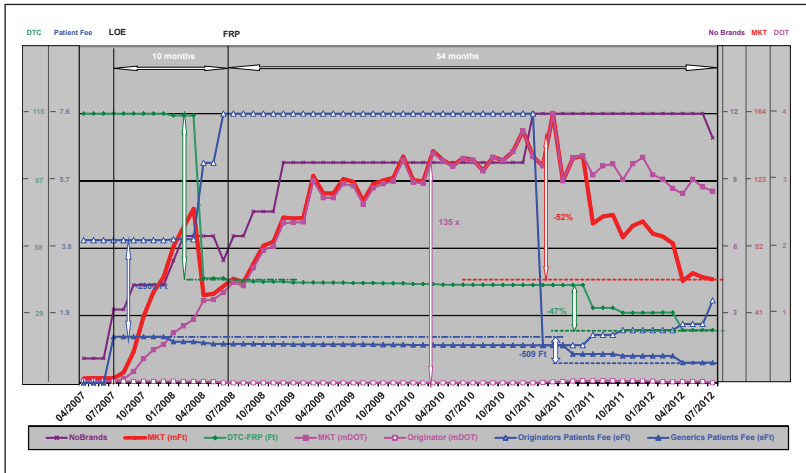


5.3.2. Development of the losartan 100 mg market in Hungary (April 2007 to July 2012)

At the beginning of the period being assessed, losartan was reimbursed by 70%. However, after January 2007 the reimbursement rate was cut to 55%. The originator brand, Cozaar (Merck Sharp & Dohme (MSD)) suffered its LOE in the fourth month of the period under consideration and lost the right to reimbursement in mid 2008 due to its high price compared to the relevant generics. Cozaar (MSD) regained reimbursement status after its price decreased to the same level as the generics in mid 2011. The losartan market was initially small but an extreme increase in sales took place after the market entry of the generics; this resulted in market saturation at a consumption level more than 130 times higher than before patent expiry. The increase in consumption could be mostly due to switching from cheaper off-patent angiotensin-converting enzyme (ACE) inhibitors, and partly to switching from

on-patent ACE inhibitors. As a consequence of the lack of real competition, prices did not change, and the market share (in terms of value and volume (DOT)) grew in parallel between mid 2008 and mid 2011. The sales volume seriously started to decline in parallel with the DTC in October 2011, as a result of the modified reference pricing system (preferential price range) (see Fig. 5.12).

Fig. 5.12. Market development of 100 mg losartan, 2007–2012

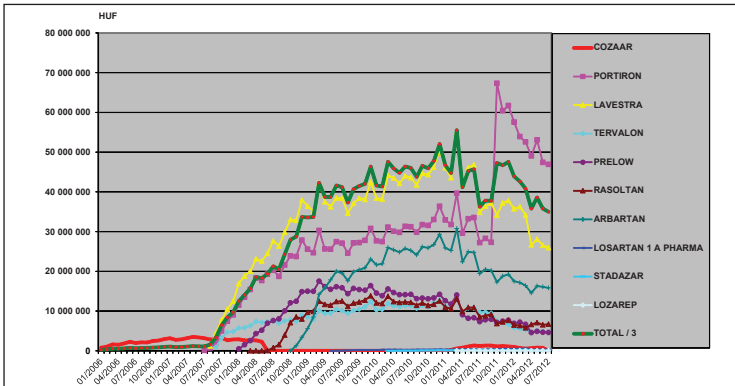


Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF.

5.3.3. Development of market shares on the losartan 100 mg market in Hungary (January 2006 to July 2012)

Generics knocked the originator out of the market within a year. The first products to enter the market – Lavestra (KRKA) and Portiron (Gedeon Richter) – were able to keep their high market share throughout the period analysed. Only one late entry to the market, Arbartan (Teva) approached the sales level of the first two companies (see Fig. 5.13). Since the implementation of the modified reference pricing system (preferential price range) in October 2011, Portiron (Gedeon Richter) has taken over the market leader position from Lavestra (KRKA).

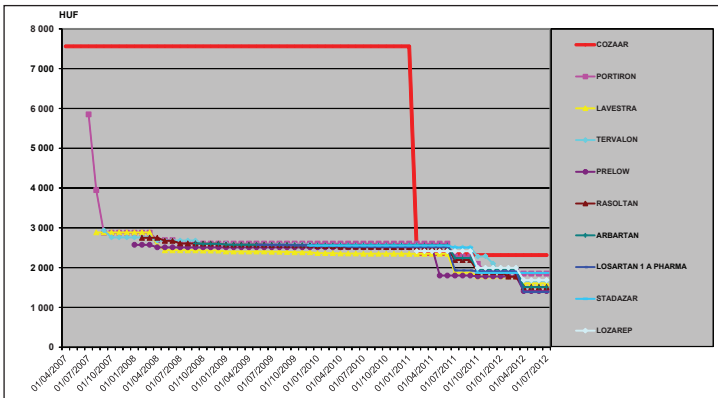
Fig. 5.13. Sales of various losartan 100 mg presentations, 2005–2012



5.3.4. Development of prices on the losartan 100 mg market in Hungary (April 2007 to July 2012)

The reference price was first calculated 10 months after the market entry of the first generic, leading to a 61% price drop. After the first drop in the reference price, it has remained fairly constant until mid 2011 (see Fig. 5.14). In October 2011 and April 2012 there were additional price decreases due to the modified reference pricing system (preferential price range) that was introduced.

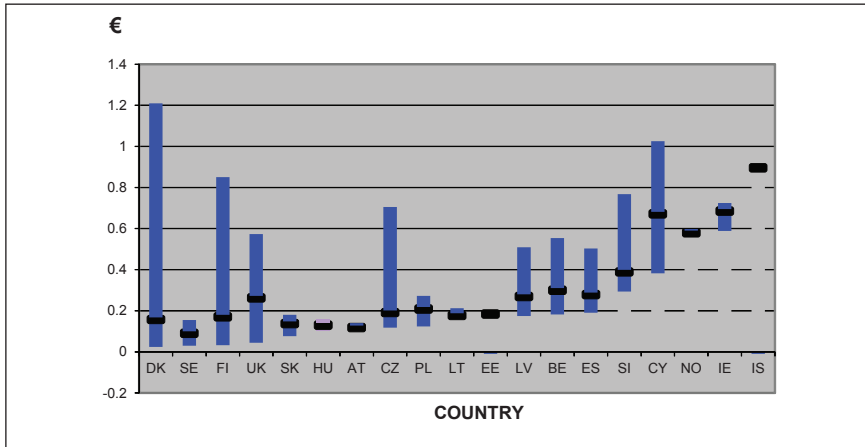
Fig. 5.14. Prices of various losartan 100 mg monthly presentations, 2007–2012



5.3.5. Unit prices of losartan 100 mg – an international perspective, 1 July 2012

By international comparison, the unit prices of losartan 100 mg are lower in Hungary (see Fig. 5.15); however, the lowest prices in Finland, Denmark, Sweden and the United Kingdom are only a fraction of the lowest price in Hungary.

Fig. 5.15. Losartan 100 mg unit prices, international perspective, 1 July 2012



Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

5.3.6. Conclusions on the development of the losartan 100 mg market in Hungary (2005–2012)

The losartan market was small until the entry of generics companies, the promotion activities of which – along with the the low price level compared to valsartan – led to an extreme increase in consumption. Despite the significant drop in unit prices after the first reference price was set (10 months after the

expiry of the patent), the introduction of generics did not lead to cost saving. Presumably most new patients were recruited from among those that were previously treated with ACE inhibitors. Companies with a strong sales force and without any real price competition were able to maintain their market share until mid 2011.

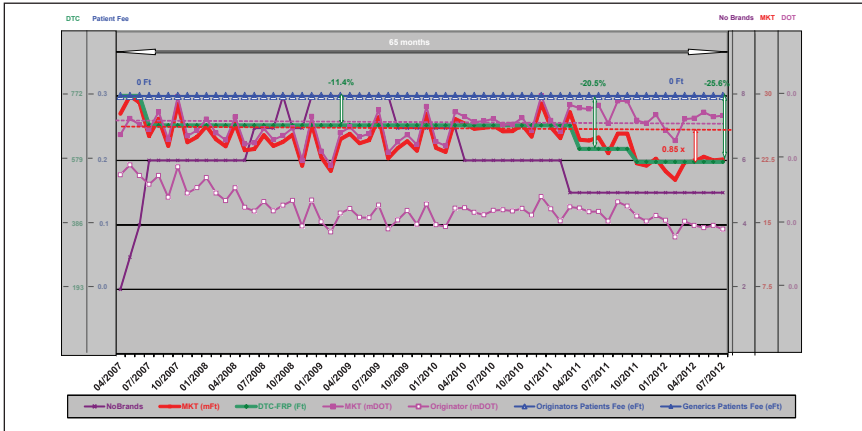
The price level of ARBs began to decline again after the introduction of the modified reference pricing system with the preferential price range in October 2011.

Hungarian prices are rather low in an international comparison; however, it should be mentioned that the lowest unit prices in Finland, Denmark, Sweden and the United Kingdom are well below, as is the case in other large markets (such as that of clopidogrel).

5.4. ANALYSIS OF THE FENTANYL 50 MCG/HOUR MARKET (JANUARY 2005 TO JULY 2012)

5.4.1. Development of the fentanyl 50 mcg/hour market in Hungary (April 2007 to May 2012)

Fentanyl is an opioid analgesic that is indicated for the relief of chronic pain. The dispensing of fentanyl is strictly regulated due to the possibility of abuse. The fentanyl market is medium sized. The originator brand – Durogesic (Johnson&Johnson) – suffered its LOE before the beginning of the period being analysed. Fentanyl is nominally a 100% reimbursed active substance in its most frequently used indication; however, since January 2007, patients have to pay a co-payment of HUF 300 (about €1) for each package. Due to the originator's patient-sensitive pricing strategy (that is, that there is no difference between the originator and generic patient fee), Durogesic (Johnson&Johnson) was able to maintain its relative position on the opioid patch market (see Fig. 5.16).

Fig. 5.16. Market development of 50 mcg/h fentanyl, 2007–2012

Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF

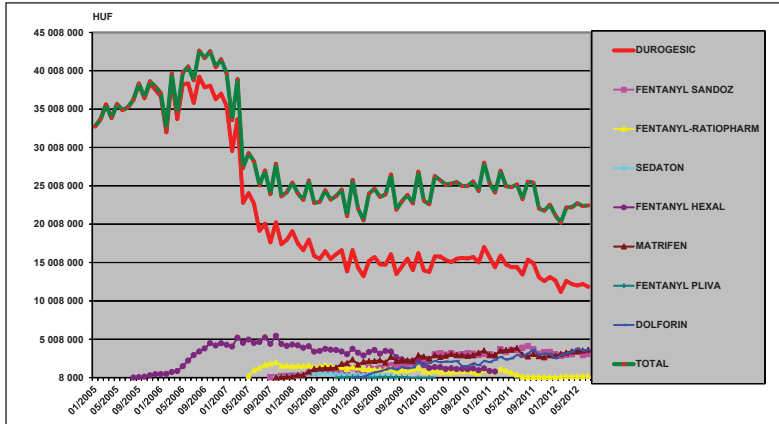
5.4.2. Development of market shares on the fentanyl 50 mcg/hour market in Hungary (January 2005 to May 2012)

Despite the numerous competitors, the originator brand Durogesic (Johnson&Johnson) was able to keep around 60% market share across five years (due to its patient-sensitive pricing strategy) (see Fig. 5.17). The entry of the generics into the market has not had a significant effect on turnover and sales volume, due to the stability of prices and the special nature of the indication of the drug; namely, the fact that opioid pain killers are most used in the final stages of cancer care (for terminal patients). The highest market share among the generics was attained by Sandoz, Gedeon Richter and Nycomed.

5.4.3. Development of prices on the fentanyl 50 mcg/hour market in Hungary (April 2007 to July 2012)

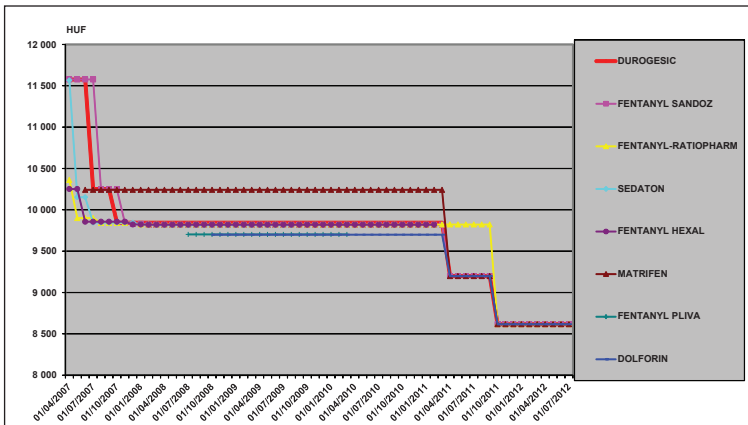
Unit prices dropped dramatically in the latter part of 2007, in line with the end of patent protection; however, a long period followed without any price change

Fig. 5.17. Sales of various fentanyl 50 mcg/h transdermal patches, 2005–2012



(2007–2011). Significant price decreases occurred from the second half of 2011 onwards (see Fig. 5.18), as a consequence of the modified reference pricing system (preferential price range) that was implemented.

Fig. 5.18. Prices of various fentanyl 50 mcg/h transdermal x 5 patches, 2007–2012



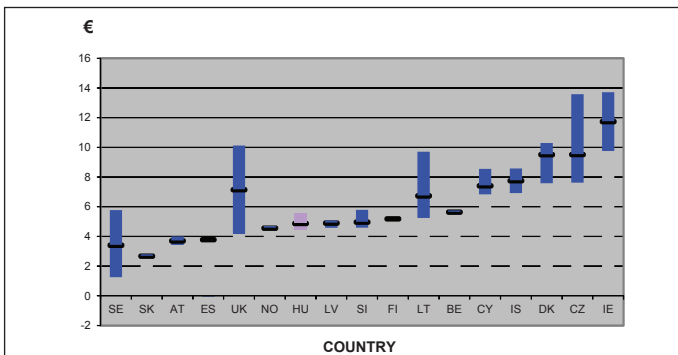
5.4.4. Unit prices of fentanyl 50 mcg/hour – an international perspective, 1 July 2012

Regarding unit prices for fentanyl 50 mcg/hour, Hungary is positioned in the middle of the country basket. The lowest prices (in Sweden) are considerably lower than in Hungary (see Fig. 5.19).

5.4.5. Conclusions on the development of the fentanyl 50 mcg/hour market in Hungary (2005–2012)

The fentanyl market is a closed market, meaning that there are no opportunities to treat patients with alternative drugs. The consumption of fentanyl has remained practically constant from 2005 to 2011.

Fig. 5.19. Fentanyl 50 mcg/hour patch unit prices, international perspective, 1 July 2012



Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

Owing to the particularity of the reference pricing system (no reference price was set for a long time), all products remained at nearly the same price level for a long period and the originator product was able to maintain its dominant position on the market.

As a consequence of the lack of incentives for price competition, only three generic companies were able to achieve significant market shares (presumably with intensive marketing activity).

The price level of fentanyl started to decline again after the introduction of the modified reference pricing system with the preferential price range in October 2011.

The variance in unit prices is lower in the case of fentanyl patches, both domestically as in an international comparison. In terms of unit prices, Hungary is in the middle of the country basket, with the lowest prices (in Sweden) at a considerably lower level than in Hungary.

5.5. ANALYSIS OF THE RISPERIDONE 4 MG MARKET (JANUARY 2005 TO JULY 2012)

5.5.1. Development of the anti-psychotics market in Hungary (January 2009 to July 2012)

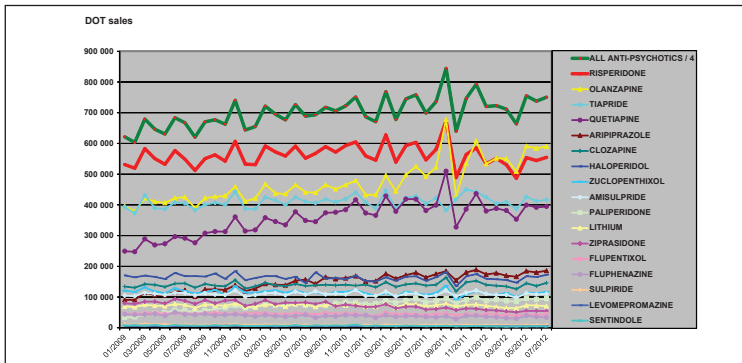
The anti-psychotic market is one of the biggest pharmaceutical market segments in Hungary, in terms of its value. The main indication for anti-psychotic agents is the treatment of serious psychotic disorders, such as schizophrenia or bipolar disorder. Olanzapine became the anti-psychotic molecule with the highest sales volume (in terms of DOT), after the expiry of its patent protection (see Fig. 5.20). The amount of risperidone sold (in terms of DOT) remained almost unchanged in the period analysed.

5.5.2. Development of the risperidone 4 mg market in Hungary (April 2007 to July 2012)

The risperidone market is large and risperidone traditionally received 100% reimbursement. However, since January 2007, patients have to pay a co-payment

(per package) of HUF 300 (about €1). The risperidone market is a good example to demonstrate the originator companies' post-patent switching strategy: the sales volume of 4 mg risperidone dropped dramatically before the patent expired, due to switching patients from the off-patent tablet form to the patent-protected prolonged-release infusion form of the drug. As a consequence of the lack of real competition between the different generic molecules, the prices did not change for a long time (from the beginning of 2008 until the third quarter of 2011) (see Fig. 5.21). The sales volume began to decline dramatically in parallel with the DTC in October 2011, due to the modified reference pricing system (preferential price range) that was introduced.

Fig. 5.20. DOT sales of various anti-psychotics, 2009–2012

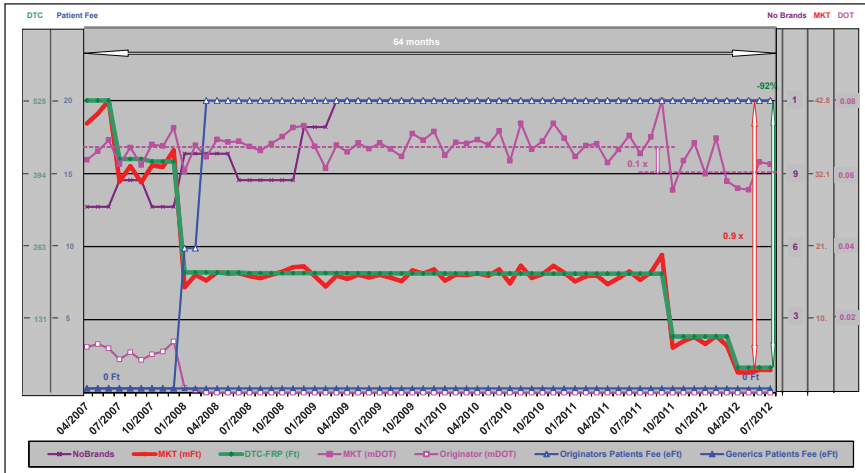


Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF.

5.5.3. Development of market shares on the risperidone 4 mg market in Hungary (January 2005 to May 2012)

After the entry of generics, the originator drug (Risperdal (Johnson&Johnson)) was withdrawn, presumably to avoid having to enter the international system of price referencing. The majority of patients taking risperidone were switched to the parenteral form of risperidone. Three companies took over the majority of the remaining risperidone oral market: Egis, Gedeon Richter and Valeant.

Fig. 5.21. Market development of 4 mg risperidone, 2007–2012



The size of the oral risperidone market decreased in terms of value dramatically after the implementation of the modified reference pricing system with the preferential price range (see Fig. 5.22).

5.5.4. Development of prices on the risperidone 4 mg market in Hungary (April 2007 to July 2012)

The first significant drop in unit prices occurred in April 2007 when (at the same time as the changes to the reference pricing system were introduced) Rispons (Actavis) cut the price of the active substance by 50% with the aim of achieving a dominant position in the market. This calculation by Actavis failed to bear fruit, however, as other companies also cut their prices and the market shares remained more or less similar. The second price cut took place on 1 January 2008 (see Fig. 5.23), knocking the originator product (Risperdal (Johnson&Johnson)) out of the market. Prices remained the same until the introduction of the modified reference pricing system (preferential price range) in October 2011, when Valeant cut the price significantly, similarly aiming to attain a dominant market position (and again, the assumption that this would work proved to be wrong).

Fig. 5.22. Sales of various risperidone 4 mg presentations, 2005–2012

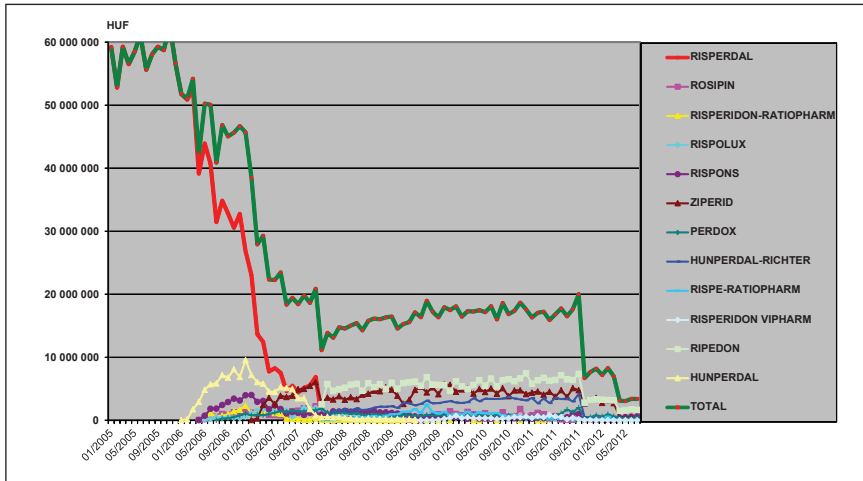
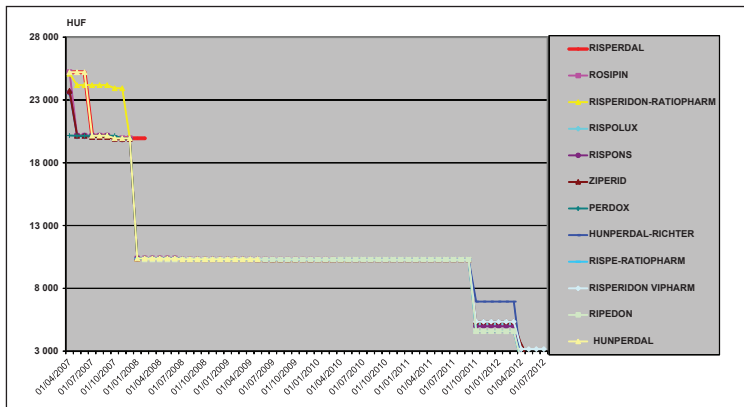
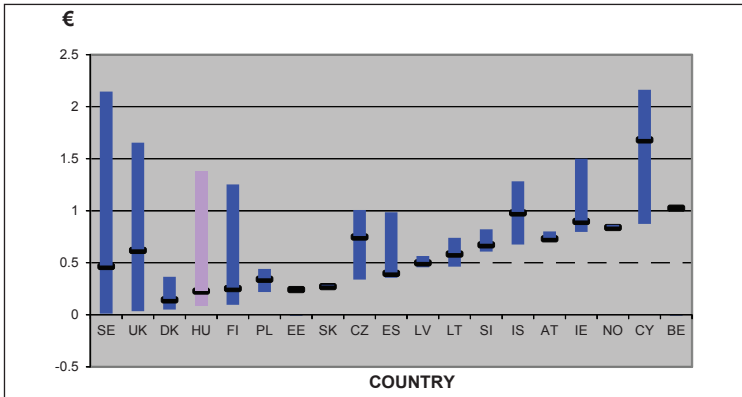


Fig. 5.23. Prices of various risperidone 4 mg monthly presentations, 2007–2012



5.5.5. Unit prices of risperidone 4 mg – an international perspective, 1 July 2012

The price of a risperidone 4 mg tablet in Hungary is among the cheapest in Europe; however, the Swedish price is still significantly lower (see Fig. 5.24).

Fig. 5.24. Risperidone 4 mg tablet unit prices, international perspective, 1 July 2012

Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

5.5.6. Conclusions on the development of the risperidone 4 mg market in Hungary (2005–2012)

The story of risperidone is a striking example of the fact that cutting expenditure after patent expiry does not necessarily result in cost saving: patients can be switched to more expensive products. Companies often try to prolong the life cycle of products with follow-up pharmaceutical forms that are not interchangeable with generics.

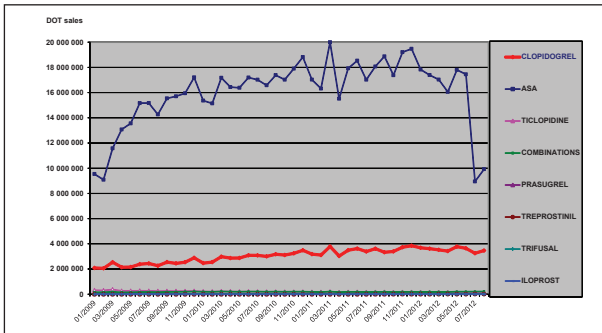
Interface management between hospitals and the outpatient sector is an important issue in terms of containing costs. Savings in hospitals can lead to high costs in the outpatient sector. Anti-psychotics are clear examples of this, as treatment initiated in hospital may need to be continued, once the patient leaves the hospital.

5.6. ANALYSIS OF THE CLOPIDOGREL 75 MG MARKET (JANUARY 2005 TO JULY 2012)

5.6.1. Development of the B01AC molecules market in Hungary (January 2009 to July 2012)

B01AC molecules are indicated for the prevention of various atherothrombotic events. See Fig. 5.25 for the DOT sales analysis.

Fig. 5.25. DOT sales of B01AC molecules, 2009–2012



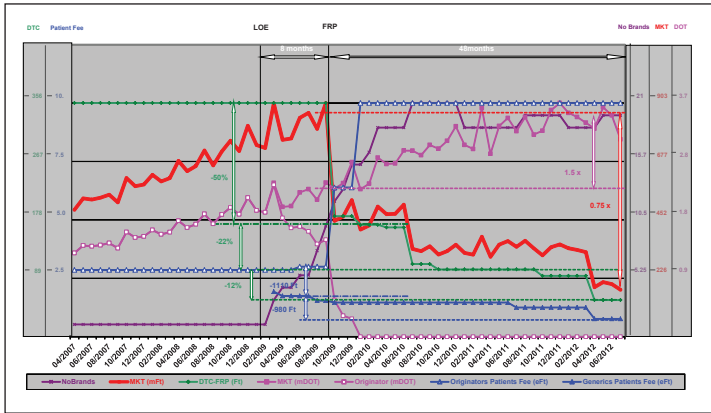
Notes. MKT (mFt): market (million HUF). DTC-FRP (Ft): daily therapeutic cost of fixed reference price (HUF). MKT (mDOT): market (million days of treatment). eFt: thousand HUF

5.6.2. Development of the clopidogrel 75 mg market in Hungary (April 2007 to June 2012)

Clopidogrel was reimbursed by 90% at the time of its launch, but the reimbursement rate dropped to 55% by August 2012. The originator brand – Plavix (Sanofi) – had the most sales by brand in Hungary before the expiry of its patent in March 2009 (see Fig. 5.26). The first time the reference price was set represented a price cut (and subsequently reduced the DOT turnover) by approximately 50%. Other substantial price cuts took place in July 2010 and April 2012. Despite the fact that

the DOT turnover has increased 1.5 times since the patent expiry, the sales value is only approximately 25% of the sales value at the time of patent expiry.

Fig. 5.26. Market development of 75 mg clopidogrel, 2007–2012



5.6.3. Development of market shares on the clopidogrel 75 mg market in Hungary (January 2005 to May 2012)

The originator brand, Plavix (Sanofi) lost its market share within a few months due to the strong price competition (see Fig. 5.27). The clopidogrel market is unusual compared to the other molecules, in terms of the number of players and their concentration: the penetration of the market of each of the huge number of different generic brands is quite similar, and none of the brands has an outstanding market share. As a result of the continuous price competition, the sales value is declining, despite the growing DOT turnover.

5.6.4. Development of prices on the clopidogrel 75 mg market in Hungary (April 2007 to July 2012)

The originator brand, Plavix (Sanofi) lost its market share within a few months, due to the strong price competition (see Fig. 5.28). Unit prices have been falling

since March 2009, although the price of the cheapest product is only about 6% of the originator price.

Fig. 5.27. Sales of various clopidogrel 75 g presentations, 2005–2012

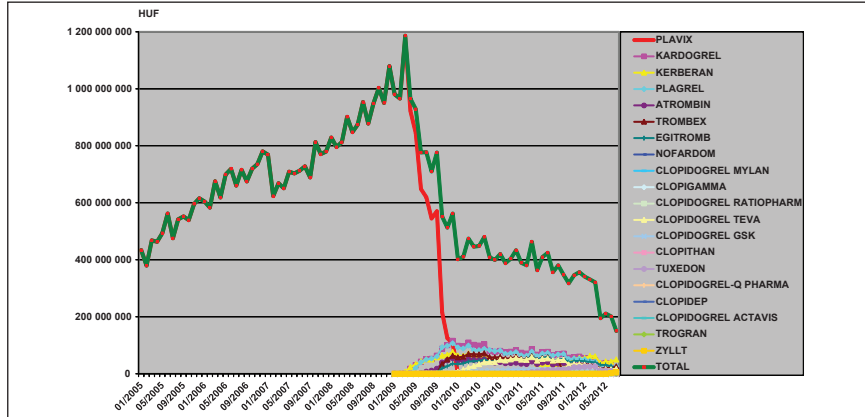
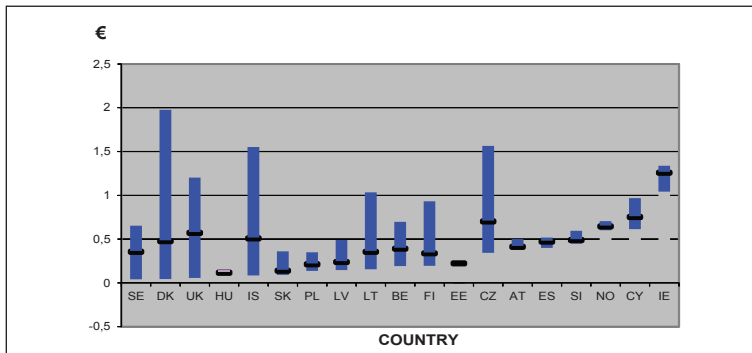


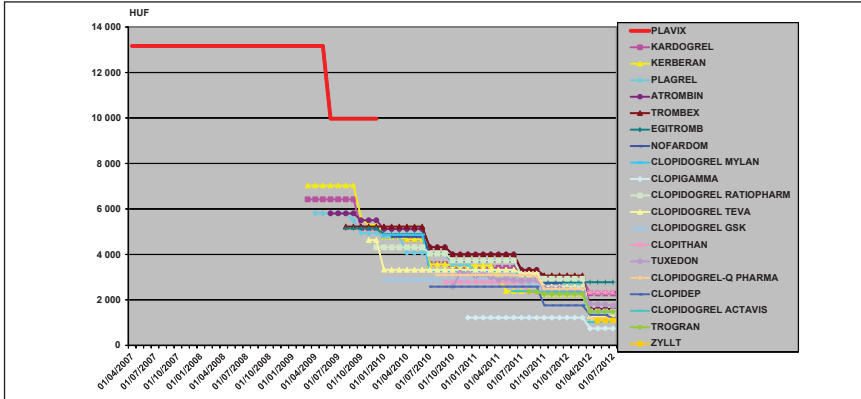
Fig. 5.28. Prices of various clopidogrel 75 mg monthly presentations, 2007–2012



5.6.5. Unit prices of clopidogrel 75 mg – an international perspective, 1 July 2012

The price of 75 mg clopidogrel tablets in Hungary are among lowest in Europe, and the variance in price is one of the lowest in Europe (see Fig. 5.29).

Fig. 5.29. Clopidogrel 75 mg tablet unit prices, international perspective, 1 July 2012



Notes. The dark line indicates the simple arithmetical average of the reimbursable products in the country. The country codes refer to the ISO 3166-1 Alpha-2 country codes (ISO, 2013).

Source: European Integrated Price Information Database (EURIPID) (accessible only to European health care authorities) – data collated in 2012.

5.6.6. Conclusions on the development of the clopidogrel 75 mg market in Hungary (2005–2012)

Clopidogrel seems to be one of the best functioning generics markets. Sales dropped rapidly after the first reference price was set, although significant price decreases also took place later. The number of competitors is high, and the concentration on the market is low.

One reason for the strong competition might be that the drug may only be prescribed by specialists, and generics companies do not specifically target their sales activity towards specialists.

There was a significant delay (eight months), however, between the entry of generics into the market and setting the first reference price.

Hungarian unit prices for clopidogrel are among the lowest in Europe, with a very low variance.

Several companies have lowered their clopidogrel prices by small increments since the patent expiry, but no individual company has been able to achieve a substantial market share. The market remains fragmented.

REFERENCES

- Baumgärtel C (2012a). Generic clopidogrel – the medicines agency’s perspective. *GaBI Journal*, 2(1):89–91.
- Baumgärtel C (2012b). Myths questions, facts about generic drugs in the EU. *GaBI Journal*, 1(1):34–38.
- EMA (2008). *Guideline on the investigation of bioequivalence*. London, European Medicines Agency Committee for Medicinal Products for Human Use (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003011.pdf, accessed 18 June 2013)
- European Commission (2009). *Communication from the Commission. Executive summary of the pharmaceutical sector inquiry report* (COM(2009) 351 final). Brussels, European Commission (http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf, accessed 28 May 2013).
- European Commission (2012). Pharmaceuticals sector inquiry [web site]. Brussels, European Commission (<http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>, accessed 28 May 2013).
- European Parliament, European Council (2001). Council Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use. *Official Journal of the European Communities*, L31:67–128 (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:311:0067:0128:en:PDF>, accessed 28 May 2013).
- Gaál P et al. (2011). Hungary: health system review. *Health Systems in Transition*, 13(5):1–266.

- Himmel W et al. (2005). What do primary care patients think about generic drugs? *International Journal of Clinical Pharmacology and Therapeutics*, 43(10):472–479.
- Hungarian Ministry of Health, Social and Family Affairs (2004). 32/2004. (IV. 26.) ESzCsM rendelet a törzskönyvezett gyógyszerek és a különleges táplálkozási igényt kielégítő tápszerek társadalombiztosítási támogatásba való befogadásának szempontjairól és a befogadás vagy a támogatás megváltoztatásáról [Decree 32/2004 (IV. 26.) of the Minister of Health, Social and Family Affairs on the criteria of the inclusion of registered medicines and special nutritional formulae into social health insurance financing and on the modification of the inclusion decision or the extent of the subsidy]. *Hungarian Gazette*, 56:5594–5626.
- Hungarian Ministry of Health, Social and Family Affairs (2005). 52/2005 (XI. 18.) *EüM rendelet az emberi alkalmazásra kerülő gyógyszerek forgalomba hozataláról* [Decree 52/2005 (XI. 18.) of the Minister of Health on the marketing of medicines for human use]. Budapest, Complex Kiadó Ltd.
- Hungarian Ministry of Health, Social and Family Affairs (2007a). 5/2007. (I. 24.) *EüM rendelet a társadalombiztosítási támogatással rendelhető gyógyszerek kereskedelmi áráséről* [Decree 5/2007 (I. 24) of the Minister of Health on the margins of reimbursed pharmaceuticals]. Budapest, Complex Kiadó Ltd.
- Hungarian Ministry of Health, Social and Family Affairs (2007b). 53/2007. (XII. 7.) *EüM rendelet a gyógyszerrendeléshez használt számítógépes program minősítésének szabályairól* [Decree 53/2007 (XXI. 7) of the Minister of Health on the regulations of software to be used for prescribing medicines]. Budapest, Complex Kiadó Ltd.
- Hungarian Parliament (2006). 2006. évi XCVIII. törvény a biztonságos és gazdaságos gyógyszer- és gyógyászati segédeszköz ellátás, valamint

a gyógyszerforgalmazás általános szabályairól [Act XCVIII of 2006 on safety and efficient supply of pharmaceuticals and medical devices as well as on the general rules of pharmaceuticals distribution]. *Hungarian Gazette*, No. 146, 29 November 2006.

ISO (2013). Country codes – ISO 3166 [web site]. Geneva, International Organization for Standardization (http://www.iso.org/iso/home/standards/country_codes.htm, accessed 3 December 2013).

Kesselheim A et al. (2008). Clinical equivalence of generic and brand-name drugs used in cardiovascular disease – a systematic review and meta-analysis. *JAMA*, 300:2514–2526.

Kesselheim A et al. (2010). Seizure outcomes following the use of generic vs brand-name antiepileptic drugs. A systematic review and meta-analysis. *Drugs*, 70(5):605–621.

Kjoenniksen I, Lindbaek M, Granas AG (2006). Patients' attitude towards and experiences of generic drug substitution in Norway. *Pharmacy World & Science*, 28(5):284–289.

Kobayashi E et al. (2011). Patients' attitudes towards generic drug substitution in Japan. *Health Policy*, 99:60–65.

McPake B, Normand C (2008). *Health economics – an international perspective. 2nd edition*. London, Routledge.

Mrozek M, Mossialos E (2004). Regulating pharmaceutical prices in the European Union. In: Mossialos E, Mrazek M, Walley T, eds. *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*. Maidenhead, Open University Press: 114–129 (http://www.euro.who.int/__data/assets/pdf_file/0008/98432/E83015.pdf, accessed 4 June 2013).

- Németh G et al. (2009). Hatékonyabbá tehetők-e a generikus gyógyszerpiacok? [Could generic markets be made more efficient?] *IME*, 8(4):12–14 (http://www.imeonline.hu/article/925/12_14.pdf, accessed 14 March 2013).
- OECD (2012). OECD health data 2012 [online database]. Paris, Organisation for Economic Co-operation and Development (<http://www.oecd.org/els/health-systems/oecdhealthdata2012-frequentlyrequesteddata.htm>, accessed 4 June 2013).
- OEP (2013). Országos Egészségbiztosítási Pénztár [National Health Insurance Fund Administration] [web site]. Budapest, Országos Egészségbiztosítási Pénztár (http://www.oep.hu/portal/page?_pageid=34,1&_dad=portal&_chema=PORTAL, accessed 23 August 2013).
- Quintal C, Mendes P (2012). Underuse of generic medicines in Portugal: an empirical study on the perceptions and attitudes of patients and pharmacists. *Health Policy*, 104:61–68.
- Simoens S (2012). A review of generic medicine pricing in Europe. *GaBI Journal*, 1(1):8–12.

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

Member States

Albania
Andorra
Armenia
Austria
Azerbaijan
Belarus
Belgium
Bosnia and Herzegovina
Bulgaria
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Georgia
Germany
Greece
Hungary
Iceland
Ireland
Israel
Italy
Kazakhstan
Kyrgyzstan
Latvia
Lithuania
Luxembourg
Malta
Monaco
Montenegro
Netherlands
Norway
Poland
Portugal
Republic of Moldova
Romania
Russian Federation
San Marino
Serbia
Slovakia
Slovenia
Spain
Sweden
Switzerland
Tajikistan
The former Yugoslav
Republic of Macedonia
Turkey
Turkmenistan
Ukraine
United Kingdom
Uzbekistan



SEMMEWEIS UNIVERSITY
HEALTH SERVICES
MANAGEMENT
TRAINING CENTRE