European Commission

Study of the policy mix for the reimbursement of medicinal products

Proposal for a best practice-based approach based on stakeholder assessment

Written by Gesundheit Österreich Forschungs- und Planungs GmbH *and* SOGETI

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SOGETI

Health and Consumers

Study of the policy mix for the reimbursement of medicinal products

Proposal for a best practice-based approach based on stakeholder assessment

(In short: Study of the policy mix for the reimbursement of medicines)

Final Report

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List of abbreviations

AED	Access with Evidence Development
AIM	Association Internationale de la Mutualité / International Association of Mutual Benefit Societies
AT	Austria
ATC	Anatomical Therapeutic Chemical Classification System
BE	Belgium
BEUC	European Consumer's Organisation
BG	Bulgaria
CAPR	Competent Authorities for Pricing and Reimbursement of Pharmaceuticals
CED	Coverage with Evidence Development
CHAFEA	Consumers, Health and Food Executive Agency
CPME	Comité Permanent des Médecins Européens / Standing Committee of European Doctors
CTC	Conditional Treatment Continuation
CY	Cyprus
CZ	Czech Republic
DE	Germany
DG	Directorate General
DG ENTR	Directorate General for Enterprise and Industry
DG SANCO	Directorate General for Health and Consumers
DK	Denmark
EAHC	Executive Agency for Health and Consumers
EASP	Escuela Andaluza de Salud Pública / Andalusian School of Public Health
EC	European Commission
EE	Estonia
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EGA	European Generic Medicines Agency
EL	Greece
ELECTRE	ELimination Et Choix Traduisant la REalité / ELimination and Choice Expressing REality
EPF	European Patients' Forum
EPR	External Price Referencing
ES	Spain
ESIP	European Social Insurance Platform
EU	European Union
EUnetHTA	European Network for Health Technology Assessment

EUROPABIO	The European Association for Bio-industries
FI	Finland
GDP	Gross Domestic Product
GÖ FP	Gesundheit Österreich Forschungs- und Planungsgesellschaft mbH
GÖG	Gesundheit Österreich GmbH / Austrian Health Institute
HR	Croatia
HTA	Health Technology Assessment
HU	Hungary
IE	Ireland
INN	International Non-Proprietary Name
IP	Intellectual Property
IT	Italy
LT	Lithuania
LV	Latvia
MCDA	Multi-Criteria Decision Analysis
MEDEV	The Medicine Evaluation Committee
MS	Member State(s)
MT	Malta
n	Number
n.a.	not available
NCE	Number of new Chemical Entities
NICE	National Institute for Health and Care Excellence
NL	Netherlands
OECD	Organization for Economic Co-operation and Development
PAS	Patient Access Scheme
PGEU	Pharmaceutical Group of the European Union
PHIS	Pharmaceutical Health Information System
PL	Poland
PPRI	Pharmaceutical Pricing and Reimbursement Information
PT	Portugal
R&D	Research and Development
RO	Romania
SE	Sweden
SHA	System of Health Accounts
SI	Slovenia
SK	Slovakia
SMEs	Small and Medium Sized Enterprises
UK	United Kingdom
US	United States

USA	United States of America
VAT	Value Added Tax
VBP	Value-Based Pricing
WHO	World Health Organization

Executive Summary

Background

EU Member States have been struggling to address the challenge of reconciling different, partially conflicting health and non-health policy objectives related to the reimbursement of medicines: timely patient access and equity, cost-containment and sustainable funding, and granting reward for innovation to the pharmaceutical industry. In the European Union, there is, as the High Level Pharmaceutical Forum welcomed, the development of a shared understanding that pricing and reimbursement policies need to balance these objectives.

The pharmaceutical sector comprises several different stakeholder groups with different roles and responsibilities. As a result, they are likely to assess the importance of the various policy objectives differently. Major stakeholders in this area are competent authorities responsible for pricing and reimbursement and public payers, pharmaceutical industry (research-oriented as well as generic industry), patients and consumers, and health professionals such as doctors and pharmacists.

The responsibility for pharmaceutical pricing and reimbursement lies, in principle, with the EU Member States under the condition that they comply with overall EU legislation such as the Transparency Directive. All EU Member States have developed their national pharmaceutical pricing and reimbursement policy framework in order to achieve the defined policy objectives. There are common reimbursement practices which are applied in several EU Member States, but since most of these policies can be designed differently, each country implements the policies in its own way.

Reimbursement policies can be targeted at specific product groups (differentiation per therapeutic value, patent status and existence of competitor medicines). Recent practices and arrangements, such as value-based pricing or managed-entry agreements, are primarily relevant for new, typically high-cost, medicines, whereas reference price systems and demand-side measures, such as generic substitution and International Non-Proprietary Name (INN) prescribing, are typical measures targeted at off-patent medicines.

Given the trade-offs between policy objectives and possible differences in the assessment of policy objectives and measures by the stakeholders, the challenge remains of how to develop the most appropriate policy mix to meet the different goals and expectations.

Aim of the study

The objective of this study was to investigate which policy mix related to the reimbursement of medicines the consulted stakeholders would consider as ideal and, based on their assessments investigated in a Multi-Criteria Decision Analysis (MCDA), to develop a proposal for the best practice-based approach for such a policy mix, by reconciling the different – often conflicting – policy objectives.

Specific objectives of this study were:

1. To identify relevant policy practices related to the reimbursement of medicines in European countries (EU Member States and the EEA countries);
2. To develop a list of policy objectives and a catalogue of reimbursement policy measures, classified per product group, to be assessed in a stakeholder consultation;
3. To perform a European-wide stakeholder consultation in this catalogue of reimbursement policy measures;
4. To analyse and discuss the results of the stakeholder consultation via the MCDA method in order to address potential trade-offs between identified policy measures; and
5. To draw conclusions for a proposal of a reimbursement policy mix considered by the stakeholders as the best practice.

Methodology

This study was performed by a consortium of SOGETI Luxembourg S.A. and Gesundheit Österreich Forschungs- und Planungsgesellschaft mbH (GÖ FP), together with the Andalusian School of Public Health (EASP) as sub-contractor, following the Request for Specific Services N°EAHC/2012/Health/18 (for the implementation of Framework Contract N°EAHC/2010/Health/01 Lot) launched by the Executive Agency for Health and Consumers (EAHC, called Consumers, Health and Food Executive Agency, CHAFEA since January 2014) in autumn 2012. The study started in February 2013, and it ended in January 2014 after a planned duration of 12 months.

Literature review

A systematic literature review was performed in order to identify and gather evidence of relevant policy measures related to pharmaceutical reimbursement in the European countries. The search was conducted in several databases (e.g. MedLine, Embase, Econlit, OECD Publications, Cochrane Effective Practice and Organisation of Care Group, WHO, etc.) to retrieve publications (in all EU languages) on reimbursement policies in all EU Member States (including Croatia) and the European Economic Area (EEA) countries (Iceland, Lichtenstein, Norway) published between 1995 and February 2013. Additionally, grey literature was searched via GoogleScholar, a hand search of selected bibliographies and a PPRI (Pharmaceutical Pricing and Reimbursement Information) network query with competent authorities for pharmaceutical pricing and reimbursement. Exclusion criteria were non-coverage in geographic terms and non-coverage related to the time period under investigation, policy measures strictly linked to pharmaceutical pricing (e.g. distribution margins, VAT rate), policies not addressing medicines (e.g. medical devices), research of purely theoretical character, and law texts. The search addressed both the out-patient and the in-patient sectors. The literature review was designed as a bibliometric review.

List of policy objectives and policy measures

Based on expert knowledge as well as on information from the literature review and from EU processes such as the High Level Pharmaceutical Forum, a long list of policy objectives (assessment criteria) and reimbursement policy measures was established. The policy measures were categorized in terms of: 1) type of product (four groups depending on the patent status and availability of competitor medicines); 2) the setting in which they tend to be used (out-patient/in-patient sector); 3) the stakeholders they usually target; 4) whether, or not, they are classified as supply-side measures or demand-side measures.

For the stakeholder consultation, the broader lists were reduced to short lists of seven policy objectives and 16 policy measures. Inclusion criteria included the frequency of being mentioned in literature and relevant policy documents, the clarity and comprehensiveness of the definition and, related to the measures, the frequency of their implementation in practice and some considerations to keep a balance between different categorisations (e.g. demand-side/supply-side measures) to which the medicines were classified to.

The seven policy objectives selected were: timely access to medicines; equitable access to medicines; reward for innovation; cost-containment / control of pharmaceutical expenditure/budget; long-term sustainability (for the health care system); promotion of a more rational use of medicines; and increased competition.

The short list of reimbursement practices to be assessed by the stakeholders included 16 policy measures (listed in alphabetical order): co-payment; differential pricing; discounts / rebates / price negotiations / clawback; external price referencing; generic substitution; INN prescribing; managed-entry agreements; pharmaceutical budgets; pharmaco-economic evaluation; positive list; reference price systems; reimbursement process; reimbursement rates; reimbursement review; tendering; and value-based pricing.

The short lists of policy objectives and measures were agreed upon with the EAHC/European Commission.

Stakeholder survey

An online questionnaire, using the survey tool QuestBack®, was performed with eight stakeholder groups in the 28 EU Member States. The targeted stakeholders were: 1) consumers; 2) patients (in the analysis, a combined group of 'consumers and patients' was created); 3) competent authorities for pharmaceutical pricing and reimbursement; 4) public payers (combined group of 'authorities and payers' in the analysis); 5) generic medicines industry; 6) research-based pharmaceutical industry (including biotech companies) (combined group of 'industry'); 7) doctors; 8) pharmacists (combined group of 'healthcare professionals'). The survey addressed the out-patient sector only.

Relevant stakeholders were asked to comment which preference they attribute to the seven listed policy objectives, and to assess whether the 16 policy measures were able to contribute to the achievement of each of the policy goals.

The questionnaire was piloted with two representatives of each stakeholder group in August 2013. Based on the lessons learned from the pilot, the online questionnaire was revised and rolled out on 26 September 2013. The online survey was performed till the end of October 2013, with two extensions of the deadline in-between.

Multi-Criteria Decision Analysis

A Multi-Criteria Decision Analysis (MCDA) methodology was applied to weight the set of policy objectives (assessment criteria) and to score identified reimbursement policy measures. The algorithm ELECTRE III, an outranking method, was chosen as the most appropriate method, since it allows for the concept of weak preferences and thus reflects real world decision-processes better compared to other outranking methods.

Since the ELECTRE algorithm compares parameters with a broad range of input-values, its results are highly sensitive to changes. Thus, large sensitivity analyses were performed to test the stability of the selected methodology. These analyses confirmed the robustness of the methodology.

Results

Literature review

A total of 244 publications were selected to be analysed in the bibliometric literature review after two selection processes.

In terms of policy objectives, 39% of the total of included publications did not state any underlying policy objectives, whereas 11% mentioned more than one policy goal. The most frequently mentioned policy goal (26% of the included publications) was sustainable funding and/or cost-containment. Studies relating to equitable access to medicines and reward for innovation were much less frequent (4% respectively in both cases).

The top five reimbursement policies most frequently mentioned were: co-payment, reimbursement rates, reference price systems, positive lists and the reimbursement process. More than every second publication addressed either HTA or pharmaco-economics. Generic substitution, reimbursement reviews, tendering and INN prescribing were mentioned in 35%-22% of all included publications. 9% of all included publications referred to managed-entry agreements, and around 7% mentioned value-based pricing. Reimbursement policies mentioned in low frequency were auction-like systems, profit control or delisting from positive lists.

Stakeholder survey

Answers to the stakeholder survey came primarily from associations which represented the selected stakeholder groups at national level and, in three cases, from EU-wide level. We had a preliminary response rate of 41% (109 responses from a total of 266 contacted institutions), with the group of competent authorities for pricing and reimbursement and generic medicines industry having the highest response rates (around 60%). However, some respondents could not completely answer the questionnaire due to missing capacity, and a few incomplete questionnaires had to be excluded from the analysis. In total, 81 filled questionnaires (adjusted response rate of around 30%) were included in the analysis.

In terms of stakeholder representativeness, most of the fully completed questionnaires were submitted by the pharmaceutical industry (38%; thereof 24% of research-based industry and 14% of generic medicines industry), followed by authorities and payers (33%; thereof 22% of competent authorities and 14% of public payers) and pharmacists (15%). In geographical terms, most of the completed questionnaires were received from Austria (n=7), followed by Belgium, Bulgaria, Portugal and Slovenia (n=5 for each of these countries).

Multi-Criteria Decision Analysis

All seven selected policy objectives were considered important by the participating stakeholders; they all indicated weights above the value of 30 (on a scale of 0 to 50 expressing the level of preference). Overall, the policy objective of 'equitable access to medicines' was given the highest priority, followed by 'long-term sustainability' and 'timely access to medicines'. Lower weights were attributed to 'reward for innovation' and 'increased competition'. The two policy objectives of 'equitable access to medicines', which relates to fair and affordable access for all population groups, including vulnerable people, in a given society or country, and 'long-term sustainability' were given high priority by all stakeholder groups, whereas differences among stakeholders were related to the other goals: 'reward for innovation' was of high priority for pharmaceutical industry but less so for consumers/patients and authorities/payers; 'timely access to medicines' was a priority for consumers/patients and industry but to a lesser extent for health professionals and authorities/payers; 'cost-containment' was the policy objective to which authorities/payers gave particular priority; 'promotion of a more rational use of medicines' was important for industry, health professionals and authorities/payers, but less relevant for consumers/patients. Within the group of pharmaceutical industry, the research-based pharmaceutical industry gave high priority to 'equitable access', 'timely access' and 'reward for innovation', whereas 'increased competition', 'timely' and 'equitable access' and 'promotion of a more rational use' were highly ranked policy objectives for the generic medicines industry. No substantial differences could be observed between the EU Member States of different economic wealth. Still, 'cost-containment' and 'increased competition' appear to be given higher priority in those EU Member States with comparably lower income.

Overall, stakeholders assessed 'pharmaco-economic evaluation' as the most appropriate reimbursement policy to achieve the selected policy objectives. 'Value based pricing' and 'reimbursement process' were ranked second and third respectively, followed by 'managed-entry agreements'. Four measures ('reimbursement review', 'positive list', 'reimbursement rates', 'generic substitution') were all ranked fifth. The 'reference price systems' and 'pharmaceutical budgets' were ranked sixth, followed by 'differential pricing' and 'INN prescribing' (both ranked seventh). 'Co-payment' and 'discounts / rebates / price negotiations / clawback' (both ranked eighth), 'tendering' (ninth) and 'external price referencing' (tenth) were considered to have the comparably lowest ability to achieve the different policy objectives.

An analysis per stakeholder group shows a common pattern for specific measures: for instance, pharmaco-economic evaluation and also generic substitution tend to be the preferred policy measures, whereas discounts / rebates / price negotiations / clawback and, particularly, external price referencing are given low priority by most stakeholder groups. High priority is given to generic policies such as generic substitution, INN prescribing and reference price systems by the generic medicines industry, but also by public payers and pharmacists, whereas research-based industry preferred measures particularly targeted at new medicines such as value-based pricing and managed-entry agreements (adding to the high preferences for the pharmaco-economic evaluation and reimbursement process). Within the combined groups of stakeholders, differences were not only visible between research-based industry and generic medicines industry but also between consumers and patients. Interestingly, the patients assessed some measures differently than the other stakeholders, for instance, they expressed comparably higher preference for discounts / rebates / price negotiations / clawback and external price referencing, whereas the reimbursement process and value based pricing were ranked last by them.

'Pharmaco-economic evaluation' and 'value-based pricing' were assessed as particularly appropriate for the policy goals of reward for innovation and promotion of a more rational use of medicines. A reimbursement process appropriately designed was seen as a key policy measure to ensure timely, and also equitable, access to medicines. Managed-entry agreements were considered as supportive to the goals of timely access to medicines and reward for innovation. Generic substitution was given the highest priority when it came to the policy objectives of equitable access to medicines, cost-containment/control of pharmaceutical expenditure/budget, long term sustainability and increased competition.

A weighted analysis (i.e. every stakeholder group has the same influence on the outcome of the ranking, regardless of their quantitative participation in the stakeholder survey) among the four stakeholder groups did not show major differences compared to the overall ranking. This suggests the robustness of the chosen methodology which was also confirmed by a large number of sensitivity analyses. Within the sensitivity analyses it could be proven that using fewer criteria leads to a lack of information regarding all stakeholders' preferences as each criterion reflects a different policy focus. Accordingly, the multi-criteria approach showed the need for a consensus-finding decision-making process. Taking all criteria and therefore

all stakeholders' preference structures into account, three clusters of policy measures were identified (high, middle, low rank clusters). The policy measures in the high rank cluster reflect those measures being most suitable for all stakeholder groups. Among the limitations of the survey was the low number of representatives in some stakeholder groups (particularly doctors, but also patients and consumers). The low response rate is attributable to the fact that the questionnaire was considered too complex – both in terms of the chosen MCDA method (which required stakeholders to openly express their preferences and indicate a preference threshold) as well in terms of the reimbursement practices, several of which addressed the ex-factory price level and were not considered as relevant by some of the stakeholders.

Conclusions

The survey made it clear that specific reimbursement practices are, across all stakeholder groups, considered of high relevance, whereas a few policies are given low priority by the majority of all the respondents.

Any policy mix proposed would need to be aligned with the policy objectives which all relevant stakeholders consider of high priority: these are particularly equitable access to medicines, long-term sustainability and timely access to medicines. Still, other objectives, including those highlighted by the High Level Pharmaceutical Forum, i.e. cost-containment and reward for innovation, were also given preference and should therefore also be taken into account when designing a policy mix.

Overall, highly ranked measures are those which are rather targeted at new medicines. Two of the top 3 measures concern processes and supportive tools rather than specific policy measures: Most stakeholder groups ranked pharmaco-economic evaluations first or second. Across all stakeholder groups (except for patients), a reimbursement process with clear rules, a transparent process, documented and reproducible decisions taken in reasonable time, which will allow the in-depth consideration of sound evidence, is considered key.

According to the stakeholders' assessment, the best practice-based approach for a reimbursement policy mix should include both measures related to new medicines, including high-cost medicines, as well as generic medicines, though the policy options for new medicines were ranked higher. Value-based pricing, in a stricter understanding of joint pricing and reimbursement processes, was considered as a policy option to be explored further. Related to generic policies, stakeholders seem to have different preferences for the various policies to promote generics uptake. Of the three generic policies listed in the survey, generic substitution was definitively assessed better than reference price systems and INN prescribing.

A policy mix which the stakeholders consider as 'ideal' is not likely to include high co-payments, arrangements such as discounts, rebates, price negotiations or clawback, tendering applied in the out-patient sector, and external price referencing.

Since we do not know the reasons for the stakeholders' preferences (not scope of this study), this would need to be further explored.

Policy recommendations

- The design of the best practice-based mix of reimbursement policies is likely to require a different approach depending on the policy goals which a country aims to give highest priority to.
- A policy mix considered as 'ideal' should take into account the different approaches to the different groups of medicines (particularly the two groups of new, high-cost medicines and generics).
- Sound evidence, gained through pharmaco-economic evaluations, for instance, appears to be a major prerequisite in policy decisions. Ways on how to further develop and implement pharmaco-economics should be explored.
- Good processes, characterized by very clear rules, transparency, consideration of sound evidence, documentation and reproducible decisions taken in reasonable time, seem to be another major element in pharmaceutical reimbursement. Investment in improving reimbursement processes should be made.
- Reviews are another key element whose implementation should be further explored as part of an 'ideal' policy mix.
- Stakeholders should be asked to explore the confidentiality issues which might negatively impact defined policy goals.
- In order to achieve equitable access to medicines, a highly prioritized policy objective among all stakeholders, reimbursement policy measures should be designed in a way to avoid financial burden for the patients.

1 Introduction

1.1 Objectives

EU Member States have been struggling to address the challenge of reconciling different, partially conflicting policy objectives related to the reimbursement of medicines: patient access and equity, cost-containment and sustainable funding, and granting reward for innovation to the pharmaceutical industry. Processes such as the High Level Pharmaceutical Forum (2005 to 2008) and the Platform on Access to Medicines in Europe under the Process on Corporate Responsibility in the field of Pharmaceuticals (2010 to 2013), led by the European Commission and involving Member States and stakeholders, and the 'Reflection process - Towards modern, responsive and sustainable health systems' of the sub-group on 'Cost-effective use of medicines', led by the Netherlands, should support the Member States in implementing policies to address this challenge.

The general objective of this study was to explore which policy mix related to the reimbursement (funding) of medicines the consulted stakeholders consider as ideal and, based on their assessments investigated in a Multi-Criteria Decision Analysis (MCDA), to develop a proposal for the best practice-based approach for such a policy mix (reconciling the different – often conflictive – policy objectives).

Specific objectives of this study were:

1. To identify relevant policy practices related to the reimbursement of medicines in European countries (specific objective 1);
2. To develop a list of policy objectives and a catalogue of reimbursement policy measures, classified per product group, to be assessed in a stakeholder consultation (specific objective 2);
3. To perform a European-wide stakeholder consultation in this catalogue of reimbursement policy measures (specific objective 3);
4. To analyse and discuss the results of the stakeholder consultation via the MCDA method in order to address potential trade-offs between identified policy measures (specific objective 4); and
5. To draw conclusions for a proposal of a reimbursement policy mix considered by the stakeholders as the best practice (specific objective 5).

1.2 Activities and deliverables

This study was performed by a consortium of SOGETI Luxembourg S.A. and Gesundheit Österreich Forschungs- und Planungsgesellschaft mbH (GÖ FP), together with the Andalusian School of Public Health (EASP) as sub-contractor, following the Request for Specific Services N°EAHC/2012/Health/18 (for the implementation of Framework Contract N°EAHC/2010/Health/01 Lot) launched by the Executive Agency

for Health and Consumers (EAHC, called Consumers, Health and Food Executive Agency, CHAFEA since January 2014[1]) in autumn 2012.

The specific objectives of the study were addressed in different work packages (see Table 1.1).

Table 1.1: Introduction – Overview of the Work Packages according to study objectives and activities

Objective	Work Package	Activities
1	WP 1: Literature review	To identify relevant policy practices related to the reimbursement of medicines in European countries (EU Member States and EEA countries)
2	WP 2: Development of a catalogue of policy measures and assessment criteria	To list policy objectives (assessment criteria) and reimbursement policy measures, to classify them per product group and select those policy objectives and policy measures to be consulted in the stakeholder survey
3	WP 3: Stakeholder survey	To explore stakeholder preferences (weights) concerning reimbursement policies on medicines in line with the selected policy objectives (assessment criteria)
4	WP 4: Multi-Criteria Decision Analysis (MCDA)	To collate all preferences of stakeholders regarding reimbursement policy measures according to the defined assessment criteria and thus obtain information about the policies preferred by different stakeholders
5	WP 5: Set of policy recommendations	To propose a reimbursement policy mix considered by the stakeholders as the best practice in accordance with the assessment criteria

The study started in February 2013 and had a planned duration of 12 months. In July 2013, an interim report presented the results of the literature review (objective 1), the proposal for selected policy objectives and a catalogue of reimbursement policy measures (objective 2) and the methodology for the stakeholder consultation and the Multi-Criteria Decision Analysis (MCDA) (objectives 3 and 4).

Following the interim report, the methodology for the MCDA was refined, and the stakeholder consultation was prepared and piloted in August 2013. From the end of September 2013 till end of October 2013, stakeholders were consulted. Their assessments were analysed and collated in November/ December2013 and filled into the MCDA algorithm. Results and conclusions were presented in a draft final report submitted to the EAHC/European Commission in December 2013. Considering the feedback on the draft final report, this final report was produced in January 2014.

[1] In this report, which relates to activities predominantly performed in 2013, we refer to the previous name EAHC.

1.3 Outline of this report

This report is split into four content chapters which follow, to a great extent, the defined work packages. However, some in-depth results already presented in earlier documents (e.g. the literature review in the Interim Report) are not described in this report.

Chapter 2 – Background and context: In this chapter, we explore the rationale for this study and draw a comprehensive picture of reimbursement practices related to medicines in the European countries, also based on the literature review undertaken.

Chapter 3 – Methodology: The methodology chapter presents, in different sub-sections: the list of policy objectives (assessment criteria) for which the stakeholders will be asked to express their preferences; the catalogue of reimbursement measures to be commented on in the stakeholder survey; the design of the stakeholder consultation, including the selection of stakeholder groups, representativeness and the survey tool; the chosen MCDA methods, including sensitivity analyses.

Chapter 4 – Results and analyses: In this chapter, we present the results of the stakeholder survey and analyse the stakeholders' preferences for policy objectives and policy measures in total and per sub-groups (e.g. per stakeholder group). We also discuss trade-offs and limitations.

Chapter 5 – Conclusions: In the concluding chapter, we propose a reimbursement policy mix which stakeholders consider as the best practice, and we discuss next steps for research and practice.

The report is accompanied by an Executive Summary, a reference section and annexes.

2 Background

2.1 Context

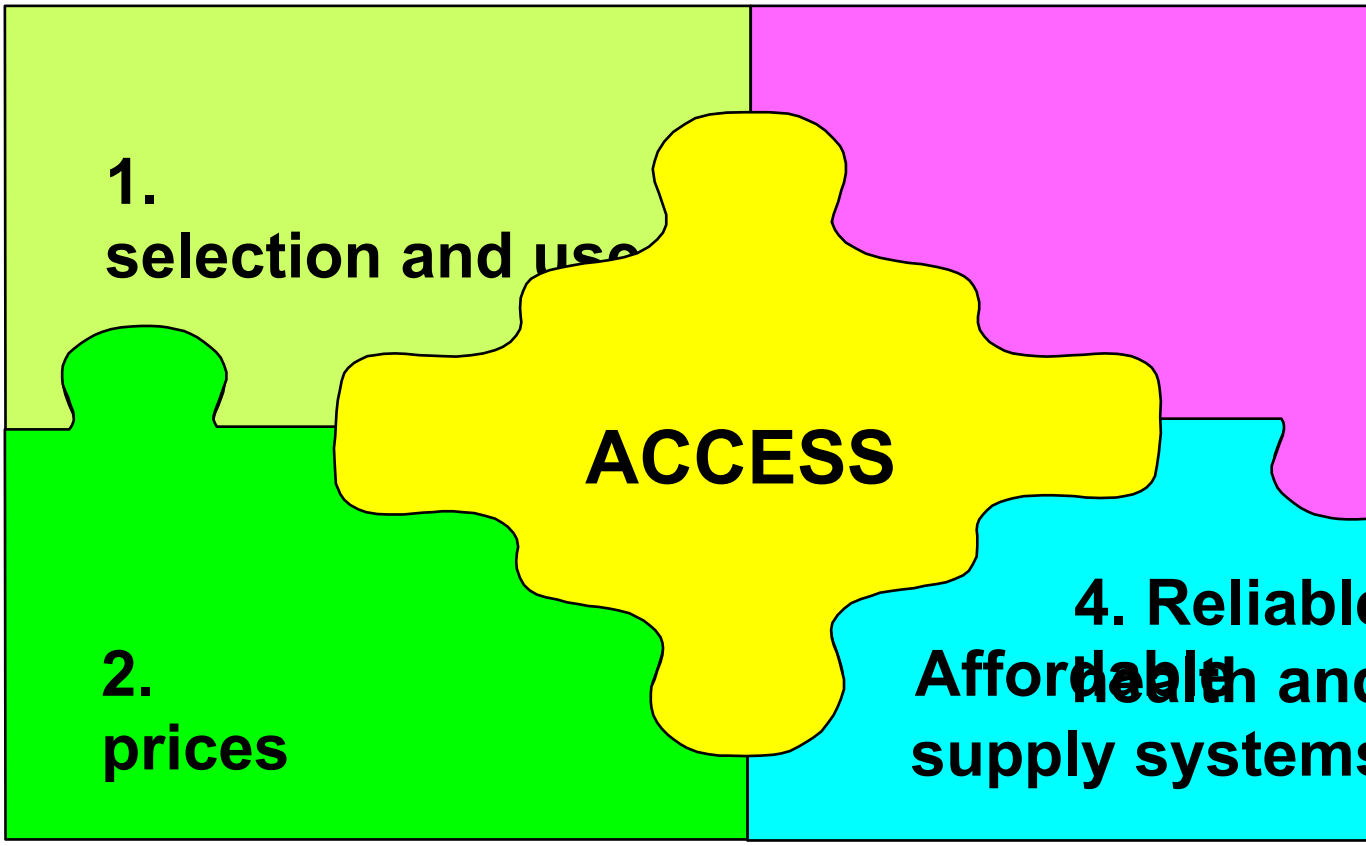
A national pharmaceutical policy is needed: to present a formal record of values, aspirations, aims, decisions and medium- to long-term government commitments; to define the national goals and objectives for the pharmaceutical sector; to set priorities; to identify the strategies needed to meet those objectives, and identify the various actors who are responsible for implementing the main components of the policy [1]. That is the case for countries all over the world though the focus of the policy goals may differ. Low-income countries are likely to struggle to assure the quality of the medicines. Medium-income countries, with emerging pharmaceutical markets and aiming at extending health coverage, require securing access to medicines for basic public health programmes for the poor, who represent the majority of the population, at the same time considering the demands of a wealthier urban population. High-income countries such as the European Union (EU) Member States aim to ensure access to all important treatments and support for innovation through the research and development of new medicines and treatments [2]. Given the economic pressure resulting from the global financial crisis, ageing populations and the expectations of medical progress, cost-containment measures and a focus on encouraging a more rational use of medicines have been of key importance for European policy makers in recent times [3].

The major requirements which a national pharmaceutical policy is expected to meet are: 1) a regulatory framework which should ensure good quality of medicines from production throughout the supply chain; 2) mechanisms to provide an equitable access to medicines to the population, particularly to vulnerable groups; 3) strategies which support financial sustainability of the system in order to be able to meet the previously mentioned aims [4,5].

More than 35 years ago, the World Health Organization (WHO) developed the concept of 'essential medicines' which are defined as medicines that satisfy the priority health-care needs of the population. They should be selected with due regard to disease prevalence, evidence on efficacy, safety and comparative cost-effectiveness. Essential medicines are intended to be available at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford [6]. Countries are encouraged to develop their national essential medicines list. WHO has established and updated the 'WHO essential medicines list' but this list merely aims to serve as a model; it is the responsibility of the Member States to specify which medicines are essential according to the country-specific characteristics and needs [7]. In order to achieve access to essential medicines, WHO proposed a framework for coordinated action consisting of four elements (see also Figure 2.1): 1) rational selection and use of medicines (e.g. reimbursement lists based on treatment guidelines, regularly updated guidelines based on best evidence, trainings); 2) affordable prices (e.g. price information, generic policies); 3) sustainable financing (e.g. increase in public funding, increase in health insurance coverage, better use of out-of pocket payments); 4) reliable health

and supply systems (e.g. integrate medicines in health sector development, assure medicines' quality, promote rational use) [8].

Figure 2.1: Ensuring access to essential medicines – WHO framework for collective action



Source:[8]

Though the 'essential medicines' concept is considered by some people as a model for poor countries only, it has, in fact, its relevance for high-income countries as well [9]. Even if the reimbursement lists in European countries are not called 'essential medicines list', they are based on the idea of prioritizing and selecting best 'value for money' medicines which will be then covered by public funds.

While a European regulatory framework regarding quality assurance of medicines (e.g. marketing authorisation, pharmacovigilance, falsified medicines) has been developed, the decisions on the pricing and reimbursement of medicines remain the competence of the EU Member States under the condition that EU provisions (e.g. the Transparency Directive [10]) are respected. It is thus up to the Member States to define the most appropriate mix of pricing and reimbursement strategies at national level.

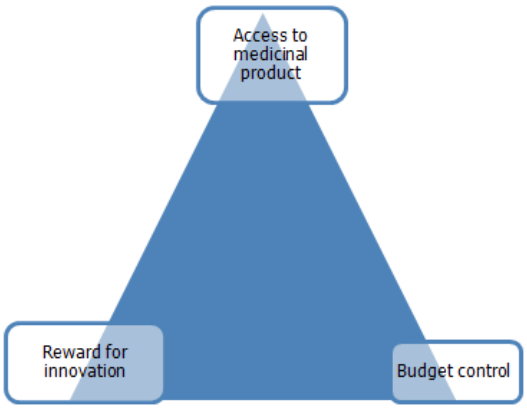
2.2 Policy goals in European countries

The above-mentioned policy goals, as discussed in the previous section 2.1, are public health objectives. In addition, goals from other policy areas might come into play. In the field of medicines, particularly industry policy goals are also of relevance: they aim to promote research and development (R&D) and innovation and to provide an attractive environment for the pharmaceutical industry. These industry goals need to be reconciled with the public health goals which are, in some cases, in conflict with cost-containment measures because of their ability to disincentivize the pharmaceutical industry [11]. This trade-off between 'static efficiency', in which consumer welfare is maximised by getting the most health value from expenditure spent, and 'dynamic efficiency', in which the R&D incentives serve to generate growth in the capacity to prevent conditions and cure diseases in the future, is considered as probably the most difficult one, which seems system-inherent [12].

In the European Union, three, partially conflicting, policy goals are considered as core values which need to be balanced when Member States implement pharmaceutical pricing and reimbursement policies. These are '(1) timely and equitable access to pharmaceuticals for patients all in the EU, (2) control of pharmaceutical expenditure for Member States, and (3) reward for valuable innovation within a competitive and dynamic market that also encourages Research & Development' [13] (cf. Figure 2.2). This was stated in the Final Conclusions and Recommendations of the High Level Pharmaceutical Forum, a major EU process running from 2005 till 2008 (cf. section 2.3). It should be noted that for several countries, particularly those strongly hit by the global financial crisis, cost-containment is a necessity, and this strongly conflicts the 'real' public health goals.

The first goal of timely and equitable access includes several components: 1) regulatory procedures which incentivize bringing medicines to the market without unreasonable delay (this might be conflicting with the need for in-depth and time-intensive HTA reports and pharmaco-economic evaluations to assess the value of the medicine as the basis for an informed decision); 2) incentives and disincentives for pharmaceutical companies to launch medicines on some national markets, and at specific sequences (e.g. manufacturers may decide to launch medicines later in low-price countries so as not to negatively impact the price in other countries applying external price referencing [14,15]); 3) fair access (e.g. the reimbursement scheme ensures the affordability of, at least essential, medicines, and provides particular safeguard mechanisms for vulnerable groups 4); the regulation of medicine prices throughout the supply chain (distribution margins, taxes, duties); 5) the actual continuous availability of the medicines on the market (to avoid or at least successfully manage medicine shortages); 6) gaps in availability on small markets. Some of these elements will be addressed in further detail in section 2.7.

Figure 2.2: Policy objectives defined in the European Pharmaceutical Forum process



Source: [13]

Another policy goal in this field would be to ensure competition in the pharmaceutical sector, wherever appropriate (e.g. on the generics market or elsewhere where competitor medicines exist). In the Pharmaceutical Sector Inquiry published by DG Competition [16], concerns were raised about barriers which might delay the market entry of generic medicines. This is likely to be detrimental to both patients and payers.

A literature review of the reimbursement policy measures related to medicines, which was performed in the course of this study (details are provided in section 2.6), showed that in the literature on EU Member States and EEA (European Economic Area) countries, which was published between 1995 and February 2013, the policy goals were not always mentioned: 39 percent of all 244 included studies did not state the underlying policy goals. The most frequently mentioned policy goal (in 26% of the included publications) was sustainable funding and/or cost-containment. Publications which referred to the policy goal of cost-containment/sustainable funding usually addressed a wide range of policies: among those, the reference price system was mentioned most frequently. Tendering and managed-entry agreements, which were less frequently mentioned in the total of included publications, were found quite frequently in publications on cost-containment. Studies on equitable access to medicines were much less frequent (in four percent of the 244 included publications), and they were usually related to the design of co-payments, solely or in combination with further measures such as reimbursement rates and reimbursement measures. Reward for innovation was addressed in only four percent of the included publications, which primarily related to innovative medicines; these studies tended to mention HTA and pharmaco-economic evaluations. A low number of publications (less than four percent) addressed other policy goals. Within this small group, a more rational use of medicines was highlighted as a policy goal; relevant publications often addressed demand-side policies (i.e. those targeted at physicians, patients, pharmacists). 11 percent of the total of included publications mentioned more than one policy goal.

2.3 EU Processes

In order to address some of the above mentioned policy goals and the inherent trade-off between them, the European Commission launched several processes, targeted particularly at policy makers in pharmaceutical pricing and reimbursement.

In response to the 'Pammolli report' [17] in 2000, which had raised concerns about the competitiveness of the European pharmaceutical industry lagging behind the US, the 'G-10 Medicines Group' was established, consisting of ten selected Member States and stakeholder representatives. Their final report published in 2002 [18] recommended that Member States should examine the scope for improving the time taken between the granting of a marketing authorisation and pricing and reimbursement decisions, and should explore ways of increasing generic penetration of individual markets, including generic prescribing and dispensing.

In July 2003, the European Commission adopted the 'A stronger European-based pharmaceutical industry for the benefit of the patient – a call for action' Communication which outlines the Commission's proposals for advancing the G10 recommendations. A key pharmaceutical pricing and reimbursement action proposed was to 'provide a forum for member states to generate and share information on common relative effectiveness issues in the context of pricing and reimbursement decisions' [19].

To follow up on these recommendations, the High Level Pharmaceutical Forum was set up in 2005 as a three-year process. It involved EU institutions, all EU Member States, industry, health care professionals, patients and insurance funds represented in the three Working Groups which were focused on three main topics: information to patients on diseases and treatment options, pricing and reimbursement policies, and relative effectiveness.

In the Working Group on Pricing and Reimbursement, guiding principles and ideas were discussed which aimed to help Member States balance the conflicting policy objectives, through the implementation of national pricing and reimbursement practices [20]. In the so-called 'tool box' exercise, for six selected practices (internal reference pricing, cost sharing, payback, prescription information, price control, generic substitution), expertise from Member States and stakeholders and evidence of the literature were collected in order to offer a view on what each practice brings for each of the three policy goals which need to be balanced [21]. Further topics were discussed: the Working Group addressed burning issues such as the challenge of how to ensure availability to medicines in small national markets in Europe [22], how to improve access to orphan medicines for all affected EU citizens and how to recognise, assess and reward valuable innovative medicines [23]. They aimed at clarifying how some EU Member States use assessments of innovative medicines in their pricing and reimbursement decisions [24] and started work on collecting evidence about practices of risk-sharing schemes and conditional reimbursement (managed-entry agreements) in the Member States [25].

Several of these topics were followed up in one of the projects of the Platform on Access to Medicines in Europe under the Process on Corporate Responsibility in the field of pharmaceuticals. This process was launched in 2010 as a voluntary multi-stakeholder process which aimed to find non-regulatory solutions to several of the new challenges. The Platform on Access to Medicines in Europe was one of three working areas and consisted of six projects:

- Mechanism of coordinated access to orphan medicinal products: developing a concept of a coordinated access to orphan medicines based on the set-up of programmes between companies and groups of competent authorities and results of the ongoing project on a mechanism for clinical added value on orphan medicines.

- Capacity building of managed-entry agreements for innovative medicines: to clarify the various approaches to managed-entry agreements (also referred to as risk-sharing, outcome-based or performance-based agreements) ensuring access to innovative medicines.

- Facilitating supply in small countries: to clarify the specific non-regulatory bottlenecks for the access of medicines on small markets to all concerned parties with a view to defining possible specific approaches to pricing and reimbursement of medicines in these countries.

- Promoting good governance of non-prescription medicines: to identify the necessary elements to ensure informed and adequate uptake of medicines after a change of their classification from being subject to medical prescription to not being subject to medical prescription.

- Market access for biosimilars: to define the necessary conditions within the pharmaceutical environment to ensure informed and adequate uptake of biosimilars.

- Prioritisation: in order to ensure that the European Commission, Member States and relevant stakeholders are closely associated with the revision of the Priority Medicines Report 2013, the European Commission set up the 'Prioritisation' working group under the umbrella of the Process on Corporate Responsibility in the Field of Pharmaceuticals.

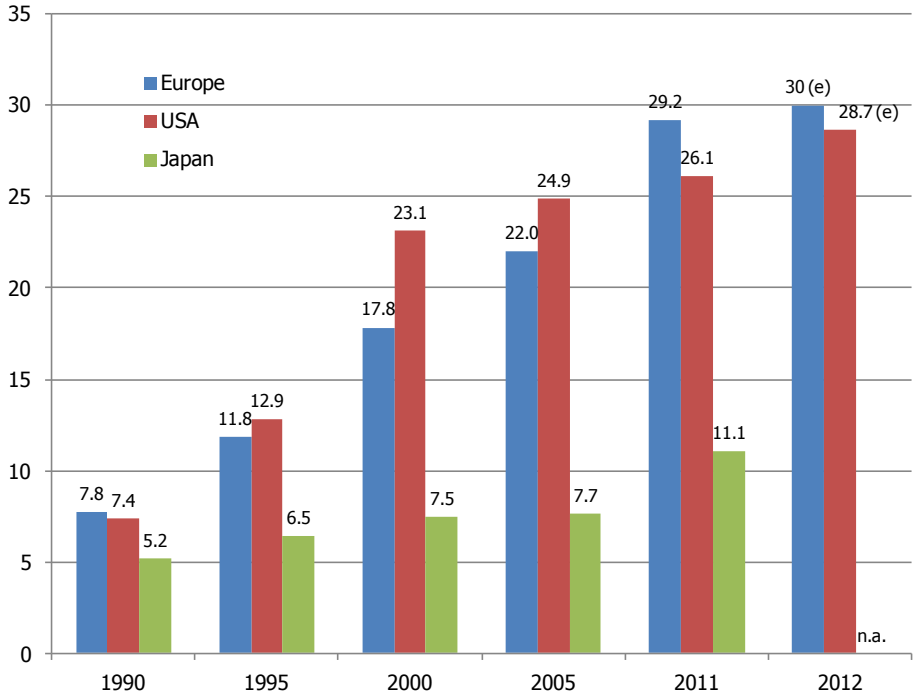
The outcomes of the first five working groups of Platform on Access to Medicines in Europe were published after endorsement by the Steering Group in April 2003 [26]. In July 2013, the Priority Medicines Report [27] was published.

Furthermore, as part of the 'Reflection process - Towards modern, responsive and sustainable health systems', a sub-group on Cost-effective use of medicines was established led by the Netherlands; work on five defined objectives is on-going, including the one on 'cost effective use of medicines' [28]. The present study is related to this cost-effective use of medicines sub-group.

2.4 Business and economic framework

In 2012, Europe's research-oriented industry accounted for a total production of € 210 billion (leaders were Switzerland, Germany, Italy, UK, Ireland and France), corresponding to a pharmaceutical market value of € 163 billion (at ex-factory prices) and a total employment of 700,000 people (estimated data [29]). In 2012, industry invested € 30 billion in research & development (R&D) in Europe, which was higher than the investment in the USA and it shows an overall increasing trend [29] (see Figure 2.3).

Figure 2.3: Pharmaceutical R&D expenditure in Europe, USA and Japan (in billion Euro), 1990-2012



(e) = Estimate, n.a. = not available

Source: Illustration by authors, based on figures produced by EFPIA [29]

From the late 1990-ties on, there has been a debate about the competitiveness of Europe's pharmaceutical industry compared with that of the US model. The 'Pammolli report` 2000, which led to the establishment of the 'G-10 Medicines Group' (cf. section 2.3), expressed concern that the European industry has been losing competitiveness as compared to the US industry: 'As a whole, Europe is lagging behind in its ability to generate, organise, and sustain innovation processes' [17]. The authors of the 'Pamolli report' analyzed the development of prices and market shares in the European countries and concluded that national European markets were not competitive enough, particularly in some countries where prices and market shares were found not to vary substantially after patent expiry [17]. In a more recent analysis by Pammolli and colleagues, based on the information from R&D projects related to more than 28,000 compounds investigated since 1990, a decline of R&D productivity in medicines in the past two decades was observed. At the same time,

when the researchers investigated the potential variations in productivity with regard to the regional location of companies, they found that, despite the differences in the composition of the R&D portfolios of companies based in the USA and Europe, there was no evidence of any productivity gap between Europe and the USA [30].

Globally, the number of new chemical entities (NCE) brought to the market saw a dramatic rise in mid-1980-ties but it steadily declined from 1997 till 2003. From 2003 till 2006, it was stable at about 30 launches annually [12]. The downward trend in the new millennium was observed in several key launch countries [31]. In 2011, 35 new medicines were launched [32].

Europe is the second largest global market for pharmaceutical sales, with a share of 26.7% in 2012 (compared to 41.0% in the USA) [29]. 18% of the sales of new medicines launched during the 2007-2011 period were on the European market (compared with 62% on the US market) [29].

Overall, the European region (as defined by WHO), with a share of 13.8% of the world population, accounts for 34.1% of total pharmaceutical expenditure, ranking second after the Americas region (North, Central and Latin America, 41.5% of total pharmaceutical expenditure, data as of 2005/2006) [33].

Total pharmaceutical expenditure, which has been increasing since the 1990-ties, however, at lower growth rates in the new millennium, has recently seen a decrease in some European countries (cf. Table 2.1) The decline usually occurred in those countries which were hit by the global financial crisis and had to implement austerity measures (see section 2.7).

Table 2.1: Total and public pharmaceutical expenditure in European countries, 1990, 1995, 2000, 2005-2011

	Total pharmaceutical expenditure in the out-patient sector (in billion Euro)										Public pharmaceutical expenditure (in billion Euro)										Total pharmaceutical expenditure as % share of current health expenditure										Public pharmaceutical expenditure as % share of current health expenditure									
	1990	1995	2000	2005	2006	2007	2008	2009	2010	2011	1990	1995	2000	2005	2006	2007	2008	2009	2010	2011	1990	1995	2000	2005	2006	2007	2008	2009	2010	2011	1990	1995	2000	2005	2006	2007	2008	2009	2010	2011
Austria	1.1	1.5	2.5	3.3	3.4	3.7	3.9	3.7	3.7	3.8	0.6	0.9	1.7	2.2	2.3	2.5	2.7	2.5	2.5	2.6	10%	10%	10%	13%	14%	14%	14%	13%	12%	12%	6%	6%	7%	9%	9%	9%	9%	9%	8%	8%
Belgium	1.9	2.9	n.a.	5.1	5.1	5.3	5.7	5.9	6.1	6.0	0.9	1.2	n.a.	2.8	2.8	3.0	3.4	3.6	3.7	3.9	16%	18%	n.a.	17%	17%	17%	17%	16%	16%	16%	7%	8%	n.a.	9%	9%	9%	10%	10%	10%	10%
Bulgaria	n.a.	n.a.	n.a.	0.6	0.7	0.7	0.8	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.1	0.1	0.1	0.2	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	34%	37%	35%	35%	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	8%	8%	7%	6%	n.a.	n.a.
Cyprus	n.a.	n.a.	n.a.	0.2	0.2	0.2	0.2	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.04	0.04	0.05	0.1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	22%	21%	21%	22%	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	5%	5%	5%	5%	n.a.	n.a.
Czech Republic	0.2	0.7	0.9	1.8	1.8	1.8	2.1	2.2	2.2	2.3	0.2	0.6	0.7	1.4	1.3	1.2	1.3	1.5	1.4	1.5	24%	28%	25%	26%	23%	22%	21%	20%	20%	20%	22%	24%	19%	19%	17%	15%	13%	14%	13%	13%
Denmark	0.7	1.0	1.3	1.7	1.8	1.9	1.9	1.9	1.9	1.8	0.2	0.5	0.7	0.9	1.0	1.1	1.0	1.0	1.0	0.9	8%	9%	9%	9%	9%	9%	8%	8%	8%	7%	3%	5%	5%	5%	5%	5%	5%	4%	4%	3%
Estonia	n.a.	n.a.	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	n.a.	n.a.	0.03	0.1	0.1	0.1	0.1	0.1	0.1	0.1	n.a.	n.a.	2.3%	2.4%	2.4%	2.2%	2.2%	2.4%	2.2%	2.2%	n.a.	n.a.	1.0%	1.1%	1.0%	0.9%	0.9%	1.0%	1.1%	1.1%
Finland	0.7	1.0	1.5	2.1	2.0	2.1	2.3	2.2	2.2	2.3	0.3	0.5	0.7	1.1	1.1	1.1	1.2	1.2	1.2	1.3	10%	14%	16%	17%	15%	16%	16%	15%	15%	14%	5%	6%	7%	9%	8%	8%	8%	8%	8%	8%
France	14.6	18.5	23.9	31.7	32.6	33.9	34.7	35.4	35.9	36.2	9.0	11.7	16.0	22.2	22.6	23.6	23.4	24.0	24.3	24.6	17%	15%	17%	17%	17%	17%	17%	17%	16%	16%	11%	10%	11%	12%	12%	12%	11%	11%	11%	11%
Germany	15.4	23.9	28.8	36.1	36.3	38.2	39.7	41.5	42.4	41.4	11.3	17.0	20.9	26.6	27.0	29.0	30.4	32.1	32.4	31.3	15%	13%	14%	16%	15%	16%	16%	15%	15%	15%	11%	9%	10%	12%	11%	12%	12%	12%	12%	11%
Greece	0.4	1.2	2.0	4.0	4.6	5.4	n.a.	6.6	6.0	5.4	0.2	0.9	1.3	2.9	3.5	4.3	n.a.	5.2	4.6	4.0	15%	16%	20%	22%	24%	26%	n.a.	28%	29%	29%	8%	12%	12%	16%	18%	20%	n.a.	23%	22%	21%
Hungary	0.0	0.4	n.a.	2.3	2.3	2.3	2.5	2.3	2.6	2.6	n.a.	0.3	0.6	1.4	1.4	1.2	1.2	1.1	1.2	1.3	n.a.	27%	n.a.	31%	32%	32%	32%	33%	34%	34%	n.a.	18%	18%	19%	20%	16%	16%	16%	17%	17%
Ireland	0.3	0.4	0.9	2.0	2.3	2.5	2.7	2.7	2.6	2.5	0.2	0.3	0.6	1.4	1.7	1.8	2.1	2.0	2.0	1.9	13%	12%	15%	17%	18%	18%	18%	17%	19%	18%	8%	8%	10%	12%	13%	13%	13%	13%	14%	14%
Italy	11.0	13.7	20.5	25.0	25.9	25.3	25.4	25.0	24.7	23.6	6.6	5.5	9.4	12.8	13.3	12.5	12.3	12.3	12.0	11.0	21%	21%	23%	21%	21%	20%	19%	18%	18%	17%	13%	8%	10%	11%	11%	10%	9%	9%	9%	8%
Latvia	n.a.	n.a.	n.a.	0.2	0.2	0.3	0.3	0.3	n.a.	n.a.	n.a.	n.a.	n.a.	0.1	0.1	0.1	0.1	0.1	n.a.	n.a.	n.a.	n.a.	n.a.	23%	23%	27%	21%	24%	n.a.	n.a.	n.a.	n.a.	n.a.	7%	8%	7%	8%	9%	n.a.	n.a.
Lithuania	n.a.	n.a.	n.a.	0.4	0.4	0.5	0.5	0.5	0.5	0.5	n.a.	n.a.	n.a.	0.1	0.2	0.2	0.2	0.2	0.2	0.2	n.a.	n.a.	n.a.	34%	31%	28%	26%	27%	27%	26%	n.a.	n.a.	n.a.	12%	11%	11%	10%	10%	10%	9%
Luxembourg	0.1	0.1	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.2	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2	15%	12%	11%	10%	10%	11%	10%	10%	9%	9%	13%	10%	9%	9%	9%	9%	9%	8%	8%	7%
Netherlands	1.9	2.8	3.9	5.9	6.0	6.4	6.5	6.6	6.7	6.8	1.2	2.5	2.3	3.2	4.7	5.1	5.2	5.2	5.3	5.3	10%	12%	12%	11%	11%	11%	11%	10%	10%	10%	7%	10%	7%	6%	9%	9%	9%	8%	8%	8%
Poland	n.a.	n.a.	n.a.	4.3	4.6	4.9	5.7	5.1	5.7	5.7	n.a.	0.7	1.1	1.6	1.8	1.8	2.2	2.0	2.2	2.3	n.a.	n.a.	n.a.	30%	29%	27%	25%	25%	24%	24%	n.a.	16%	11%	11%	11%	10%	9%	9%	10%	10%
Portugal	0.8	1.6	2.4	3.3	3.4	3.6	3.6	3.5	3.4	3.1	0.5	1.0	1.3	1.9	1.9	2.0	2.0	2.1	2.2	1.7	25%	24%	22%	22%	23%	22%	21%	20%	20%	19%	16%	15%	12%	12%	13%	13%	12%	12%	12%	10%
Romania	n.a.	n.a.	n.a.	1.2	0.6	1.7	1.9	1.6	1.8	2.2	n.a.	n.a.	n.a.	0.6	0.6	0.8	0.9	0.6	0.7	1.0	n.a.	n.a.	n.a.	28%	15%	27%	26%	25%	25%	30%	n.a.	n.a.	n.a.	13%	15%	12%	12%	8%	10%	14%
Slovakia	n.a.	n.a.	0.6	1.1	1.2	1.3	1.5	1.5	1.6	1.5	n.a.	n.a.	0.5	0.8	0.9	0.9	1.1	1.1	1.1	1.0	n.a.	n.a.	35%	33%	31%	29%	29%	28%	28%	29%	n.a.	n.a.	29%	24%	23%	20%	21%	20%	19%	20%
Slovenia	n.a.	n.a.	n.a.	0.5	0.5	0.5	0.6	0.6	0.6	0.6	n.a.	n.a.	n.a.	0.3	0.3	0.3	0.3	0.4	0.3	0.3	n.a.	n.a.	n.a.	22%	22%	21%	20%	20%	20%	20%	n.a.	n.a.	n.a.	13%	13%	12%	12%	12%	11%	11%
Spain	3.7	6.4	9.7	15.1	15.8	16.7	17.8	18.3	18.5	17.2	2.7	4.6	7.1	10.8	11.3	11.9	12.7	13.4	13.4	12.2	19%	20%	22%	21%	20%	19%	19%	19%	19%	18%	13%	14%	16%	15%	14%	14%	14%	14%	14%	13%
Sweden	1.1	2.1	3.0	3.6	3.8	3.9	4.0	3.7	4.1	4.4	0.8	1.5	2.1	2.2	2.3	2.4	2.4	2.2	2.4	2.6	9%	13%	15%	14%	14%	14%	14%	13%	13%	13%	6%	9%	10%	9%	8%	8%	8%	8%	8%	7%
United Kingdom	7.4	12.5	16.0	19.4	20.2	21.0	18.5	n.a.	n.a.	n.a.	5.0	8.0	12.5	16.1	17.1	17.6	15.7	n.a.	n.a.	n.a.	14%	16%	15%	13%	13%	13%	12%	n.a.	n.a.	n.a.	10%	10%	12%	11%	11%	11%	10%	n.a.	n.a.	n.a.

No data for Croatia and Malta

Total pharmaceutical expenditure in the out-patient sector = Pharmaceuticals and other medical non-durables dispensed to out-patients according to System of Health Accounts (SHA) classification

Source: Eurostat, OECD Health data 2013

2.5 European policy framework

Following the subsidiarity principle, pharmaceutical pricing and reimbursement is, as confirmed in the Pharmaceutical Forum Process [20], a national competence of the EU Member States.

Typical pricing policies concern setting, monitoring/reviewing and adopting of medicine prices throughout the supply chain, i.e. setting the medicine prices at ex-factory price level, different pricing policies such as external price referencing or cost-plus pricing, distribution margins and taxes [34]. Reimbursement is defined as 'coverage of the cost by a third party payer (e.g. Social Health Insurance/National Health Service)' [35].

In practice, there is a strong link between pricing and reimbursement [36-38]. Specific pricing policy measures such as value-based pricing or internal price referencing (e.g. therapeutic reference pricing) concern the reimbursement sector only, and the statutory wholesale and/or pharmacy mark-up is only applicable for reimbursable medicines in some countries (e.g. France), for instance [39,40]. In several EU Member States the processes of pricing and reimbursement are also interlinked in organisational terms [36]. The G-10 Medicines report states that 'the Commission and Member States should secure the principle that a Member State's authority to regulate prices in the EU should extend only to those medicines purchased by, or reimbursed by, the State' (Recommendation 6, [18]).

In the following, we will present some measures. The definitions of the below mentioned policies were taken from the Glossary of the WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies [35].

Pharmaceutical policies measures might be divided into supply-side and demand-side measures: Supply-side measures 'are primarily directed towards specific stakeholders in the healthcare system that are responsible for medicine regulation / registration/quality assurance, competition among manufacturers, intellectual property rights, pricing, and reimbursement' [41]. Typical reimbursement practices in the out-patient sector, which are defined as supply-side measures, include:

- *reimbursement list:* defined as a 'list which contains medicines with regard to their reimbursement status', which can either be a positive list (list of medicines that may be prescribed at the expense of the third party payer) or a negative list (list of medicines which cannot be prescribed at the expense of the third party payer);

- *reimbursement rates:* defined as 'the percentage share of the price of a medicine or medicinal service, which is reimbursed/subsidised by a third party payer. The difference in the full price of the medicine or medicinal service is paid by the patients.' Countries may decide if they cover those medicines eligible for reimbursement (so-called reimbursable medicines to be put on a positive list) fully or partially. They can define specific reimbursement rates at the level of the product (product-specific eligibility), per disease group (disease-specific eligibility) and per

patient group (e.g. higher reimbursement rates for the vulnerable groups); other options are also possible (e.g. in Denmark and Sweden, the level of reimbursement depends on the individual pharmaceutical expenses of a patient and her/his family during a year);

- *reimbursement reviews:* defined as a 'review process of a reimbursement decision (i.e. a decision about the reimbursement status and reimbursement rates of medicines), which may, or may not, include the price'. Reimbursement reviews can be done systematically (e.g. once a year) for all reimbursed medicines or a group (e.g. specific indication), or out-of-schedule;

- *reference price systems*: defined as a policy in which 'the third party payer determines a maximum amount (= reference price) to be reimbursed for medicines with a given active ingredient or in a given therapeutic class. If the price of the medicine exceeds the reference price, the insured must pay the difference between the reimbursed fixed amount (reference price) and the actual pharmacy retail price of the medicine in addition to any co-payments'.

Demand-side policies are 'directed at stakeholders such as health care professionals prescribing medicines (usually physicians), pharmacies and patients/consumers who prescribe, dispense and ask for medicines' [41]. Major demand-side measures include:

- *co-payments:* a measure targeted at patients/consumers which is defined as 'the insured patient's contribution towards the cost of a medical service covered by the insurer. [...] Co-payment is a form of out-of pocket payment. [...] With regard to co-payment applied to the medicines, commonly applied variants in European countries are prescription fees, percentage reimbursement / co-payment rates and, but to a less extent, deductibles';

- *prescription monitoring*: a measure targeted at prescribers which is defined as 'the act of assessing/observing prescribing practices of physicians, [...] sometimes accompanied by feedback provided to prescribers and in a few cases also sanctions';

- *INN prescribing*: a measure targeted at prescribers which is defined as 'requirements for prescribers (e.g. physicians) to prescribe medicines by their INN, i.e. the active ingredient name instead of the brand name. INN prescribing may be allowed (indicative INN prescribing) or required (mandatory/obligatory INN prescribing)';

- *generic substitution*: a measure targeted at pharmacists which is defined as the 'practice of substituting a medicine, whether marketed under a trade name or generic name (branded or unbranded generic), with a less expensive medicine (e.g. branded or unbranded generic), often containing the same active ingredient(s). Generic substitution may be allowed (indicative generic substitution) or required (mandatory/obligatory generic substitution).'

In addition to this categorisation into supply-side and demand-side measures, it is common understanding that specific reimbursement practices are particularly relevant for some types of medicines. In this respect, generic medicines (or other off-patent medicines) are seen as a policy option allowing payers to provide less expensive, but equally effective medicines to the population. From the above mentioned policies, reference price systems, INN prescribing and generic substitution are particularly designed to promote generics uptake [34,42]. Tendering in the out-patient sector is a practice applied in a few European countries in which payers tender a specific molecule and will select the best offer. This is, for instance, done in the Netherlands with the so-called preferential pricing policy, which brought about major short term savings, but the long-term impact on accessibility is not clear [43,44]. Other countries which applied and apply tendering in the out-patient sector are Belgium (they have stopped it), Cyprus, Denmark, and Malta [45].

Currently, several on-patent medicines, among them some blockbusters, had their patent expired or are expecting it in recent future. Globally, for the years 2009-2014, medicines with sales of more than $ 142 billion / € 105 billion were expected to face generic competition among the leading developed markets [46]. This phenomenon, known as 'patent cliff', is a threat for the targeted pharmaceutical companies but it offers savings for the public payers; the money saved this way can be used to fund innovation and further medicine purchase.

At the same time, policy makers are confronted with the market entry of new, often high-cost medicines. Some of them are orphan medicinal products, which 'are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 per 10,000 persons in the community when the application for marketing authorisation is made' [47].

In the light of the entry of new, high-cost medicines, new policy measures have been implemented or are under discussion, such as:

- *managed-entry agreements (risk-sharing schemes)*: They are defined as 'an arrangement between a manufacturer and a payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact' [48]. There are different types of managed-entry agreements, e.g. access with evidence development (AED), conditional coverage, conditional treatment continuation (CTC), coverage with evidence development (CED), outcome guarantees, patient access scheme (PAS); their implementation varies among the EU Member States. UK, Italy, Germany and Poland have the lead in applying these arrangements [49].
- *value-based pricing (VBP)*: This is not so much a specific reimbursement measure but rather a practice for setting and managing prices of reimbursable medicines. In a broad definition, it is meant for countries to set prices for new medicines and/or decide on reimbursement based on the therapeutic value that the medicine offers [50]. The concept of value-based pricing has gained momentum, though as a pharmaceutical pricing and reimbursement policy in a narrower sense, compared to

external price referencing, VBP is in place in only few European countries. Sweden has been applying value-based pricing since the mid-1990-ties, and the UK will introduce it for new brand medicines later in 2014.

For the assessment of the value, supportive tools such as health technology assessment (HTA) or economic evaluations are of key importance (see also section 2.7).

2.6 Reimbursement policy practices in literature

In the course of this project, we performed a systematic literature review with the aim to identify and gather evidence on relevant policy measures related to pharmaceutical reimbursement in European countries.

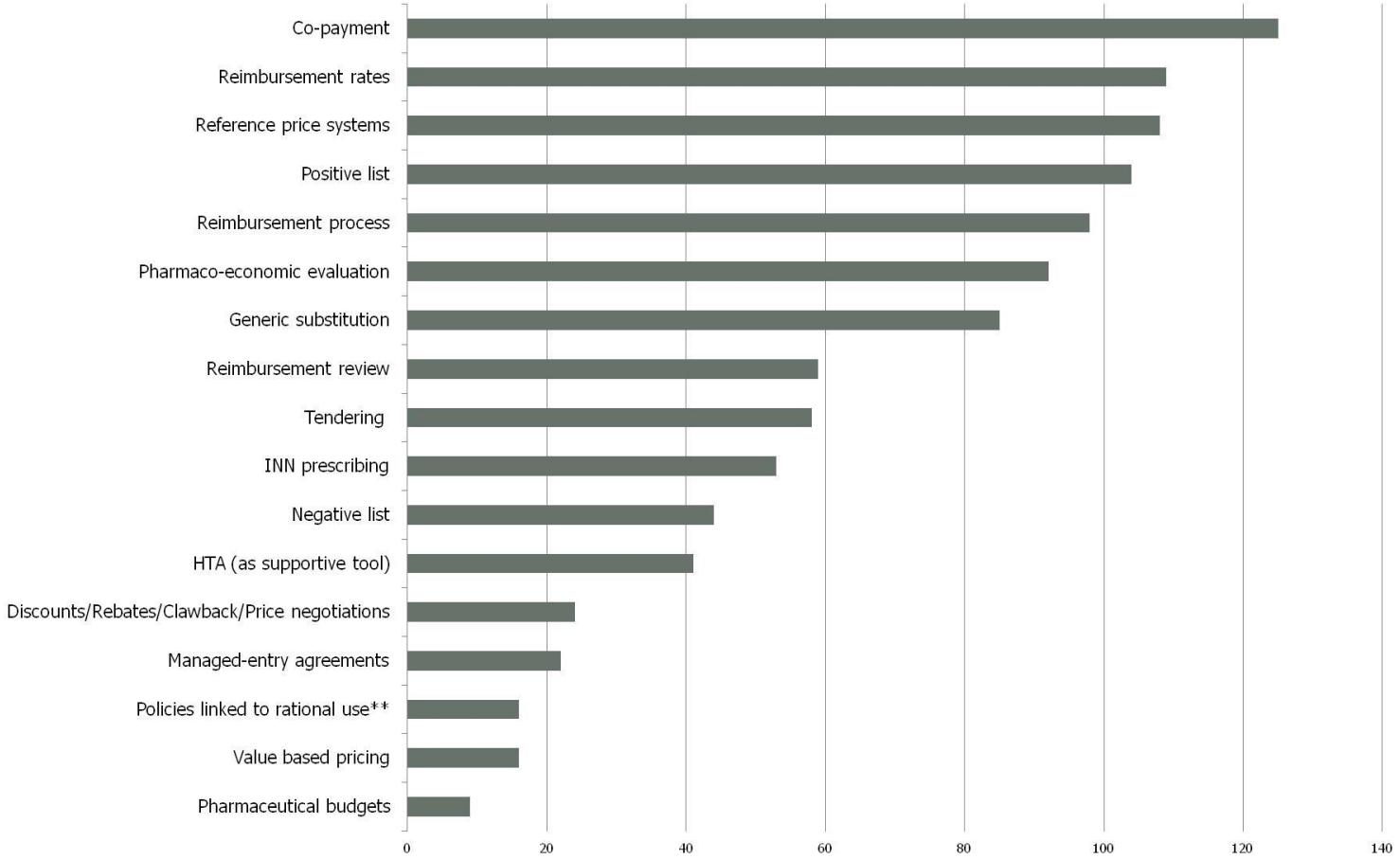
In line with a defined search strategy, we conducted a search of several databases (MedLine, Embase, Econlit, OECD Publications, Cochrane Effective Practice and Organisation of Care Group, WHO, National Health Services Economic Evaluation Database, etc.) to retrieve publications (in all EU languages) on reimbursement policies in all EU Member States (including Croatia) and the EEA countries (Iceland, Lichtenstein, Norway) published between 1995 - February 2013. Additionally, grey literature was searched via GoogleScholar, a hand search of selected bibliographies and a PPRI network query. The latter is an enquiry about the situation in those countries represented in the PPRI (Pharmaceutical Pricing and Reimbursement Information) network which comprises competent authorities of 41 countries, including all 28 EU Member States, to exchange experience and share information [51-53]. In this case, the PPRI network members were asked to check a list of identified literature for completion and provide further references, particularly about country-specific literature in the national language.

We performed a bibliometric review and analysed publications to determine several parameters (reimbursement policies mentioned, countries covered, information on impact included, product groups, etc.).

A total of 1,436 publications were retrieved from the different literature sources. Thereof, 337 publications (23.5 %) entered the second review phase. For 45 (13.4 %) of these 337 publications, the full texts could not be retrieved. Further 48 publications (14.2 %) were excluded as they did not meet the inclusion criteria. As a result, 244 publications were ultimately included in the bibliometric analysis.

The search strategy (e.g. sources, inclusion and exclusion criteria) is presented in further detail in Annex 2. The search addressed both the out-patient and the in-patient sectors. One exclusion criterion was that the policy practice is not linked to reimbursement; for instance, a measure such as the distribution margin or VAT rate is was exclusively linked to pharmaceutical pricing. As a result, the practice of external price referencing, which is a major pricing policy, was not included in the literature review. This can, of course, be challenged (cf. also sections 3.2.2 and 4.4.3).

*Figure 2.4: Reimbursement policies identified in literature, from 1995 till February 2013**



Legend: * In total, 1,063 reimbursement policies were mentioned in 244 articles, several articles/publications mentioned more than one reimbursement policy.
** Examples are prescription guidelines or monitoring of prescription patterns.
Source: Literature review performed by the authors

The five reimbursement policies most frequently mentioned in the publications were: co-payment, reimbursement rates, reference price systems, positive lists and the reimbursement process. At the other end, reimbursement policies mentioned in low frequency included auction-like systems, profit control or delisting from positive lists (Figure 2.4).

More than every second publication addressed either HTA or pharmaco-economics. We classified 'HTA' (understanding it as a supportive tool) and 'pharmaco-economic evaluation' as two different policies, but their descriptions in some pieces of literature were rather vague. Studies on pharmaco-economics and HTA were published predominantly in more recent times, probably after NICE in England was established, their proportion in peer-reviewed literature is higher compared with the total of included publications, and they tended to be presented in publications which also addressed value-based pricing. The majority of these studies were related to United Kingdom, Sweden, France, the Netherlands and Germany. It should be noted that the United Kingdom, Germany and the Netherlands are the three countries on which most literature was published, in general.

Generic substitution, reimbursement reviews, tendering and INN prescribing were mentioned in 35 %-22 % of all included publications. This highlights the relevance of generic policies (generic substitution and INN prescribing) as a major component of pharmaceutical reimbursement policies. At the same time, it should be acknowledged that the high number of references to reimbursement reviews and tendering, when compared with other policies, is likely attributable to some country reports (e.g. PPRI/PHIS Pharma Profiles [40], OECD country reports [54,55]) which followed the same outline and asked to indicate whether these measures were in place. In literature, tendering commonly referred to its practice in the in-patient sector, but there are also a few publications on tendering in the out-patient sector (e.g. on the Netherlands and Denmark). These publications included, in general, a mapping exercise on the topic; however, no impact assessment of tendering in the out-patient sector appeared to have been undertaken at the time when we conducted the literature review.

9 % of all included publications referred to managed-entry agreements. They were mainly published in peer-reviewed journals, and were less descriptive but aimed to explain and understand causes and consequences of these agreements. Most literature on management-entry agreements referred to the UK, and also, but much less, to Germany and Ireland. Interestingly, though Italy had a high number of managed-entry agreements, this was not reflected in the pieces of literature published.

Less than 7 % of the publications mentioned value-based pricing. Some of them were articles solely on the UK, discussing the planned introduction of the value-based pricing. Other publications looked at several countries, usually including the UK and non-European countries such as Canada and Australia. Although Sweden had had a value-based pricing system in place for years, this country was rarely mentioned in literature in connection with value-based pricing.

We could not perform an analysis of whether the mentioned policies were related to a product group (e.g. patented medicines with and without competitors and off-patent medicines with and without competitors) as no product group was mentioned in nearly three quarters of the publications.

2.7 Developments and challenges

Based on what is discussed in political processes and literature (not limited to the literature considered in the literature review, cf. section 2.6, because in our search only literature published before March 2013 was included), we identify the following developments and challenges related to pharmaceutical reimbursement policies:

Cost-containment measures in response to the global financial crisis and concerns for affordability and health outcomes

Several European countries were strongly hit by the global financial crisis, and, as a result, had to undertake strict austerity measures in several policy areas, including healthcare and medicines. Since 2008, cost-containment measures have been taken throughout Europe but have been mainly concentrated on countries that were hit the hardest by the financial crisis, i.e. Greece, Spain, Portugal, Ireland, Iceland and the Baltic States. Measures most frequently taken include price reductions, increases in the value added tax, increases in co-payments for medicines, policies aimed at increasing generic uptake, and procedural changes, including methodological changes in the external reference price system [56]. The impact of these measures is now, a few years after their continuous implementation, reflected in the development of pharmaceutical expenditure and, particularly so, public pharmaceutical expenditure. As shown in Table 2.1, (public) pharmaceutical expenditure has shown negative growth in some of these 'crisis countries'.

Though cost-containment is considered as a necessity in many countries hit by the crisis [3], this might be in conflict with other policy objectives. Rewarding innovation might be given less attention by policy makers who (have to) focus on cost-containment.

Besides concerns raised over the long-term impact on innovation of such measures [52], there are major concerns about the impact on affordability and, as a result, on health outcomes, since cost-containment measures, such as increased private co-payments and delisting of medicines (i.e. excluding products from reimbursement), imply the risk that patients forego the needed as well as unneeded medication, discontinue treatment, or delay purchasing medicines. For Greece, there are signs of deterioration in health outcomes, including an increase in suicides and attempted suicides, particularly among vulnerable groups, as a result of the crisis [57,58], and similar effects are also seen in other countries hit by the crisis [59-61]. Related to medicines, a WHO analysis, undertaken one year before and two years after the beginning of the recession (2007-2009), concluded that the economic recession has had a mixed effect on pharmaceutical consumption, expenditure and prices. In Europe, consumption of medicines was seen to have decreased in the Baltic States

and Romania, while Ireland, which was also strongly hit by the crisis, did not experience any decline in medicines consumption [62]. However, as the crisis is still on-going, the study would need to be updated, as well as the impact of cost-containment measures and the economic recession of the availability, access to and consumption of medicines; potential long-term effects on innovation in European countries would also need to be assessed.

Medicine shortages and gaps in availability

There have been some major problems related to medicine shortages in several European countries in recent years, after the problem started in the USA, particularly in the field of generic injectable chemotherapy agents [63,64]. Meanwhile, the number of reports of medicine shortages, addressing both community pharmacy and hospitals, in the European Union has been increasing. For instance, it has been reported from the UK, where over one million branded medicine supply failures occur each year, that community pharmacy staff would spend an average of three hours each week sourcing medicines which they are not able to order from their usual wholesaler [65].

Several reasons were identified for this problem, among others also pricing and reimbursement practices in some cases. Given the different price levels of medicines across Europe [12,66], parallel trade is incentivized. However, to order to address the problem of medicine shortages, Greece decided to implement a temporary parallel trade ban [67], in consultation with the Troika, since the freedom of goods is normally considered as a value of the European Union.

Availability problems may also be a result of external price referencing which is the key pricing policy for new medicines eligible for reimbursement in most European countries (cf. section 2.5). Pharmaceutical companies may decide to launch a medicine later in countries where it would be sold at a low price so as to not negatively impact the price in other countries applying external price referencing [14,15].

Since generics which encourage competition are seen as an opportunity to achieve savings (without the trade-off between too many policy objectives, allowing for re-investment in innovation; see also section 2.5), delayed generic availability is another issue to be dealt with in this context. The Pharmaceutical Sector Inquiry [16] raised concerns about barriers which delay market entry of generics. Research-based industry has also brought up this topic [68].

Particular concerns are related to the limited availability of generics on small markets [69], which further exacerbates the existing challenge of ensuring availability of medicines on small markets [70]. To address the latter, a Working Group of the Platform of Access to Medicines was launched to develop non-regulatory approaches (cf. section 2.3)

Related to generics, the practice of tendering (in the out-patient sector), as it is, for instance, done in the Netherlands, shows well the trade-off between different policy objectives as well the potential trade-off between short-term achievements and long-

term implications. The Dutch tendering practice, called preferential pricing policy, proved successful in terms of cost-containment and the initial total savings (projected to € 355 million annually) exceeded expectations [43]. But there have been reports of short-term absences of some medicines due to logistic shortages [43,44].

A discussion about the topic of availability and delays in access to medicines would be incomplete if delays attributed to the delays in the completion of the pricing and reimbursement process were not mentioned. The current EC Transparency Directive [10] requires that the Member States make a pricing decision within 90 days and a reimbursement decision within 90 days; a 180-day limit is required for joint pricing and reimbursement decisions. While competent authorities for pricing and reimbursement have been regularly criticised for their delays in decision making, they have, however, pointed out that delays in decision making sometimes occur because they have to deal with submitted dossiers that are incomplete or do not contain all the information required for informed decision making [52].

Assessing the value of high-cost medicines

One of the major challenges for policy makers in the European countries is how to deal with new, usually high-cost medicines. This is, for instance, the case for the orphan medicinal products which are granted premium prices to compensate for small volumes. Further, one area of concern for policy makers are cost-intensive health technologies that are not medicines, but medical devices: they are usually not (price) regulated, and they have a key impact on the pharmaceutical bill since they are often part of a 'treatment package' (see below).

In the light of this challenge on how to design the pricing and reimbursement framework in a way to meet the different health and non-health policy objectives (cost-control, sustainable funding as well as rewarding innovation and encouraging investments in R&D), policies to acknowledge the 'value' of the medicine have been discussed and have, to some extent, been implemented.

The concept of 'value-based pricing' has gained momentum although there is no widely-accepted definition in this context [50]. Examples for a 'pure' value-based pricing system primarily come from outside Europe (e.g. Australia, New Zealand, Canada) [71]. As stated in section 2.5, Sweden has a value-based pricing system, in which the cost-effectiveness principle for assessing the value of a medicine is applied from a societal perspective [72]. The UK has been working on the principles of how to organise their value-based pricing system for new branded medicines which is planned to be introduced in the course of 2014 (personal communication).

In addition to these two countries in the European Union which have, or will have, a value-based pricing system as their key pricing and reimbursement framework for new medicines, value-based pricing elements are part of several reimbursement systems in Europe. According to a recent OECD report [50], all European countries included in that report (e.g. Belgium, France, Italy, the Netherlands) are shown to have a system in place that assesses the added value of medicines.

Assessing the value of medicines requires sound evidence based on Health Technology Assessment (HTA) reports and/or pharmaco-economic evaluations. Several European countries use HTA in their reimbursement decisions [3]. HTA is defined as a multidisciplinary process in which medical, social, economic, and ethical issues related to the use of a health technology (including medicines) are assessed in a systematic, transparent, unbiased, and robust manner (definition by EUnetHTA, cf. [73]). As for the other policies and instruments, the implementation of HTA may vary, and the EU Member States apply HTA in the reimbursement process in their own way. Even if reimbursement decisions based on HTA would not necessarily involve the use of pharmaco-economic evaluations (but rather understand the relative efficacy or effectiveness of a medicine as the major element of the assessment), in reality several Health Technology Assessments include some economic evaluation.

In recent years there has been an on-going discussion about external price referencing versus value-based pricing as the appropriate pricing policy for new medicines to be included into reimbursement. In Europe, external price referencing continues to be the major pricing policy for new medicines, whereas HTA and pharmaco-economics are elements of the reimbursement process that provide policy makers with sound information. External price referencing (EPR) is seen as an easy, more or less technical procedure. While designing and implementing EPR, including assuring access to up-dated and reliable price data, is a challenge not to be under-estimated, it is true that EPR is a technical methodology compared to value-based pricing which aims to assess the 'value' of the medicine for society. External price referencing has been criticized for impeding patient access to medicines (disincentivizing manufacturers to launch medicines early on a low price market, see above the discussion on the possible impact of EPR on the availability) and for discouraging innovation. To create barriers to EPR, and to avert the threat of parallel trade, pharmaceutical companies 'are likely to invest in development to produce marginal modifications (e.g. formulation, dosage) of existing products – with no benefit to patients in terms of therapeutic effect, convenience or otherwise' [12]. A major argument against external price referencing is that it reflects neither a country's willingness to pay nor its ability to pay. This is acknowledged in the value-based pricing concept. However, when a country uses an explicit threshold, which is publicly known, manufacturers have no incentive to price their product below the threshold [74].

Finally, the assessment of the 'value' of a new medicine is likely to be impaired by the limitations in existing evidence on the (additional) therapeutic value at the time of the decision on reimbursement. In response to that, several forms of 'conditional reimbursement', summarized under the term 'managed-entry agreements', have been developed and implemented in some European countries (cf. section 2.5, and for a more in-depth overview, see the report produced within the framework of the Working Group on managed-entry agreements of the Platform on Access to Medicins [49]). Such arrangements, which allow managing uncertainty, are generally seen as an opportunity to reward innovation and assure quick patient access. However, the drawbacks are that they are rather time-intensive (both for the pharmaceutical company and for the payer), that payers are likely to have difficulties explaining to the public why they will withdraw reimbursement once the health outcomes are not confirmed, and the fact that these agreements are usually confidential, which has implications for transparency (see below the following section on that topic).

Transparency versus confidentiality issues

Several of the new reimbursement practices, e.g. managed-entry agreements, are based on an arrangement the contents of which are kept confidential, though the presence of such agreements is generally known and might even be published.

The existence of confidential arrangements granted by suppliers to purchasers, e.g. discounts, rebates, bundling, has been long known, at least at an anecdotal basis, for the hospital sector. Specific medicines used in hospitals, particularly those with therapeutic alternatives and which are likely to be used for long-term treatments after the discharge of a patient from hospital, are likely sold to hospitals at high discounts, or even for free, in those European countries where such practices are allowed [75-77]. Discounts, rebates and similar, usually confidential, arrangements also exist in the out-patient sector: in 21 of the 31 European countries, discounts and rebates were surveyed to be granted in the out-patient sector to public payers by pharmaceutical companies, usually taking the form of price reductions and refunds linked to the sales volume [78].

It has been argued that these arrangements would offer advantages to the various stakeholders: they serve cost-containment purposes for payers ('hidden price cuts'), and they allow pharmaceutical companies to gain market share [78]. Furthermore, it has been argued that for countries with a limited ability to pay which are included in the reference baskets of other countries, confidential discounts and rebates are a tool to increase access to patients, as under full transparency companies might be less willing to launch a product in their country or might insist on a higher price (see above). In fact, discounts and rebates have been increasingly used as a kind of 'hidden price cuts' instead of real price cuts (e.g. during the emergency measures in Spain, a discount shared by the industry and distributors of 7.5 percent on originator products was agreed upon instead of a 'real' price cut) [56,78]. Given the widespread use of external price referencing in European countries, it creates a situation in which the official list prices, as published by the Member States, may provide at best only an indication of, but not a reflection of, the actual prices. In a joint position paper regarding the revision of EU Transparency Directive, the European Social Insurance Platform (ESIP) and Association Internationale de la Mutualité (AIM) called for a disclosure of the discounted prices as they argue that the Member States employ external price reference systems that require them to know the 'real' price in other countries [79].

The use of confidential discounts and rebates is also an issue related to 'differential pricing', however, in the current EU framework differential pricing is not possible given the wide-spread use of external price referencing in Europe and the existence of parallel trade encouraged by the free movement of goods concept. Authors advocating for differential pricing [80] argue that confidentiality is required to do differential pricing, which would allow countries to be charged according to their willingness to pay. However, examples from international donor organisations show that differential pricing does not necessarily require confidentiality.

Interface issues

Finally, it has been increasingly recognized that in the area of pharmaceutical policies a more comprehensive approach might be needed to address the existing and potential link between specific areas. Areas that require improvement include:

- **Interface between the out-patient and hospital sectors**

  The start of treatment in hospitals impacts the future use of medicines in the out-patient sector. As a result, pharmaceutical companies are likely to supply hospitals with high-volume medicines, with comparators, at large discounts and rebates, including cost-free provision (if allowed by national legislation), with the aim to facilitate starting treatment in hospitals [75-77]. Solutions to bridge the gap between the out-patient and the in-patient sectors are also urgently required for new high-cost medicines since, due to existing funding mechanisms in most European countries (different payers or funding sources for the out-patient and the in-patient sectors), public payers have an incentive to find arguments why medicinal treatment might be shifted to the other sector.

  In recent years, awareness has been raised about the need to improve cooperation at the interface of the out-patient and in-patient sectors and to find sustainable funding solutions offering appropriate incentives to all stakeholders. However, knowledge about good practice examples appears to be scarce. A few European countries (e.g. France, the Netherlands – from 2006 till 2012) implemented funding models, in which the public payer for the out-patient sector also covers (partial) costs of some, usually high-cost, medicines in the in-patient sector [75,81,82]. Several counties (regions) in Sweden, e.g. the Stockholm County, and Scotland implemented a joint reimbursement list and joint Drugs and Therapeutics Committees [83,84].

- **Personalised medicines at the interface of medicines and medical devices**

  In the EU Member States, medicines have a high level of regulation for marketing authorisation, pricing and reimbursement, pharmaco-vigilance and post-market surveillance. Medical devices are much less regulated than medicines: there is a notification of medical devices instead of marketing authorization; free pricing is usually applicable to medical devices, and there are limited reimbursement mechanisms for medical devices so costs are, in principle, borne by patients or – in the case of hospital care – by hospitals.

  Medical devices, some of which are cost-intensive high technologies, play a major role within the concept of personalised medicines (sometimes also called co-dependent technologies or stratified medicines) because a 'treatment package' is usually composed of a medicine for treatment and a medical device for diagnostic purposes. Considerable differences were found between the European countries that have reimbursement systems for combined diagnostics and therapeutics (e.g. France, Germany and the United Kingdom), whereas for other countries (e.g. the

Netherlands, Finland and Norway), no clear pathways for the evaluation and funding of personalized medicines were identified [85]. In addition, the fact that this 'treatment package' might be applied in hospital care in some countries while being delivered in the out-patient (ambulatory) sector in other countries, might also have an impact on the pricing and funding of the medicines and medical devices in the 'treatment package' (for example in the diagnosis and treatment of breast cancer [86]).

- **Interface between marketing authorization and pricing and reimbursement**

Furthermore, discussion has started on an improved cooperation between regulators in charge of marketing authorization and the authorities responsible for pharmaceutical pricing and reimbursement including Health Technology Assessment (HTA) agencies. While it is clear that the criteria for marketing authorization approval and reimbursement are different (a safe, effective and quality medicine can be considered as not cost-effective at the proposed price), there are considerations to work on a better understanding between the 'two worlds' and to also support pharmaceutical companies [87]. The instrument of early scientific dialogue, usually known as part of the regulatory field, has also been piloted by reimbursement authorities [88].

3 Methodology

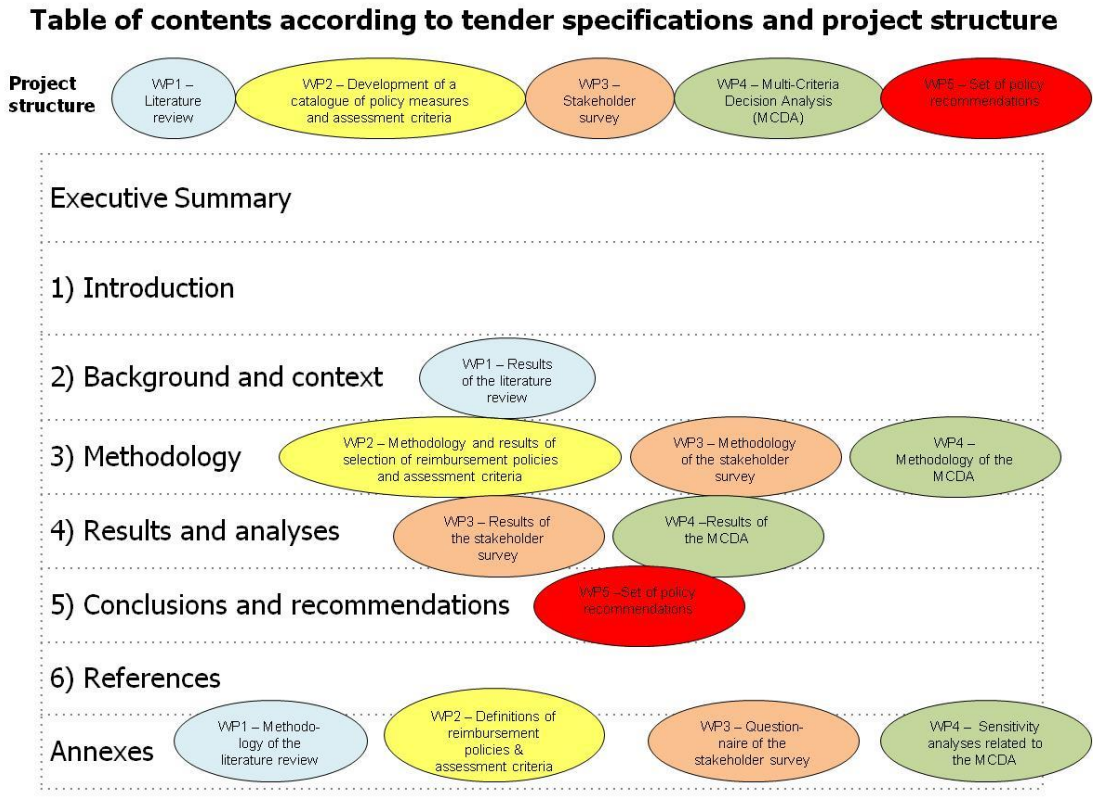
The methodology chapter is divided into different sub-sections to present, following some general methodological considerations: the definition and selection of policy objectives (assessment criteria) and reimbursement measures which stakeholders were asked to comment on; the design of the stakeholder consultation, including the selection of stakeholder groups and the survey tool; and the chosen MCDA method, including the sensitivity analyses as well as the procedure of piloting and roll-out.

The methodology of the literature review will not be presented since it was briefly addressed in Chapter 2, and it is presented in further detail in the annexes.

3.1 General methodological considerations

The aim of the study was to perform a stakeholder consultation about their preferences to the policy practices related to the reimbursement of medicines in line with defined policy objectives. The tender specifications stated that the survey should be done in writing (e.g. electronically), and the assessments of the stakeholders should be collated and discussed through a Multi-Decision Criteria Analysis (MDCA) method.

Figure 3.1: Interplay of outline of the report under consideration of the methodology parts



Given this framework, the design of the stakeholder survey and the choice of the MCDA method were strongly interlinked. In fact, the questionnaire development, particularly aspects related to the thresholds required for the selected MCDA method, was based on the decision related to the chosen MCDA method.

For the interplay of the different methodological steps, please see Figure 3.1.

3.2 Policy objectives and policy measures

The stakeholder survey aimed to explore:

- the preferences of the different stakeholders related to policy objectives relevant for the reimbursement of medicines, and
- the assessment of the stakeholders on relevant policy measures, i.e. whether these practices were considered appropriate to achieve the defined policy objectives (assessment criteria).

Thus, selecting these policy objectives and measures (classified per product group) was a major task. In a first step, a broader list of policy objectives and policy measures was set up, based on expert knowledge as well as on the information from the literature review and from political processes. In order not to discourage potential respondents with a too long questionnaire, it was decided to reduce the number of policy objectives to around five to seven and the number of policy measures to around 15 (for the criteria and process, see the section below).

A definition of the policy objectives and the policy measures under discussion, whether they were selected or not, is available in Annex 4.

3.2.1 Policy objectives

Key criteria for the inclusion of policy objectives into the study were: being frequently mentioned in literature and relevant policy documents (e.g. Pharmaceutical Sector Inquiry, WHO Nairobi Declaration) and being identified as objective(s) by the High Level Pharmaceutical Forum or other key processes; the limitations related to the scope (too broad objectives or those already captured by other terms) were the criteria for exclusion.

As a result, the following seven policy objectives were chosen:

- Timely access to medicines
- Equitable access to medicines
- Reward for innovation
- Cost-containment / control of pharmaceutical expenditure/budget
- Long-term sustainability (for the health care system)
- Promotion of a more rational use of medicines
- Increased competition.

The proposed policy objectives were agreed upon with the EAHC/EC and were tested in the pilot survey (cf. section 3.8 below). They were not changed after the piloting.

3.2.2 Policy measures

From the literature review, we identified a total of 23 reimbursement policy measures related to medicines. These were:

Auction-like systems (i.e. reimbursement procedure in which applicants for reimbursement are invited to submit (price proposals)

- Co-payment (as a form of out-of-pocket payments)
- Delisting (e.g. switches)
- Differential pricing
- Discounts / rebates / price negotiations / clawback
- Generic substitution
- HTA (as a supportive tool)
- INN prescribing
- Managed-entry agreements
- Negative list
- Pharmaceutical budgets
- Pharmaco-economic evaluation
- Positive list
- Prescription guidelines
- Prescription monitoring
- Profit control
- Reference price system
- Reimbursement list
- Reimbursement process
- Reimbursement rates
- Reimbursement review
- Tendering
- Value-based pricing.

We were aware of the fact that the processes of pricing and reimbursement are strongly interlinked [36,38] (cf. section 2.5). Still, in the literature review we focused on pure reimbursement measures and excluded medicine price-related measures. This was the reason why, for instance, external price referencing was considered as out of the scope of the literature review. However, in consultation with the EAHC/EC on the selection of criteria, it was decided that a potential inclusion of the policy measure 'differential pricing' should be accompanied by the consideration of the policy measure 'external price referencing'. As a result, external price referencing was added, and this increased the number of possible policy measures to be commented upon to a total of 24. Classifications were performed for this total of 24 possible measures.

Classification of policy measures

We classified these 24 reimbursement measures with regard to five categorisation criteria:

(1) Supply-side versus demand-side measures

Supply-side policies are defined as measures primarily directed towards specific stakeholders in the healthcare system that are responsible for medicine regulation/registration/quality assurance, competition among manufacturers, intellectual property rights, pricing, and reimbursement, whereas 'demand-side 'policies are directed at stakeholders such as health care professionals prescribing medicines (usually physicians), pharmacies and patients/consumers who prescribe, dispense and ask for medicines ([41], cf. also section 2.5).

a. **Supply-side measures** were sub-divided into three categories:
   i. **reimbursement system**: general structure and organisation of the reimbursement system in the specific country
   ii. 'pure' reimbursement tools / instruments
   iii. pricing policies strongly linked to reimbursement.
b. **Demand-side** measures relevant to reimbursement were specified according to the different stakeholders (e.g. prescribers, pharmacists, consumers).

(2) **Per type of products**, considering the patent status and the existence of competitors in the same therapeutic group:

a. Patented medicines with no competitor product within the therapeutic class;
b. Patented medicines with competitor product(s) within the therapeutic class;
c. Off-patent medicines with no competitor product within the therapeutic class on the market;
d. Off-patent medicines with competitor product(s) within the therapeutic class on market.

(3) Per setting (out-/in-patient):

a. The policy measure is only applicable to the out-patient sector.
b. The policy measure is only applicable to the hospital sector.
c. The policy measure is applicable to both the out-patient and in-patient sectors.

(4) Per key stakeholders targeted by the policy measures:

a. Patients;
b. Prescribers – by taking the decision on the medical treatment for the patient and being impacted by reimbursement decisions; doctors by prescribing medicines can importantly influence the pharmaceutical bill;
c. Pharmacists – by being key healthcare providers in the field of medicines and often the first contact points for consumers and patients; they are also impacted by reimbursement policies;
d. Pharmaceutical companies.

(5) Level in the health care system:

a. National
b. Regional
c. Individual (e.g. on hospital level).

Table 3.1: Classification of reimbursement policies per different categorisation systems

Reimbursement policy options		Type of product	Setting	Key stake-holders targeted[2]	Level
Supply-side					
Reimbursement system	Reimbursement process	1,2,3,4	O, I	Pc, Pa, Pr	N, R (in-patient)
	▪ HTA (as a supportive tool)	1, 2, (3) = usually	O,I	Pc	N, R
	▪ Pharmaco-economic evaluation	1, (3) = usually	O,I	Pc	N, R
	Reimbursement review	1,2,3,4 (focus on 1 +3)	O (usually)	Pc, Pa, Ph	N, (R)
	▪ Delisting	1,2,3,4	O (usually)	Pc, Pa, Pr	N, R
	Profit control	1,2,3,4	O	Pc	N
Pure reimbursement tools	Reimbursement list	1,2,3,4	O, I	Pc, Pa, Pr, Ph	N, (R), I
	▪ Positive list	1,2,3,4	O,I[1] ,OI	Pc, Pa, Pr, Ph	N, R (in-patient), I
	▪ Negative list	1,2,3,4	O, OI	Pc, Pa, Pr, Ph	N, (R)
	Reimbursement rates	1,2,3,4	O (usually)	Pc, Pa	N
	Design of co-payment	1,2,3,4	O (usually)	Pc, Pa	N, R
	Managed-entry agreements	1	O, I	Pc, Pa, (Pr)	N, I
Pricing policy linked to reimbursed medicines	Reference price systems	2,4	O	Pc, Pa, Pr, Ph	N, (R)
	Value-based pricing	1	O, I	Pc, Pa	N
	Discounts / rebates / price negotiations / clawback	1,2,3,4	O, I	Pc, (Pa), Ph	N, R
	Auction-like systems	2,4	O, I	Pc, (Pa), Ph	N
	Tendering	2,4 1,2, (3,4)	O I (as procurement method)	Pc, (Pa), Ph Pc, Ph	N, R
	Differential pricing	1,2,3,4	O, I	Pc, Pa	N, R
	External price referencing	1,2, (3,4)	O	Pc, Pa	N
Demand-side					
Pre-scribers	Pharmaceutial budgets	1,2,3,4	O	(Pa), Pr	N, R
	INN prescribing	2,4	O	Pc, Pa, Ph, Pr	N
	Prescription guidelines	1,2,3,4	O, I	Pr, Pa	N, R
	Prescription monitoring	1,2,3,4	O, I	Pr	N, R
Ph.	Generic substitution	2,4	O	Pc, Ph, Pr, Pa	N

[1] Different name in the in-patient sector

[2] Governments/competent authorities/public payers are not included – they implement policies to achieve defined objectives, but they are not the target of a policy

Type of product: 1,2,3,4 –4 product categories to be considered: (1) patented products with no competitor product within the therapeutic class, (2) patented products with competitor product(s) within the therapeutic class, (3) off-patent products with no competitor product within the therapeutic class on the market (4) off-patent products with competitor product(s) within the therapeutic class on the market.

Setting – in the sense of: the specific reimbursement policy is applicable in the in- or out-patient sector: O = out-patient, I = in-patient, OI = both out-patient and in-patient sector, considering interface aspects

Key stakeholders targeted (intended primary target groups of the policies): Pa = Patients, Pr = Prescribers, Ph = Pharmacists, Pc = Pharmaceutical companies

Level: N = national, R = regional, I = individual

Terms in brackets indicate 'is affected, but is not a primary focus of the policy'.

Table 3.1 provides the outcome of the categorisation process: most of the reimbursement measures under discussion were considered as supply-side measures, and were usually, but not exclusively, applied at national level. All of the measures under consideration were applicable in the out-patient sector; a few of them also in the in-patient sector. Apart from a few demand-side measures, pharmaceutical industry was nearly always targeted by reimbursement policy measures, and so were the patients in many cases. Many of the measures are, in general, applicable to all types of medicines, but a few of them are tailored to specific product groups: value-based pricing and managed-entry agreements are targeted at new on-patent medicines, whereas generic substitution and INN prescribing are typical tools to promote generics uptake and increase competition of medicines where competitors in the same therapeutic class exist (cf. section 2.5).

The categorisation process has limitations. Some measures might be applicable, in principle, to all or several settings, or types of products, or they might target all or several stakeholders. Nonetheless, the dimensions might differ. We thus considered the practical relevance when we categorized the reimbursement measures. For instance, pharmaco-economic evaluations to assess the (added) therapeutic value of a medicine can, in principle, be done for medicines of all product groups, but in reality it is a key measure applicable for on-patent medicines with no competitors (indicated as such in Table 3.1), since for off-patent medicines other measures to enhance competition among therapeutic alternatives are more likely to be applied.

Selection of policy measures

In order to decrease the number of reimbursement policy measures, which might be of interest in the stakeholder consultation, to a feasible number, and, at the same time, not to miss out on relevant policies, we applied the following selection criteria:

- Frequency of being mentioned in literature (referring to the results of the literature review);
- Frequency in practice (frequently used measures in many European countries);
- Clear and comprehensible definition of the policy measure;
- Similar practical implementation in the different countries (a policy might have different designs);
- Common understanding across Europe;
- Balanced mix of supply-side and demand-side measures;
- Balanced mix of measures relevant for all product types and those for specific medicines (e.g. new medicines, generics);
- Balanced mix of measures targeting different stakeholders;
- Implementation of the measures at national level.

Table 3.2 presents how much the selected policy measures fulfil the selection criteria, and whether the measures were selected.

Following this selection process, the short list of reimbursement practices to be surveyed in the questionnaire covers 16 policy measures. These are (in alphabetical order):

- Co-payment
- Differential pricing
- Discounts / rebates / price negotiations / clawback
- External price referencing
- Generic substitution
- HTA (as supportive tool)
- INN prescribing
- Managed-entry agreements
- Pharmaceutical budgets
- Pharmaco-economic evaluation
- Positive list
- Reference price systems
- Reimbursement rates
- Reimbursement review
- Tendering and
- Value-based pricing.

Scope of the selected policy measures

Reimbursement policy measures may be implemented in different ways: for instance, a reference price system may be implemented at ATC 5 level, i.e. a comparison at the active ingredient level, or the cluster of comparable medicines might be defined at ATC 4 level or some other broader level. Furthermore, the implementation in the out-patient sector might differ from the one in the in-patient sector. Tendering is a good example: while it is a procurement method for all, particularly for the high-cost, on-patent medicines in the in-patient sector, this practice is, when applied in the out-patient sector, particularly intended to encourage competition in the off-patent market (e.g. the preferential pricing policy in the Netherlands, cf. section 2.5).

In consultation with EAHC/EC, it was decided that, in the course of this project, the stakeholder survey should be limited to the out-patient sector, i.e. to policy measures applied in the out-patient sector commented upon by stakeholders in the out-patient sector.

In the survey, stakeholders were asked to relate to the chosen policy measures 'in the light of the broadest possible interpretation'. To ensure a clear understanding, examples were given for each policy measure on how to interpret it (cf. section 3.7).

Table 3.2: Selection matrix for reimbursement policies

	Reimbursement policy options	Frequency in the literature review	In place in European countries (EU MS, EEA c.)	Clear definition (y/n)	Scope of product groups	Stake-holders targeted	Implementation at national level	Selected
Reimbursement system	Reimbursement process	xx	Standard	y	several	> 1	y	✓
	▪ HTA (as a supportive tool)	xx	Used for specific medicines (e.g. high-cost medicines)	y	focus on new med.	1	y	
	▪ Pharmaco-economic evaluation	xx	Used for specific medicines (e.g. high-cost medicines)	y	focus on new med.	1	y	✓
	Reimbursement review	xx	Done in a few countries (systematically or ad-hoc)	n	several, focus on new med.	> 1	y	✓
	▪ Delisting	x	A common measure, particularly in recent years	y	several	> 1	y	
	Profit control	x	A few countries	y	several	1	y	
Pure reimbursement	Reimbursement list	xxx	All countries	y	several	> 1	y	
	▪ Positive list	xxx	Majority of countries	y	several	> 1	y	✓
	▪ Negative list	xx	Few countries	y	several	> 1	y	
	Reimbursement rates	xxx	All but 5 MS	y	several	> 1	y	✓
	Co-payment	xxx	All countries, different design and extent	y	several	> 1	y	✓
	Managed-entry agreements	x	New measure, some countries	n	focus on new med.	> 1	y	✓
Pricing policy linked to reimbursed medicines	Reference price systems	xxx	21 of 28 MS	y	focus on med. with competitors	> 1	y	✓
	Value-based pricing	x	Very few countries	n	focus on new med.	> 1	y	✓
	Discounts / rebates / price negotiations / clawback	x	Commonly applied, different design	n	several	> 1	y	✓
	Auction-like systems	x	A few countries	y	focus on med. with competitors	> 1	y	
	Tendering	xx	Few countries (out-patient sector)	y	several	> 1	y	✓
	Differential pricing	x	Not applied	y	several	> 1	y	✓
	External price referencing	xxx	24 of 28 MS	y	several	> 1	y	✓
Prescribers	Pharmaceutical budgets	x	A few countries	y	several	> 1	y	✓
	INN prescribing	xx	Several countries	y	focus on med. with competitors	> 1	y	✓
	Prescription guidelines	x	Majority of countries	n	several	> 1	y	
	Prescription monitoring	x	Majority of countries	y	several	1	y	
P h	Generic substitution	xx	Majority of countries	y	focus on med. with competitors	> 1	y	✓

EEA = European Economic Area, EU = European Union, MS = Member State(s), med. = medicines, n = no, Ph. = pharmacist(s), Pc = pharmaceutical companies, y = yes
Notes: Frequency in literature: x = low frequency (in less than 4% of the identified publications, xx = medium frequency (in 4-9% of the identified publications), xxx = high frequency (in more than 10% of the identified publications). Pls. note that external price referencing was not included in the literature review due to its dominant character as a pricing policy.

3.3 Stakeholder selection and cooperation

3.3.1 Stakeholder groups included

The tender specifications (see Annex 1) required the analysis to cover the following four stakeholder groups: patients, 'research-based' pharmaceutical industry including biotech companies and Small and Medium Sized Enterprises (SMEs), generic medicines industry, public healthcare payers. These four stakeholder groups reflect the major groups in this field, and, as major stakeholders, they were also involved in the processes of the Pharmaceutical Forum and the Corporate Social Responsibility.

In addition, we proposed to address additional stakeholder groups in the consultation. Our suggestions included:

- consumers, since healthcare is not only an issue of sick people, but also of all the healthy European citizens (taxpayers);
- competent authorities for pricing and reimbursement, since they might be not covered by the group of payers in all Member States but they are of key importance as they are directly involved in policy making;
- doctors, since by prescribing medicines they can importantly influence the pharmaceutical bill, while being impacted by reimbursement policy measures, particularly specific demand-side measures;
- pharmacists, since, apart from also being impacted by reimbursement policy measures (particularly specific demand-side measures) they are key healthcare providers in the field of medicines and often the first contact points for consumers and patients.

This proposal was consulted and agreed upon with the EAHC/EC. As a result, the survey was addressed to eight stakeholders (summarized in Table 3.3). In the analysis, two stakeholders of a similar field were combined in order to learn whether any differences can be found in the analysis of the single (eight) groups or combined (four) groups.

Table 3.3: Selected stakeholder groups

Combined groups	**Stakeholder groups**
Consumers and patients	(1) Consumers (2) Patients
Authorities and payers	(3) Competent authorities for pharmaceutical pricing and reimbursement (4) Public healthcare payers
Industry	(5) Generic medicines industry (6) Research-based pharmaceutical industry (including biotech companies)

Healthcare professionals	(7) Doctors (8) Pharmacists

The stakeholders consulted should primarily represent the national level in the 28 EU Member States.

After consultation with the EAHC/EC, it was decided not to include stakeholders from the in-patient sector (hospitals/hospital associations/hospital pharmacists) in the stakeholder survey as the focus of the study is on the out-patient sector, and in some respect there are considerable differences between out-patient and hospital pricing and reimbursement policies.

3.3.2 Involving the stakeholders

In order to obtain responses from the most competent person of each stakeholder group in the respective countries, we decided to identify potential respondents via the European associations.

We approached the following associations at the European level:

- European Federation of Pharmaceutical Industries and Associations (EFPIA) and The European Association for Bio-industries (EUROPABIO) for the innovative medicines industry;
- European Generic Medicines Agency (EGA) for the generics industry;
- European Patients' Forum (EPF) for patients;
- the European Consumer's Organisation (BEUC) for consumers;
- the Standing Committee of European Doctors (CPME);
- the Pharmaceutical Group of the European Union (PGEU);
- the CAPR (Competent Authorities for Pricing and Reimbursement of Pharmaceuticals) network led by Directorate-General Enterprise of the European Commission, the public payers' organisation 'The Medicine Evaluation Committee' (MEDEV) and the PPRI network for the groups of the payers and the competent authorities for pharmaceutical pricing and reimbursement.

On 2 August 2013, we sent letters to BEUC, CPME, EFPIA, EGA, EPF, EUROPABIO, MEDEV and PGEU in which we officially informed them about this study and the planned stakeholder survey. We asked for their support by identifying possible respondents in their national associations and sharing their contact details with us. Our request was accompanied by a supporting letter of the EC with an advance notification to the European associations. All contacted associations responded, usually after only a short time; two associations were delayed in replying due to the summer holiday season and answered after a reminder at the beginning of September 2013. All contacted associations reacted positively to our request. All but one provided us

with the needed contact details; one association did not want to share contact details but offered to forward the link to the questionnaire to their members.

The secretariat of PPRI is located with the Austrian Health Institute, one of the consortium members. The survey was pre-announced to the PPRI network members during a network meeting in March 2013.

One important limitation is that most associations do not cover all 28 EU Member States. Thus, a few associations offered back-up solutions, such as providing contact details of similar but non-member associations or, in the case of industry, of companies with whom they cooperate.

3.4 Survey tool

The tender specifications (see Annex 1) asked for a 'written consultation in respect of applicable legislation on data protection'.

We decided to perform the consultation via an online survey tool and chose the software tool QuestBack® (previously called Globalpark®). The questionnaire was available between 26 September and 12 November 2013 via the following link: http://ww2.umfragecenter.at/uc/gesundheit_oesterreich_team3/14fc/ (meanwhile closed). We offered the respondents the possibility to download the full questionnaire in a PDF format (allowing a preview of the contents) and to save the online survey while answering.

3.5 MCDA method

Multi-Criteria Decision Analysis (MCDA) was used in the present study as an instrument to compare the 16 selected reimbursement policy measures taking into account seven different, sometimes even conflicting , assessment criteria as well as identified weights and thresholds of the asked decision-makers and stakeholders. Of the various existing MCDA methods, an outranking approach using an algorithm called ELECTRE III (for further information see Annex 5) was found to be most suitable for the purpose of the study, which was to identity a policy mix based on the best practice approach taking into account the preferences of the stakeholders in the field.

One of the advantages of ELECTRE III is the fact that it allows for the inclusion of the concept of weak preference (between strong preference for e.g. a policy objective and being indifferent) and therefore reflects the real world decision-making processes better than other outranking methods. Based on the preferences of stakeholders for different policy objectives and their assessment of the contribution of selected policy measures to policy objectives (assessment criteria), the algorithm can create a ranking of policy measures - general or only for defined subgroups, e.g. for single stakeholder (groups) or (groups of) countries. It is possible that policy measures are ranked equally but considered indifferently.

As the ELECTRE algorithm compares parameters with a broad range of input-values, its results are sensitive to changes. Therefore, broad sensitivity analyses have been performed to test the stability of the underlying method and its appropriateness for the questions addressed in the present study (for the results of the sensitivity analyses, see Annex 13).

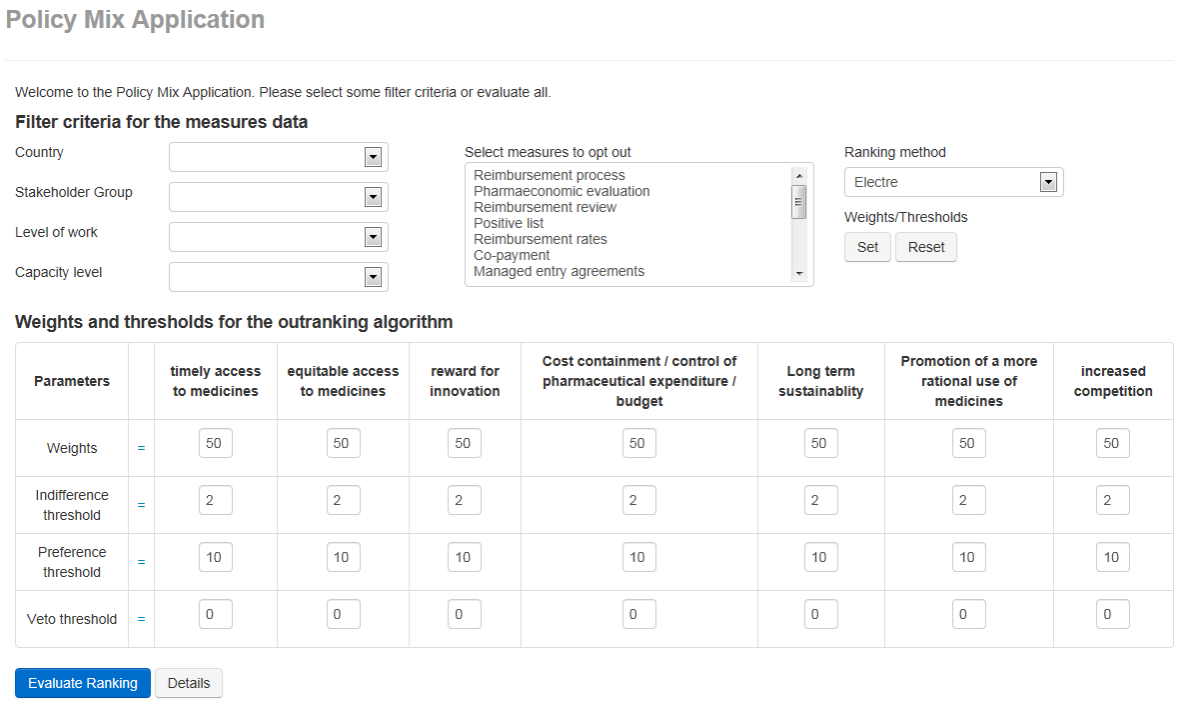
3.6 MCDA tool

As soon as agreement has been reached on the selected MCDA methodology (ELECTRE III), an electronic tool was developed to run several analyses for the total of (cleared) data from the stakeholder survey, and for specific groups (filtering specific countries and specific stakeholder groups). The tool is also designed to provide detailed information on the input variables (derived from the filled questionnaires) and the different calculation steps for the ELECTRE algorithm.

The tool was tested in summer 2013 with 'dummy' data since real data from the survey were not available at that time. In October 2013, the 'reality testing' was done with preliminary data; in mid-November 2013 the final data were entered. As in the course of time new ideas for analysis (e.g. building clusters of stakeholders and countries, weighting results) were developed, the tool was adopted accordingly.

See below a screenshot of the MCDA tool which was made available to the European Commission.

Figure 3.2: MCDA tool (screenshot)



The tool is also suitable for performing parts of the sensitivity analyses, e.g. by opting out single measures (for the results of the sensitivity analyses, cf. Annex 13).

3.7 Design of the questionnaire

The MCDA requires different elements, such as the identification of the assessment criteria, the determination of their importance, and the prioritising of the policy measures.

Therefore, the design of the questionnaire was strongly linked to the chosen MCDA methodology.

The questionnaire was split into three parts, following a general introduction which explained the rationale of the survey, offered some procedural and organisational information and asked for some key information (e.g. stakeholder group, country) from the respondents.

- *Part 1: Assessing preferences for defined policy objectives*

  Respondents were asked to indicate which relevance (low priority = 0 to high priority = 50) they attribute to the seven selected policy objectives (see section 3.2.1).

  It was decided to define the assessment of preferences for the policy objectives as well as for the policy measures (see below) via values on a broader scale in the form of a continuous rating tool. We used a sliding scale as a visual support.

  This decision for a larger scale, in contrast to a 5-level scale, for instance, offers a larger spectrum of answer possibilities und thus secures higher accurateness. Respondents could also choose to be indifferent (value 25), and they had the possibility not to answer at all ('I cannot assess').

- *Part 2: Assessment of reimbursement policy measures related to defined policy objectives*

  All reimbursement policy measures were linked to the same assessment criteria. Respondents were asked to assess the selected policy measures (see section 3.2.2) by answering the following question:

  How much do the mentioned policy measures (e.g. positive list, reference price system) contribute to the following objective?

  Assessment Criteria 1 (e.g. timely access to medicines): values to be entered between 0-50.

  Respondents were invited to indicate their assessment through values between 0 and 50 (no contribution = 0 to high contribution = 50). They were asked to assess

all selected 16 policy measures for each of the seven assessment criteria (policy objectives).

- *Part 3: Indicating thresholds*

  As for the performance of the (MCDA) 'thresholds' (indifference threshold, preference threshold, veto threshold), the respondents were asked to provide these thresholds, indicating them on a scale from 0 to 50. For definitions and details, see Annex 5 - MCDA methodology paper.

To support the respondents, the questionnaire was accompanied by a set of definitions of all listed policy objectives and policy measures, which could be opened in the online questionnaire as well as downloaded as a PDF file, and in fact sheets on the 28 EU Member States, which provided key information on the pharmaceutical systems in the countries, particularly on the reimbursement practices related to medicines (see also section 3.10). The full questionnaire is accessible in Annex 6. Stakeholders could also listen to audio files reading the definitions or watch several videos guiding them through the questionnaire.

3.8 Pilot and roll-out

Before the roll-out, we piloted the online survey with representatives of all stakeholder groups. The pilot was launched on August 9, 2013, and most respondents replied during August 2013; a few of them answered at the beginning of September 2013. A total of nine respondents (response rate: ~65 %) from six stakeholder groups (no replies from pharmacists or doctors), plus five staff members of the consortium and representatives of DG Sanco participated in the pilot. Their reactions to the questionnaire were, in general, mainly positive though the complexity of the questions was considered as a challenge. Based on the experiences made and lessons learned in the pilot (e.g. further refinement of the definitions/descriptions of the policy measures was needed; reduction in the length of the survey, etc.), we revised the questionnaire accordingly.

On 26 September 2013, we sent personalised links of the online questionnaire to a total of about 375 people in the 28 EU Member States (cf. Annex 7 for invitation e-mail). They were asked to respond by 7 October; the deadline was then extended till 14 October and later to 30 October 2013 (cf. Annex 7 for reminder(s). Data confidentiality was also guaranteed- Some activities (personal calls, contacts to the European associations) were undertaken to increase the response rate (see also section 3.10). Some European associations came back to us during the survey to learn about the response rate of their members and offered to approach their members to increase the response rate.

3.9 Data validation and compilation

We critically assessed the data from the online survey with regard to completeness and consistency, and in some cases we had to exclude data sets.

The following steps were taken to obtain the final data set for the MCDA:

- Compilation of pilot data results (of 9 stakeholders) and the results of the personalised stakeholder survey (of 76 stakeholders) = yielding a preliminary data set of 85 stakeholders[2].
- Adjustment of thresholds as soon as data quality problems with thresholds occurred:
  - In case the preference threshold was indicated lower than the indifference threshold, values were exchanged;
  - Missing values for thresholds were replaced by mean values of all stakeholder groups.
- In the questionnaire, respondents had to indicate the stakeholder group they belong to. There was also the possibility to state the option 'others'. For the MCDA, we needed the allocation of the respondents to one of the selected 8 stakeholder groups. Therefore, the respondents who selected 'others' (n=7) were recoded to the 8 stakeholder groups.
- Data quality problems with some stakeholder answers: Some of the stakeholders (n=9) only partially completed the questionnaire. Five incomplete data sets could be filled with mean values of the same stakeholder group. However, four incomplete questionnaires of patient organisations had to be excluded due to the high number of incomplete data.

Data validation was realised in the time period between the end of October and November 12, 2013. The final data set was entered into the electronic tool by November 13, 2013. The analyses were done in the time period between November 13 and December 13, 2013. Several sensitivity analyses were run in parallel. Cf. Annex 5 – MCDA methodology paper, cf. chapter 4 for results and cf. Annex 13 for results of the sensitivity analyses.

3.10 Quality assurance

In this study, quality was assured through the following instruments and approaches:

- *To ensure clear understanding*

  The questionnaire addressed different stakeholder groups which had a different level of knowledge of all or some of the reimbursement practices. Another challenge was that the policy measures can be and are, in reality, implemented in different ways (see section 2.5). To ensure a common understanding of the policy measures, as well as of the policy objectives, definitions were provided in the questionnaire (next to the policy objectives/policy measures and as a separate document for download), which also provided practical examples of how to understand the respective measure. The definitions had been reviewed by the EAHC/EC.

  The questionnaire aimed to be written in a clear and concise language; it was copy-edited.

[2] The final data set for the MCDA contained 81 completed questionnaires.

- *To inform the respondents*

  The questionnaire was accompanied by background information, both on the selected MCDA methodology (a methodology paper was made available for download) and the reimbursement practices. In addition to the definitions as mentioned above, fact sheets with key information on the countries were available for download in the online questionnaire; this was intended to help the respondents of stakeholder groups less familiar with reimbursement policies to get a better picture of the policies via learning about them in the context of their own countries.

  Furthermore, the study authors were available for queries and clarification; in some cases, we guided respondents through the questionnaire.

- *To critically review and test the methodology*

  There are different methodologies to perform a Multi-Criteria Decision Analysis (MCDA). After an in-depth internal discussion, our team decided to use the ELECTRE III approach.

  In addition to the consultation with EAHC/EC who provided valuable feed-back on the chosen methodological approach, the methodology was peer-reviewed by three external researchers.

  The online survey was piloted and revised on the basis of the lessons learned (see above). Respondents of the pilot survey were actively motivated to provide feed-back on the questionnaire. In the roll-out survey, respondents were also asked whether specific policy objectives or policy measures were missing in the questionnaire, and whether they had other comments.

  A number of sensitivity analyses were run (see Annex 13) in order to check whether the chosen methodology was sound.

- *To have a high response rate*

  We secured the cooperation and support of the European associations for the survey. They helped us to identify the most appropriate respondents in their national associations, and several of them motivated, via supportive e-mails or in personal discussions, their members to participate.

  We were responsive to requests and did our best to motivate reluctant respondents and to guide them through the survey. The deadline was extended twice, and reminders were sent twice to respondents who had not replied. For selected stakeholder groups and countries with a low response rate, we phoned people to motivate them to participate. At a PPRI (Pharmaceutical Pricing and Reimbursement Information) meeting with competent authorities for pricing and reimbursement at the end of October 2013, we personally approached respondents whose answers were still missing.

- *To ensure good data management*

  The data taken from the online survey were critically checked. During the data validation process, some data sets had to be excluded since they were incomplete.

  We worked with an electronic tool in which the MCDA ELECTRE III algorithm was programmed to do the analysis of the entered data. The tool, which was tested before its implementation, ensured that no mistakes were made, which might have occurred with a more manual data analysis (e.g. in Excel).

4 Results and analyses

This chapter is divided into four sections. First, statistics on the results of the stakeholder survey are presented (section 4.1). They are then followed by the assessments of stakeholders on policy objectives (section 4.2) and policy measures (section 4.3) analysed via the chosen MCDA approach. This chapter ends with a discussion section, including limitations (section 4.4).

4.1 Responses to the stakeholder survey

The stakeholder survey was piloted in August 2013 yielding 14 responses: nine from six different stakeholder groups (no replies from pharmacists or doctors) plus answers of five staff members of the consortium and representatives of DG Sanco.

After the refinement of the questionnaire taking into account the results of the pilot survey (cf. section 3.8), the roll-out of the final online survey started on 26 September 2013. The stakeholder survey was conducted in the time period between 26 September 2013 and 12 November 2013. Personalised e-mail invitations (cf. Annex 7) including the link to the online survey were sent to about 375 persons of more than 260 different institutions/organisations in all 28 EU Member States. Two reminders were sent per e-mail to the respondents in October 2013. Additional telephone calls to selected stakeholders helped motivate them to contribute to our survey.

Table 4.1: Overview of the responses per stakeholder group (incl. pilot results)

Stakeholder group	Contacted institutions/ organisations	Completed question-naires received	Answer: No competence or resources to complete the survey	Pilot results	Response rate	
					Number	In %
Competent authorities for pricing and reimbursement of medicines & public payers	46	24	1	3	**28**	60.87%
Consumers	39	5	9	1	**15**	38.46%
Doctors	33	1	6	-	**7**	21.21%
Generic medicines industry	20	9	1	2	**12**	60.00%
Patients	53	8	4	1	**13**	24.53%
Pharmacists	25	12	1	-	**13**	52.00%
Research-based pharmaceutical industry	50	17	2	2	**21**	42.00%
Total sum	**266**	**76**	**24**	**9**	**109**	**40.98%**

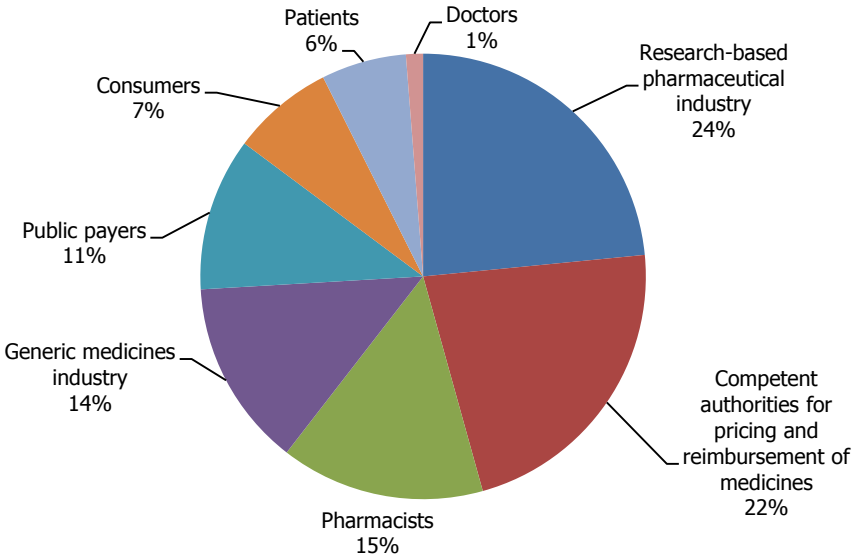
Of the 375 contacted persons, 76 completed the questionnaire (20 %). 24 persons said that they did not have the time or resources (33 %) or that the scope of the survey did not correspond to their field of competency (66 %).

Due to data quality problems (cf. section 3.9), four (partly incomplete) questionnaires of patient organisations had to be excluded from the MCDA. In total, 81 completed

questionnaires (9 respondents to the pilot survey and 76 minus 4 questionnaires of the roll-out phase) were taken into account for conducting the MCDA.

81 completed questionnaires represent about 30 % of the 266 contacted institutions.

Figure 4.1: Stakeholder representation in the MCDA



Legend: n=81

The majority of the completed questionnaires (38 %) came from the pharmaceutical industry (either representing associations of research-based or generic companies), 33 % from competent authorities for pricing and reimbursement of medicines and public payers, and 15 % from pharmacists.

Three groups of stakeholders (consumers, patients and doctors) consistently reported problems with completing the questionnaire. Of the 15 answers of consumer organisations, seven replied that they did not have the competency in the field of reimbursement of medicines and preferred refraining from answering to the survey. Additional two consumer organisations reported a lack of time to respond to the questionnaire resulting in a total of 60 % of negative replies from consumer organisations. 30 % of the answers from patient organisations were negative (mostly no competence in the field of reimbursement of medicines). However, most of the negative replies (85 % of the answers) were received from medical associations of doctors who stated that most of them did not have the time/resources to complete the complex survey.

Participation in the survey not only varied across stakeholder groups but also between countries.

Table 4.2: Completed questionnaires per stakeholder group (incl. pilot results) and country

Country	Research-based pharma-ceutical industry	Generic medicines industry	Patients *	Con-sumers	Competent authorities for pricing and reimburse-ment of medicines	Public payers	Pharma-cists	Doctors	Sum
Austria	2	1	1	1	1	1	0	0	**7**
Belgium	0	1	1**	1	1	0	1	0	**5**
Bulgaria	1	1	1	0	1	0	1	0	**5**
Croatia	1	0	0	0	0	0	0	0	**1**
Cyprus	1	0	0	0	0	1	0	0	**2**
Czech Republic	0	1	0	0	1	0	1	0	**3**
Denmark	1	0	0	1	1	0	0	0	**3**
Estonia	0	0	0	0	1	0	0	0	**1**
Germany	1	1	0	0	0	1	1	0	**4**
Greece	1	0	0	0	0	0	1	0	**2**
Finland	0	1	0	0	1	1	0	1	**4**
France	0	0	0	0	0	0	0	0	**0**
Hungary	1	0	0	0	0	1	0	0	**2**
Ireland	1	0	0	0	1	1	0	0	**3**
Italy	1	1	0	0	1	0	0	0	**3**
Latvia	0	0	0	0	1	0	0	0	**1**
Lithuania	0	0	0	0	1	1	0	0	**2**
Luxem-boug	0	0	0	0	0	0	0	0	**0**
Malta	1	0	1	0	1	0	0	0	**3**
Nether-lands	1	1	0	0	1	0	1	0	**4**
Poland	1	0	1	0	0	0	1	0	**3**
Portugal	1	1	0	1	0	1	1	0	**5**
Romania	1	1	0	0	0	0	0	0	**2**
Sweden	1	0	0	1	1	0	1	0	**4**
Slovenia	1	0	0	1	1	1	1	0	**5**
Slovak Republic	0	0	0	0	1	0	1	0	**2**
Spain	0	0	0	0	1	0	1	0	**2**
United Kingdom	0	0	0	0	1	0	0	0	**1**
EU level	1	1	0	0	0	0	0	0	**2**
Sum	**19**	**11**	**5**	**6**	**18**	**9**	**12**	**1**	**81**

Legend: The country was indicated by the respondents in the stakeholder survey.

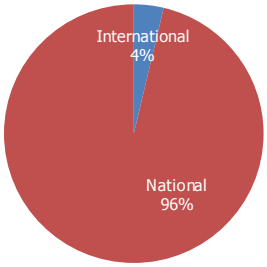
* Already excluding four completed questionnaires by patient organisations due to data quality problems (questionnaires were only partly filled).

** a patient organisation being active on EU-level

Most of the completed questionnaires were sent from Austria (n=7), Belgium, Bulgaria, Portugal and Slovenia (n=5 for each country respectively). No replies were recorded of stakeholders from France and Luxembourg.

The level of work which the stakeholders represented differed: most respondents represented national organisations. No representatives of an institution on regional level participated in the survey (cf. Figure 4.2).

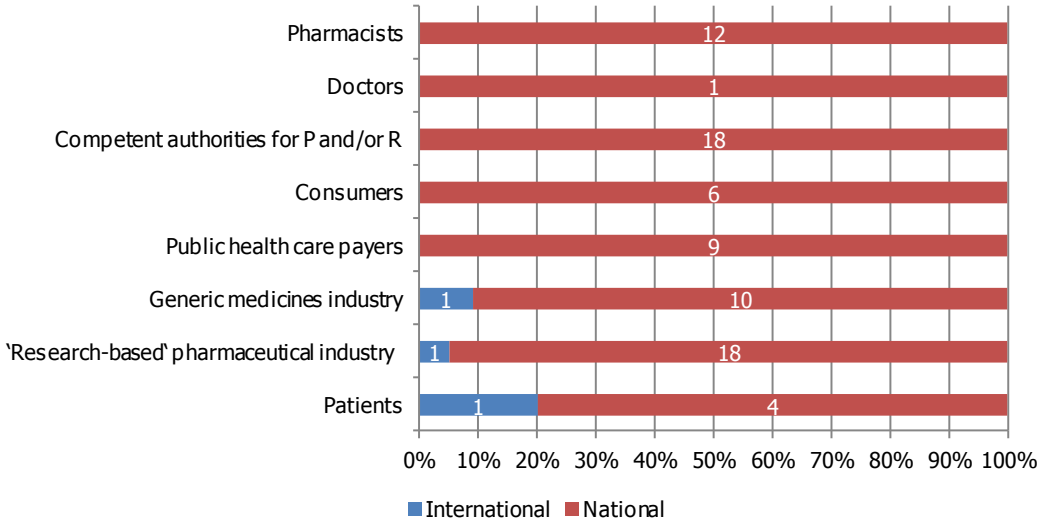
Figure 4.2: Level of work of stakeholders



Legend: n=81

Whereas competent authorities, public payers and industry (research-oriented and generic companies) are represented by their member associations' on national level, this is not always the case for patient organisations and doctor associations (e.g. in Germany, the national Chamber of Doctors exists, as well as additional relevant medical societies). To account for this split representativeness and responsibility, we addressed stakeholders of different organisational structures and asked stakeholders to indicate their 'level of work' (international, national or regional level). Only three organisations acting as representatives on EU level participated in the stakeholder query.

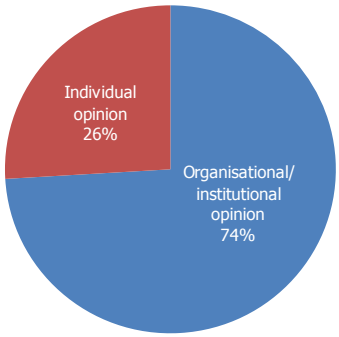
Figure 4.3: Level of work by stakeholder groups



Legend: Number in the bars indicates the number of participants per stakeholder group. P = Pricing; R = Reimbursement

Stakeholders were asked to indicate whether they were answering in their capacity as the organisation which they represent, or in their capacity as individuals (personal opinion).

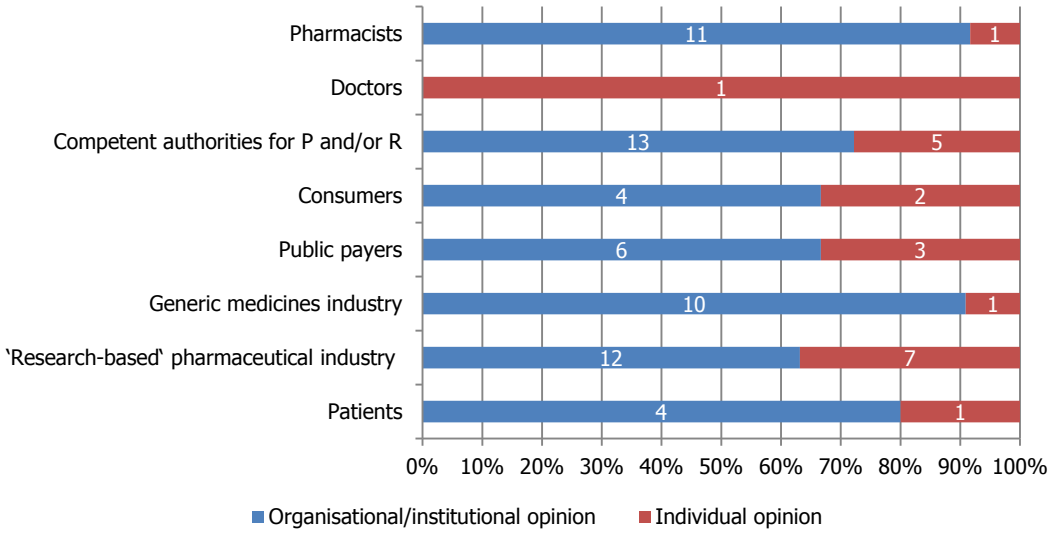
Figure 4.4: Capacity level of answering to the survey



Legend: n=81

Almost three quarters of the respondents who completed the survey indicated that they provided the institutional/organisational opinion (cf. Figure 4.4).

Figure 4.5: Capacity level of answering the survey by stakeholder group



The response from only one representative of the medical association of doctors was based on an individual opinion. More than 30% of the participants of consumer organisations, public payers and research-based pharmaceutical industry indicated that replies to the survey were their individual opinions. The study authors know from some respondents that they classified their answer as 'individual opinion' since an 'organisational/institutional opinion' would have been too cumbersome and time-intensive in order to get approval from the hierarchy.

4.2 Stakeholder assessment of the policy objectives

Stakeholders were asked to indicate which relevance they attribute to the selected policy objectives (cf. section 3.7) on a scale from 0-50, from no to high priority.

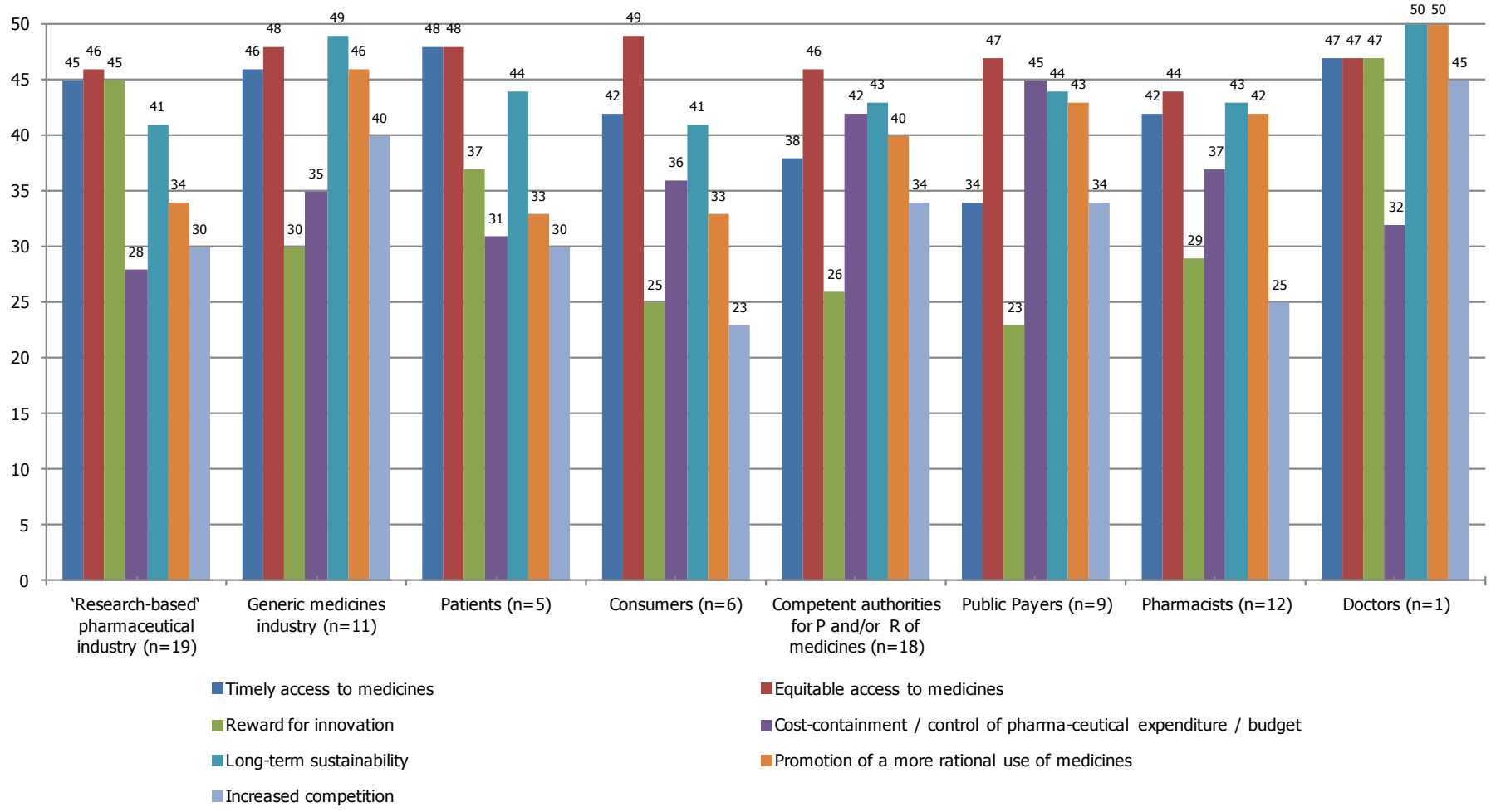
Table 4.3: Preferences for policy objectives (all stakeholders)

Policy objectives (assessment criteria)	Timely access to medicines	Equitable access to medicines	Reward for innovation	Cost-containment / control of pharmaceutical expenditure / budget	Long-term sustainability	Promotion of a more rational use of medicines	Increased competition
Weights (scale 0 'no priority'' to 50 'high priority')	42	46	32	36	43	39	32

Legend: n=81

Overall, all listed policy objectives were considered to be of high priority by the participating stakeholders, since all weights were indicated with values above 30. The policy objective 'equitable access to medicines' was of the highest priority, followed by 'long-term sustainability' and 'timely access to medicines'. Lower weights were attributed to 'reward for innovation' and 'increased competition'.

Figure 4.6: Preferences for policy objectives per stakeholder group

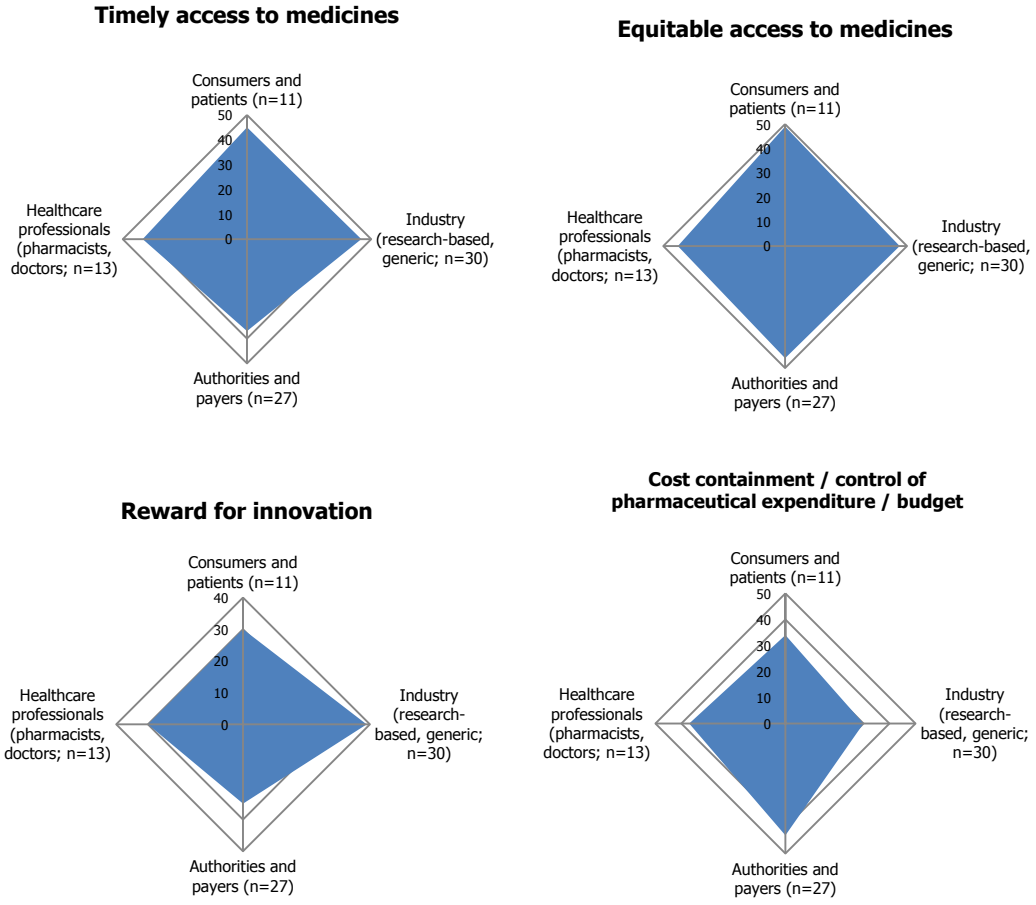


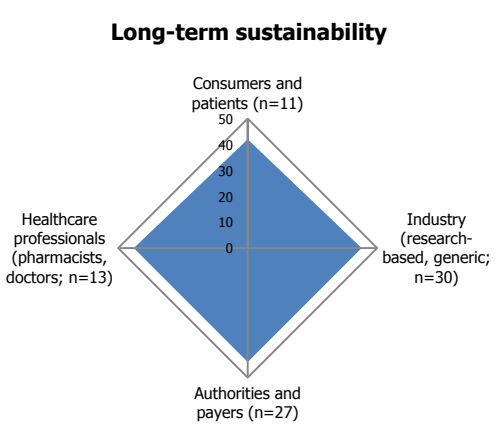
Legend: P = Pricing, R = Reimbursement

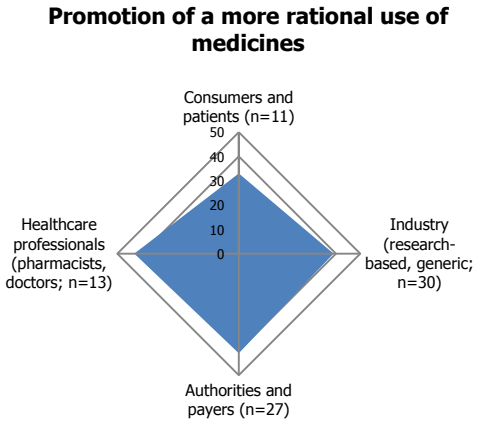
For the research-based pharmaceutical industry, 'equitable access', 'timely access' and 'reward for innovation' are of high relevance, whereas 'increased competition', 'timely' and 'equitable access' and 'promotion of a more rational use' are the preferred policy objectives for the generic medicines industry. For patient organisations, 'equitable' and 'timely access' are of equally high priority, 'long-term sustainability' ranking third. Consumer organisations displayed similar preferences. For competent authorities in the field of pricing and reimbursement, 'equitable access' followed by 'long-term sustainability' and 'cost-containment' are key policy objectives. 'Cost-containment' ranks second after 'equitable access', followed by 'long-term sustainability' for public healthcare payers. Pharmacists prefer 'equitable access', 'long-term sustainability' and 'timely access' as well as 'promotion of a more rational use of medicines'.

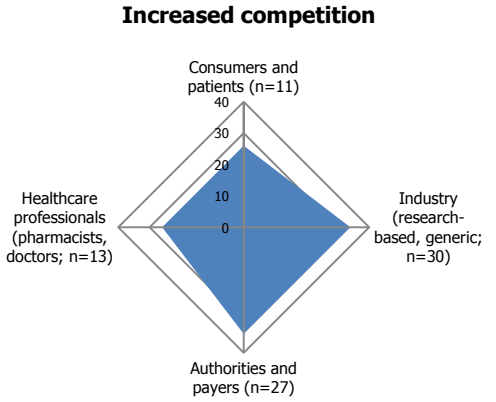
To analyse preferences across the stakeholder groups, four aggregated groups of stakeholders were formed (cf. section 3.3.1): industry (research-based and generic medicine companies), consumers and patients, authorities and payers (competent authorities for pricing and reimbursement of medicines and public healthcare payers) and healthcare professionals (pharmacists, doctors). Figure 4.7 shows the preferences for each defined policy objective per stakeholder group.

Figure 4.7: Preferences for policy objectives by aggregated stakeholder groups





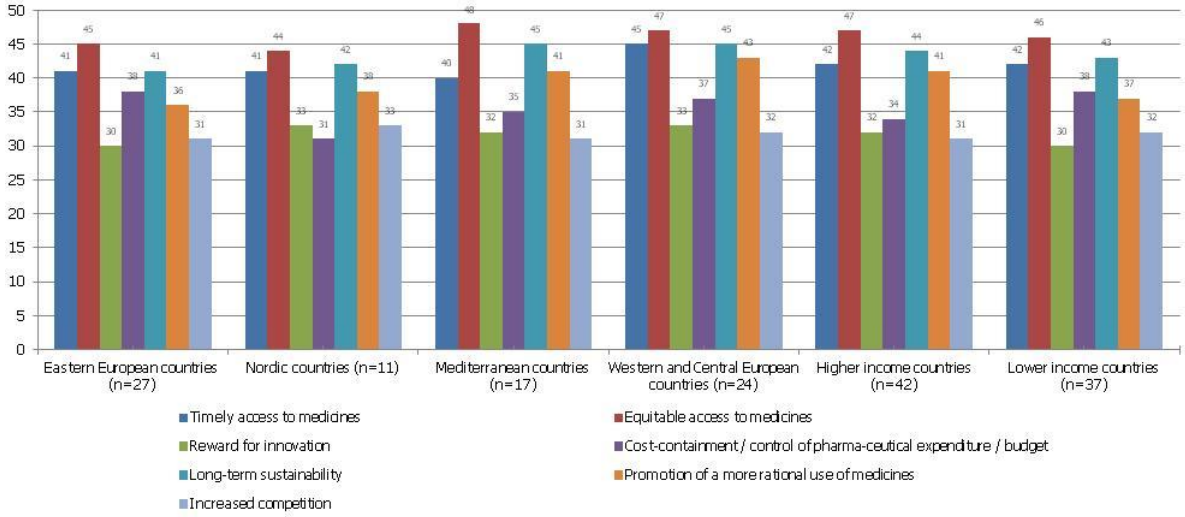




The policy objective that received most points (highest weight) was 'equitable access', and it is equally important for all stakeholders. This is also the case for the second most preferred policy objective - 'long-term sustainability', whereas 'promotion of a more rational use of medicines' is important for industry, healthcare professionals and authorities & payers, but less important for consumers & patients. 'Reward for innovation' is of high priority for the pharmaceutical industry, but to a lesser extent for consumers & patients and for authorities & payers. 'Timely access to medicines' is more important to consumers & patients and industry than healthcare professionals and authorities & payers. However consumers & patients and healthcare professionals see less need for 'increased competition' than industry or authorities & payers do. Not surprisingly, 'cost-containment' is the policy objective which authorities & payers attribute the highest priority to.

To allow for an analysis of the differences in stakeholders' preferences related to geographical regions and economic settings, different countries were aggregated to form four geographical regions and ranked into two groups of countries depending on their economic situations.

Figure 4.8: Preferences for policy objectives by aggregated geographical regions



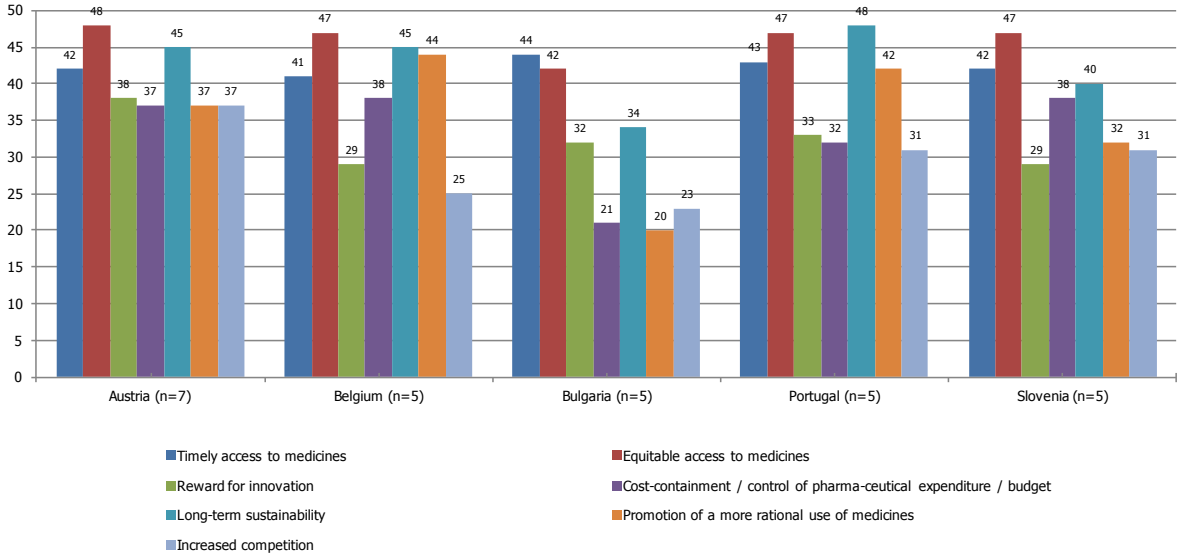
Legend: n = number of answers per group analysed; 'Eastern European countries' (11 countries) = Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovak Republic, Slovenia; 'Nordic countries' (3 countries) = Denmark, Finland, Sweden; 'Mediterranean countries' (6 countries) = Cyprus, Greece, Italy, Malta, Portugal, Spain; 'Western and Central European countries' (8 countries) = Austria, Belgium, Germany, France, Ireland, Luxemburg, Netherlands, UK; 'higher income countries' (14 countries) = countries with GDP/capita in Euro above the median of the 28 EU Member States, based on Eurostat figures as of November 21, 2013, i.e. Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Spain, Sweden, UK; 'lower income countries' (14 countries) = countries with GDP/capita in Euro above the median of the 28 EU Member States, based on Eurostat figures as of November 21, 2013, i.e. Bulgaria, Croatia, Czech Republic, Estonia, Greece, Hungary, Latvia, Lithuania, Malta, Poland, Portugal, Romania, Slovenia, Slovak Republic; No answers from Luxembourg and France.

For all geographical regions, 'equitable access to medicines' is the preferred policy objective of reimbursement policies of medicines. 'Long-term sustainability' is found second in all the geographical regions. 'Timely access' is equally important as 'long-term sustainability' for the Eastern European countries and the Western and Central European countries. 'Promotion of a more rational use of medicines' ranks third in the Western and Central European countries, the Mediterranean countries and the Nordic countries; only in the Eastern European countries 'cost-containment' is more important than rational use.

No substantial differences could be observed between higher and lower-income countries. Still, 'cost-containment' and 'increased competition' appear to be given higher priority in lower income countries. It should be acknowledged that all EU Member States are considered as high-income countries according to the definition of the World Bank [89], so the differentiation between higher and lower income countries is a ranking used among countries that as such are already seen as high-income.

Preferences for policy objectives can also be displayed at country level. Figure 4.9 shows preferences for countries where more than four completed questionnaires by different stakeholders were included in the MCDA (cf. Annex 9 for preferences at country level for all countries).

Figure 4.9: Preferences for policy objectives in selected countries



Legend: Only results of countries are shown where more than four national stakeholders completed the questionnaire.

For Austrian and Slovenian stakeholders, 'equitable access to medicines', 'long-term sustainability' and 'timely access to medicines' are the preferred policy objectives. In Belgium, 'equitable access' is followed by 'long-term sustainability' and 'promotion of a more rational use'. For Bulgarian stakeholders, the picture looks different: 'timely access' ranks before 'equitable access' and 'long-term sustainability'. 'Cost-containment' and 'promotion of a more rational use' play a minor role compared to the other countries. In Portugal, 'long-term sustainability' is the most important policy objective for the stakeholders.

4.3 Stakeholder assessment of policy measures

Stakeholders were asked to assess how much the 16 selected reimbursement practices related to medicines (cf. section 3.7) contributed to achieving each of the seven selected policy objectives. A scale from 0-50 was again used, indicating a range from no contribution to full contribution.

As a result of the questionnaire, for each stakeholder, a so-called 'performance matrix' was drawn showing the assessment results for each policy objective and measure.

Feeding the information of 81 datasets into the MCDA (cf. section 3.5), a ranking of reimbursement policies is produced, representing the preferred policy mix which stakeholders assess to be able to achieve best the policy objectives.

Table 4.4: Example – assessment results of the stakeholder group of pharmacists

Reimbursement policies	Policy objectives (assessment criteria)						
	Timely access to medicines	***Equitable access to medicines***	***Reward for innovation***	***Cost-containment / control of pharmaceutical expenditure / budget***	***Long-term sustainability***	***Promotion of a more rational use of medicines***	***Increased competition***
Co-payment	19.0	28.9	20.7	27.4	30.4	25.1	19.7
Differential pricing	13.9	25.8	20.0	18.0	18.6	7.0	16.1
Discounts / rebates / price negotiations / clawback	14.2	13.1	11.4	29.0	18.7	8.2	24.0
External Price Referencing	21.8	28.0	18.4	36.7	27.7	14.3	23.1
Generic substitution	36.1	37.3	13.5	42.1	41.4	30.6	40.6
INN prescribing	32.0	30.1	11.4	36.6	35.9	26.3	33.8
Managed-entry agreements	25.1	26.6	31.7	31.0	28.1	16.8	21.6
Pharmaceutical budgets	24.4	24.3	16.9	37.3	33.2	29.8	21.0
Pharmaco-economic evaluation	32.4	23.0	36.6	33.0	34.9	33.0	24.8
Positive list	30.0	24.2	21.3	28.7	26.6	13.9	17.8
Reference price system	33.7	24.4	21.9	40.3	30.8	22.2	30.6
Reimbursement process	41.9	25.1	24.7	37.0	33.1	22.2	26.4
Reimbursement rates	35.8	28.6	25.7	33.1	27.7	22.2	27.9
Reimbursement review	30.6	22.6	16.4	35.0	29.3	26.9	27.6
Tendering	17.7	14.9	8.6	31.6	15.6	7.9	29.1
Value-based pricing	22.3	20.9	33.1	23.0	17.9	20.1	20.1

Legend: Mean values of the assessments of pharmacists (n=12) are displayed. A scale from 0-50 was used, indicating a range from no contribution to full contribution.

Every assessment of a single stakeholder has the same influence on the overall ranking. This means that stakeholder groups that are represented by a higher number of participants in the survey have a higher influence on the ranking of the policy measures. Furthermore, the results of all stakeholders are taken into account no matter at which capacity level they replied (organisational vs. individual level, cf. Figure 4.4). Additionally to the overall ranking, we also analysed ranking positions at the different capacity levels (cf. section 4.3.4) and of weighted stakeholder groups (every stakeholder group has the same influence on the result, cf. section 4.3.6).

Table 4.5 shows the result of the selected MCDA, the ranking of policy measures according to stakeholder preferences, which is the key result of this study.

Table 4.5: Ranking of policy measures according to stakeholder preferences

	Rank
Pharmaco-economic evaluation	1
Value-based pricing	2
Reimbursement process	3
Managed-entry agreements	4
Reimbursement review	5
Positive list	5
Reimbursement rates	5
Generic substitution	5
Reference price system	6
Pharmaceutical budgets	6
Differential pricing	7
INN prescribing	7
Co-payment	8
Discounts / rebates / price negotiations / clawback	8
Tendering	9
External Price Referencing	10

Legend: n=81

Overall, stakeholders considered 'pharmaco-economic evaluation' as the most appropriate reimbursement policy to achieve the policy objectives in accordance with the preferences they had attributed to them. 'Value-based pricing' and 'reimbursement process' were ranked second and third, followed by 'managed-entry agreements'. Four measures were equally ranked fifth. 'Discounts / rebates / price negotiations / clawback', 'tendering' and 'external price referencing' were ranked last by the stakeholders. The selected MCDA approach allows ranking policy measures on equal positions.

4.3.1 Ranking by stakeholder groups

An analysis of the results per stakeholder group (cf. Table 4.6) showed somewhat different rankings of policy measures:

For the **research-based pharmaceutical industry**, 'pharmaco-economic evaluation' achieves best all the selected policy objectives. Three measures are on the second rank: 'value-based pricing', 'reimbursement process' and 'managed-entry agreements'. 'Reimbursement rates' are ranked third. The last places go to 'generic substitution' (rank 8), 'tendering' (rank 9), 'reference price system' (rank 9), 'external price referencing' (rank 10) and 'INN prescribing' (rank 10). Briefly said, research-based pharmaceutical industry seems to prefer newer and more sophisticated reimbursement policies such as 'value-based pricing' and 'managed-entry agreements', whereas traditional generic policies such as 'INN prescribing' and 'generic substitution' are scored at a lower level.

For **generic companies**, 'generic substitution' (rank 1), 'positive list' (rank 2) and 'reimbursement rates' (rank 3) contribute most to achieving all selected policy objectives. 'Co-payment' (rank 10), 'pharmaceutical budgets' (rank 11) as well as 'tendering', 'discounts and rebates' and 'external price referencing' (each rank 12) are seen as least important. 'Generic substitution' being a key reimbursement policy to increase generic shares in the pharmaceutical market is clearly preferred by the generic companies, whereas other traditional generic policies such as 'INN prescribing' (rank 8) and 'reference price system' (rank 9) are not scored highly by the generic companies. A 'positive list' is highly valued, whereas other newer and more innovative policy measures (i.e. 'value-based pricing' and 'managed-entry agreements') play a minor role for the generic industry, since they produce generics and do not sell new and innovative medicines. 'Tendering' is critically seen by the generic medicines industry since according to their feedback it might foster market concentration and drive some competitors out of business.

Table 4.6: Ranking of policy measures by stakeholder groups

Policy measures	Research-based pharma-ceutical industry	Generic medi-cines industry	Patients	Consumers	Competent authorities for P+R	Public payers	Pharmacists	Doctors
Number of completed questionnaires	*19*	*11*	*5*	*6*	*18*	*9*	*12*	*1*
Pharmaco-economic evaluation	1	4	6	5	2	2	1	3
Value-based pricing	2	5	11	1	7	3	8	3
Reimbursement process	2	6	10	6	1	3	3	4
Managed-entry agreements	2	6	5	6	6	10	6	7
Reimbursement review	5	7	9	4	7	5	6	4
Positive list	7	2	9	7	4	4	9	5
Reimbursement rates	3	3	6	6	8	8	4	4
Generic substitution	8	1	1	3	5	1	2	2
Reference price system	9	9	2	8	3	6	4	6
Pharmaceutical budgets	6	11	9	11	7	7	7	6
Differential pricing	4	6	4	9	11	12	11	4
INN prescribing	10	8	3	7	4	3	5	5
Co-payment	6	10	8	10	9	9	8	1
Discounts / rebates / price negotiations / clawback	7	12	4	11	10	11	13	1
Tendering	9	12	12	2	4	6	12	4
External Price Referencing	10	12	7	11	11	11	10	1

Legend: P+R = pricing and reimbursement

Many of the contacted **patient organisations** reported problems completing the questionnaires since they did not feel confident or believed to have insufficient knowledge of the policy field of reimbursement. Four incompletely filled questionnaires had to be excluded from the stakeholder survey, leaving only five answers from patient organisations. For patient organisations, typical generic policies such as 'generic substitution' (rank 1), 'reference price system' (rank 2) and 'INN prescribing' (rank 3) can be found on the top three ranking positions. Last positions go to 'reimbursement process' (rank 10), 'value-based pricing' (rank 11) and 'tendering' (rank 12). Ranking results of patient organisations have to be interpreted with care since many stakeholders reported difficulties in understanding and assessing the selected policy measures (e.g. differential pricing). Reimbursement policies such as 'positive list' (rank 9), 'co-payment' (rank 8), 'tendering' (rank 12) and 'reimbursement process' (rank 10) are negatively assessed (compared to the other selected measures), being seen in connection with potential contact points with patients and burdensome reimbursement procedures. 'Discounts / rebates / price negotiations / clawback' (rank 4) achieved the best ranking position (apart from the results of the assessment of one representative of medical doctors) by patient organisations.

Consumer organisations were included in the stakeholder survey, since they represent the voices of taxpayers in European countries before becoming a patient and getting into contact with healthcare systems in this context. It can be observed that consumers ranked the policy measures differently than patients. According to consumers, 'value-based pricing' (rank 1), 'tendering' (rank 2) and 'generic substitution' (rank 3) take the top three positions, whereas 'differential pricing' (rank 9), 'co-payment' (rank 10), 'discounts / rebates / price negotiations / clawback' (rank 11), 'external price referencing' (rank 11) and 'pharmaceutical budgets' (rank 11) hold the last positions. 'Tendering' achieves its top ranking position within the ranking result of consumer organisations. However, many consumer organisations replied to the invitation to participate in the stakeholder survey by saying that the policy field of reimbursement of medicines was not within their competence.

As regards **competent authorities for pricing and reimbursement** of medicines, 'reimbursement process' (rank 1), 'pharmaco-economic evaluation' (rank 2) and 'reference price system' (rank 3) are the three policy measures that achieve best all selected policy objectives. Three policy measures, i.e. 'INN prescribing', 'positive list' and 'tendering', can be found on the fourth place. 'Co-payment' (rank 9), 'discounts / rebates / price negotiations / clawback' (rank 10), 'differential pricing' and 'external price referencing' (both rank 11) are ranked last. Briefly said, 'typical and classical' reimbursement policies with clear and transparent procedures take the leading positions. 'Tendering' (rank 4) achieves a better result within the stakeholder group of competent authorities than in other stakeholder groups. It is interesting to see that 'discounts and rebates' (in the understanding and interpretation of negotiating something) are rather seen as not contributing as much to achieving the policy objectives as the other selected policy measures.

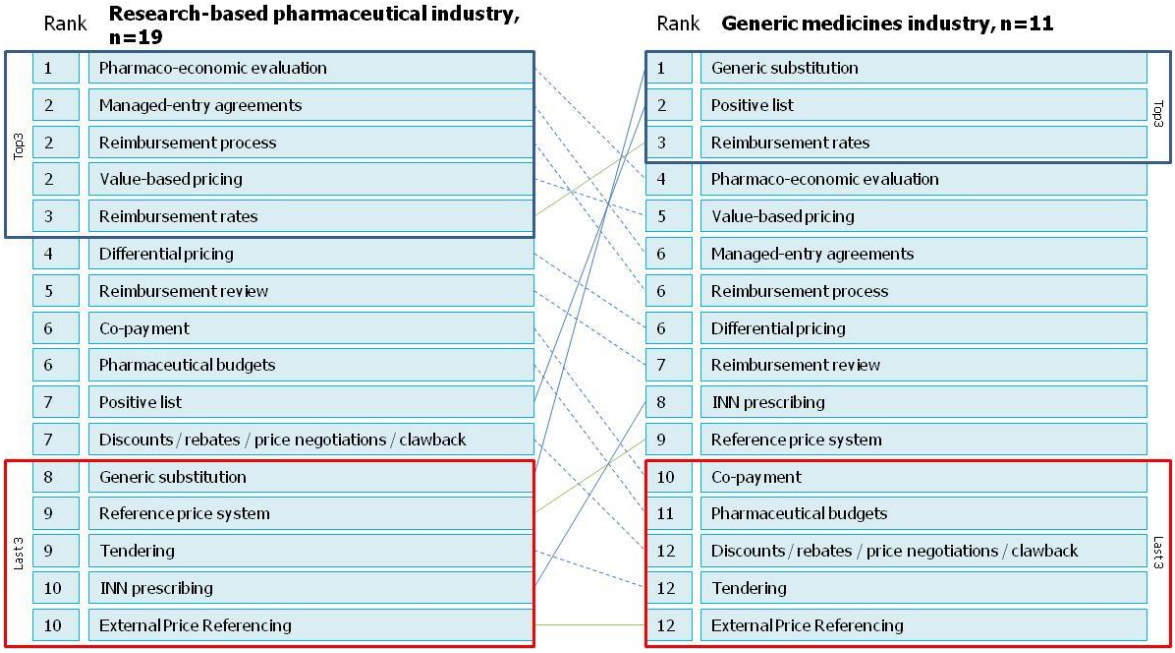
Within the stakeholder group of **public healthcare payers**, 'generic substitution' (rank 1), 'pharmaco-economic evaluation' (rank 2), 'reimbursement process', 'value-based pricing' and 'INN prescribing' (each rank 3) hold top ranking positions. 'Managed-entry agreements' (rank 10), 'discounts / rebates / price negotiations / clawback' (rank 11), 'external price referencing' (rank 11) and 'differential pricing' (rank 12) are in the lower part of the ranking results. It can be observed that public payers prefer a mixture of 'traditional' reimbursement policies, such as 'reimbursement process' (rank 3) and 'positive list' (rank 4), reimbursement policies targeted at generics and cost-containment, such as 'generic substitution' (rank 1) and 'INN prescribing' (rank 3) and 'new and more innovative' reimbursement policies such as 'value-based pricing' (rank 3). 'Differential pricing' gets its lowest ranking position with public healthcare payers. 'Discounts and rebates' as well as 'managed-entry agreements' are not favoured by payers.

'Pharmaco-economic evaluation' (rank 1), 'generic substitution' (rank 2) and 'reimbursement process' (rank 3) hold top ranking positions within **pharmacists**. 'Differential pricing' (rank 11), 'tendering' (rank 12) and 'discounts / rebates / price negotiations /clawback' (rank 13) can be found on the last positions of the ranking results. In comparison to the other selected policy measures, 'tendering' is assessed as least appropriate in contributing to the selected policy objectives, which might be due to the reported negative experiences of pharmacists with tendering in the out-patient sector [43,90].

Since **doctors** were only represented by one stakeholder, ranking results of doctors are not seen as significantly representative for this stakeholder group and were not analysed.

We also analysed in further detail the differences of the ranking results of each stakeholder group (excluding doctors) in comparison to the others. In figures 4.10 to 4.12, these comparisons for similar groups of stakeholders are drawn (research-based pharmaceutical industry vs. generic medicines industry, competent authorities vs. public payers, patients vs. consumers).

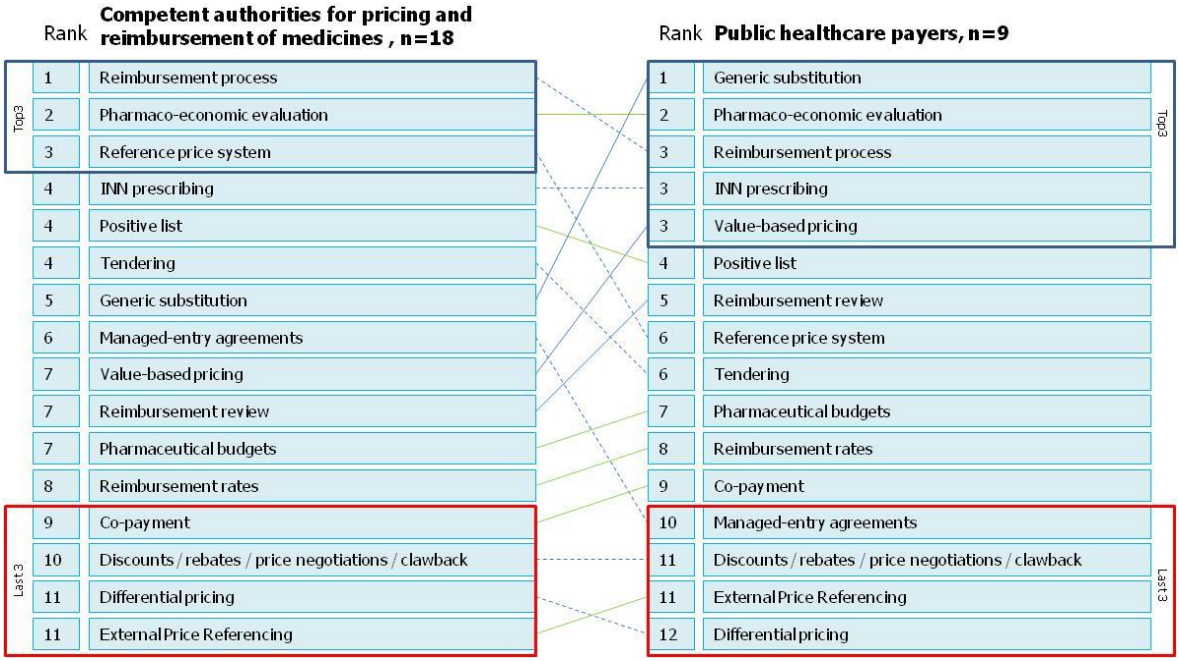
Figure 4.10: Comparison of the rankings of policy measures by research-based pharmaceutical industry and generic medicines industry



Legend: The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the generic medicines industry. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the generic medicines industry. A green straight line indicates the same rank according to the assessment of research-based industry and generic industry.

In Figure 4.10, it can be observed that the positions of the research-based pharmaceutical industry and generic medicines industry are different. The top two ranking positions of the research-based companies were assessed less positively by the generic companies, whereas the top two reimbursement policies of generic companies can be found in the lower part of the ranking results of the research-based industry. Only 'reimbursement rates' hold the same position (rank 3) in both ranking lists. The difference in the positions of these two stakeholder groups is obvious since the research-based pharmaceutical industry is more interested in innovative approaches, such as 'managed-entry agreements' and 'value-based pricing', than generic policies, such as 'generic substitution'. 'Tendering' and 'external price referencing' can be found in the lower parts of the ranking results of both stakeholder groups.

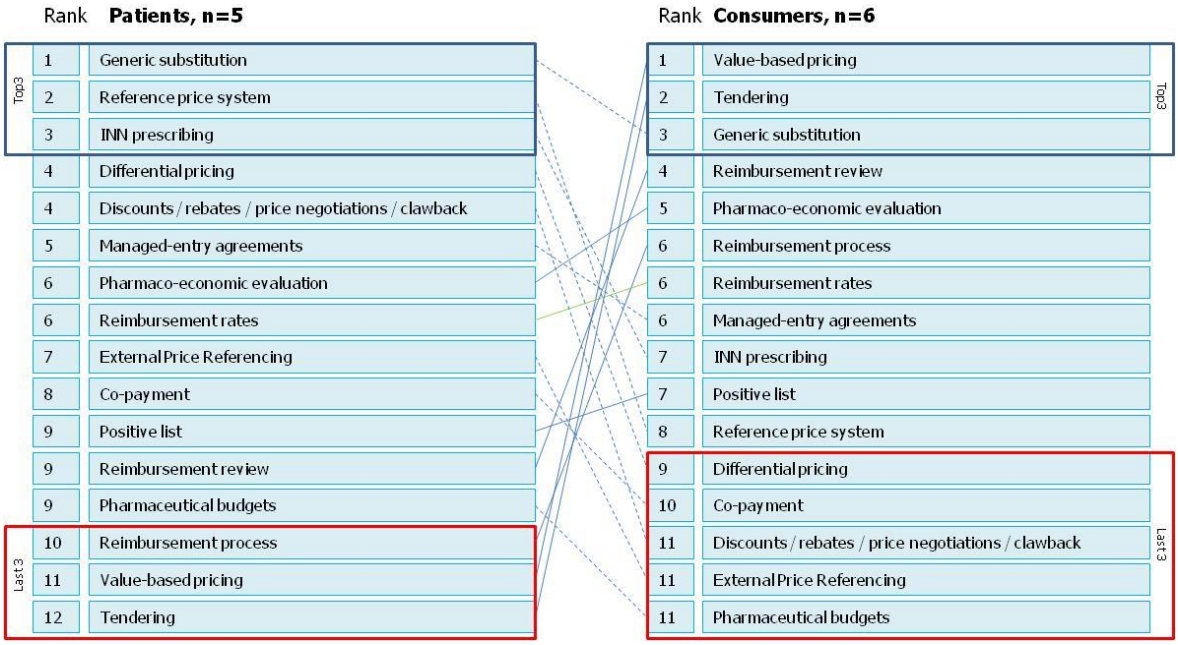
Figure 4.11: Comparison of the rankings of policy measures by competent authorities of pricing and reimbursement of medicines and public healthcare payers



Legend: The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the public healthcare payers. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the public healthcare payers. A green straight line indicates the same rank according to the assessment of competent authorities and public payers.

A comparison of the ranking results of competent authorities and public healthcare payers shows some similarities. Six policy measures (38 % of all measures) hold the same positions in both ranking lists. The two policy measures 'reimbursement process' and 'pharmaco-economic evaluations' are among the top three positions in both lists. Both stakeholders agree in their assessment of the three reimbursement measures 'discounts', 'differential pricing' and 'external price referencing' as less appropriate to achieve the policy goals; these measures hold positions in the lower part of the ranking lists.

Figure 4.12: Comparison of the rankings of policy measures by patients and consumers

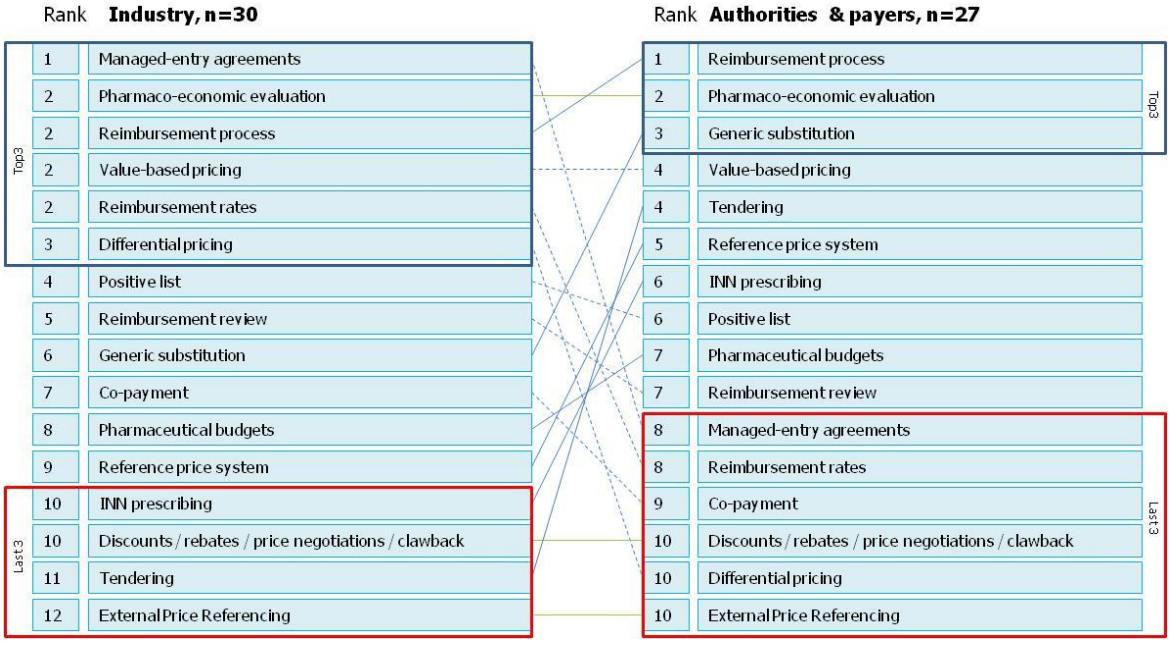


Legend: The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the consumers. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the consumers. A green straight line indicates the same rank according to the assessment of consumers and patients.

It can be observed that patients and consumers assess some reimbursement policies completely differently. Two policy measures – 'value-based pricing' (rank 11) and 'tendering' (rank 12) – which hold last ranking positions in the group of patients, hold top positions within consumer organisations – rank 1 and rank 2 respectively. Only 'generic substitution' can be found in both lists among the first three ranking positions. Only 'reimbursement rates' share the same positions (rank 6).

For a more detailed analysis, the ranking results of the four aggregated stakeholder groups (cf. section 3.3.1) are derived from the MCDA tool and are compared to each other in the figures below. Differences between the individual ranking lists of the eight stakeholders and the aggregated results are displayed in Annex 12.

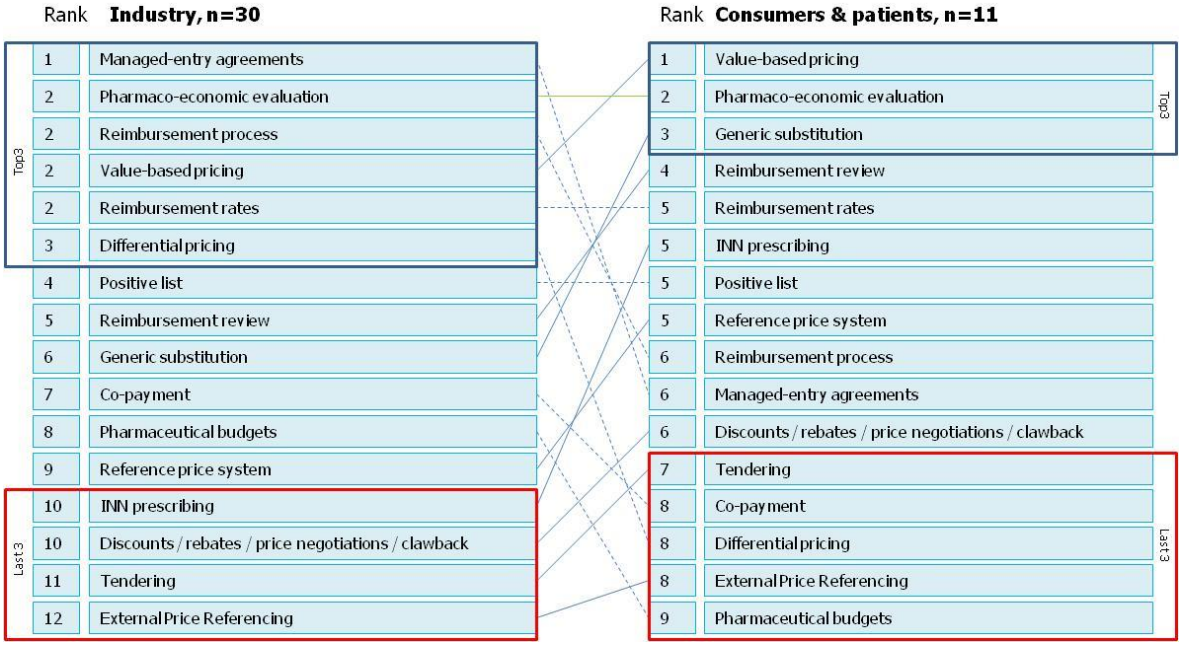
Figure 4.13: Comparison of the rankings of policy measures by aggregated stakeholder groups – industry vs. authorities & payers



Legend: 'Industry' = research-based and generic medicines industry, 'Authorities & payers'= competent authorities for pricing and reimbursement of medicines and public healthcare payers. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the authorities & payers. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the authorities & payers. A green straight line indicates the same rank according to the assessment of industry and authorities & payers.

Two policy measures, 'pharmaco-economic evaluations' and 'reimbursement process', hold top positions of the ranking lists of both industry as well as authorities & payers. However, the two aggregated stakeholder groups have contradictory opinions: three policy measures, 'managed-entry agreements', 'reimbursement rates' and 'differential pricing', rated by the industry among the top three reimbursement policies can be found at the bottom of the ranking list of authorities & payers. The number of reimbursement policies in positions at the very end of the ranking lists (either at the top or at the end) is high in both stakeholder groups: industry positively ranks six policy measures in achieving the selected objectives among the first three places, whereas authorities & payers have a larger number of six policy measures holding the last three positions of the ranking list.

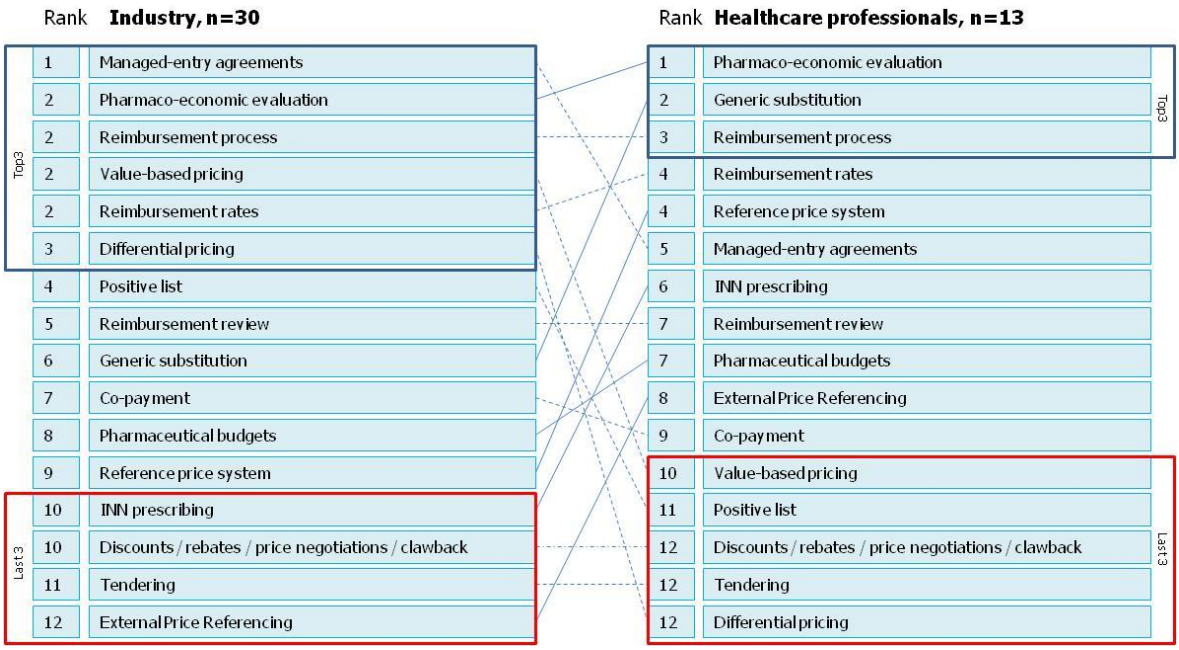
Figure 4.14: Comparison of the rankings of policy measures by aggregated stakeholder groups – industry versus consumers & patients



Legend: 'Industry' = research-based and generic medicines pharmaceutical industry, 'Consumers & patients'= patient and consumer organisations. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the consumers & patients. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the consumers & patients. A green straight line indicates the same rank according to the assessment of industry and consumers & patients.

Industry assessment has some points in common with that of consumers & patients related to the end position of the ranking lists (top and lower parts): 'value-based pricing' and 'pharmaco-economic evaluation' hold top positions and 'tendering' and 'external price referencing' hold the lowest positions. The differences in the ranking lists between industry and consumers & patients are not that remarkable as between the industry and authorities & payers.

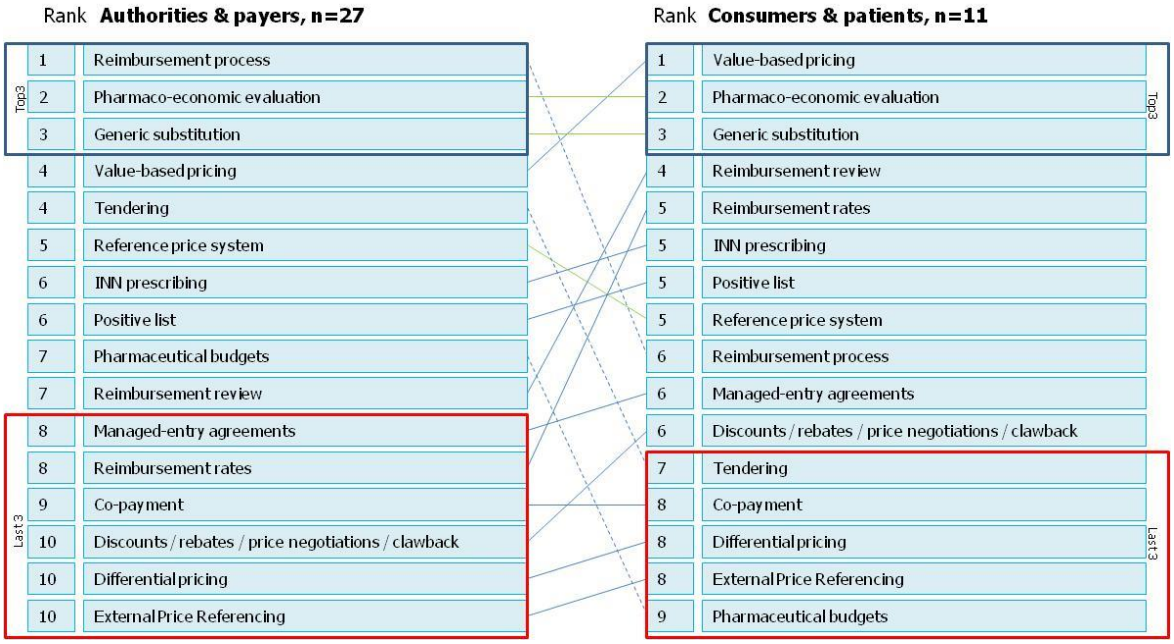
Figure 4.15: Comparison of the rankings of policy measures by aggregated stakeholder groups – industry and healthcare professionals



Legend: 'Industry' = research-based and generic medicines pharmaceutical industry, 'Healthcare professionals'= pharmacists and doctor associations. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the healthcare professionals. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the healthcare professionals. A green straight line indicates the same rank according to the assessment of industry and healthcare professionals.

On the one hand, industry and healthcare professionals see the same two policy measures as the ones contributing the most to achieving the selected policy objectives: 'pharmaco-economic evaluation' and 'reimbursement process'. On the other hand, two policy measures holding top positions within the industry - 'value-based pricing' and 'differential pricing' – are less positively assessed by healthcare professionals.

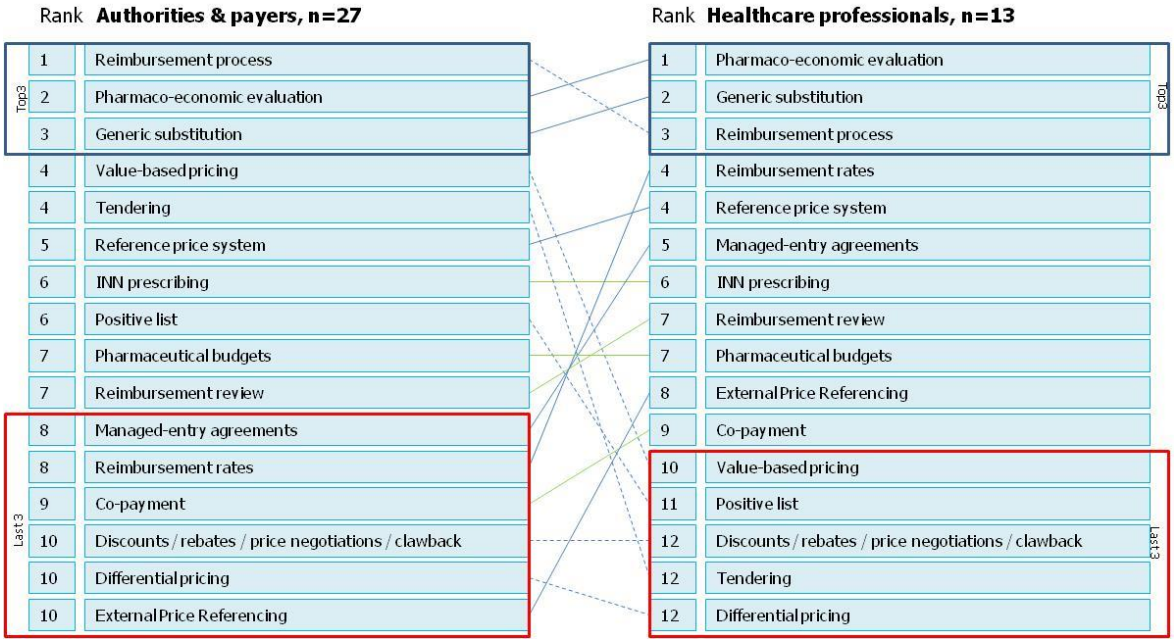
Figure 4.16: Comparison of the rankings of policy measures by aggregated stakeholder groups – authorities & payers and consumers & patients



Legend: 'Authorities & payers'= competent authorities for pricing and reimbursement of medicines and public healthcare payers, 'Consumers & patients'= patient and consumer organisations. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the consumers & patients. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the consumers & patients. A green straight line indicates the same rank according to the assessment of authorities & payers and consumers & patients.

Both aggregated stakeholder groups apparently provide a clear picture of the top three policy measures which contribute the most to achieving the selected policy objectives. Two policy measures are equally ranked among the top three positions: 'pharmaco-economic evaluations' (rank 2) and 'generic substitution' (rank 3). As far as 'co-payment', 'differential pricing' and 'external price referencing' is concerned, both aggregated stakeholder groups share the same position: these policy measures achieve last or second last positions in both ranking lists. 'Value-based pricing', which is ranked first by consumers & patients, also holds a prominent position (rank 4) with authorities & payers.

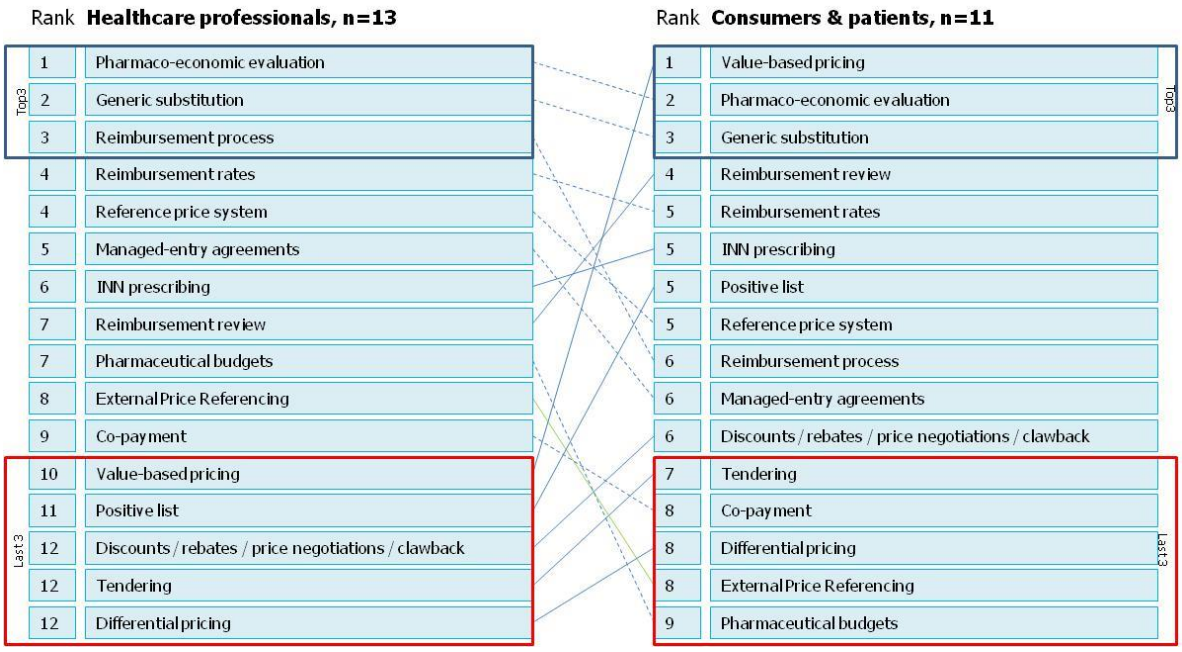
Figure 4.17: Comparison of the rankings of policy measures by aggregated stakeholder groups – authorities & payers and healthcare professionals



Legend: 'Authorities & payers'= competent authorities for pricing and reimbursement of medicines and public healthcare payers, 'healthcare professionals'= pharmacists and doctor associations. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by the healthcare professionals. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by the healthcare professionals. A green straight line indicates the same rank according to the assessment of authorities & payers and healthcare professionals.

Authorities & payers and healthcare professionals rank the same three policy measures among the top three (even though not on the same ranking positions): 'reimbursement process', 'pharmaco-economic evaluation' and 'generic substitution'. Further three measures ('INN prescribing' – rank 6, 'pharmaceutical budgets' – rank 7 and 'co-payment' – rank 9) hold the same ranks in both ranking lists. 'Tendering' (rank 12) and 'value-base pricing' (rank 10) contribute less to achieving the objectives according to healthcare professionals compared to the assessment of authorities & payers (both policy measures on rank 4).

Figure 4.18: Comparison of the rankings of policy measures by aggregated stakeholder groups – healthcare professionals and consumers & patients

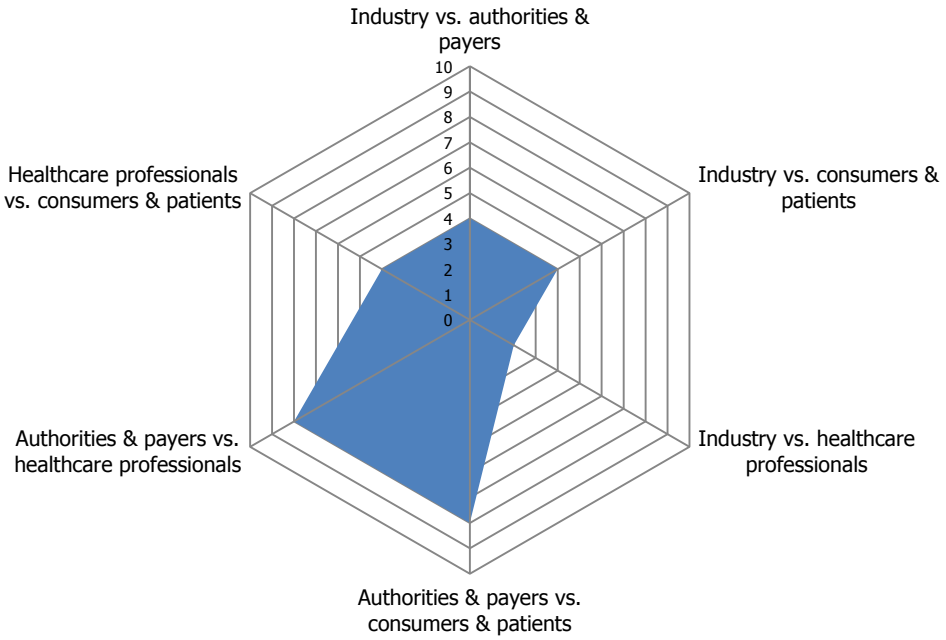


Legend: 'healthcare professionals'= pharmacists and doctor associations, 'consumers & patients'= patient and consumer organisations. The blue dotted line signals a lower rank of the respective reimbursement policy as assessed by consumers & patients. The blue straight line signals a higher rank of the respective reimbursement policy as assessed by consumers & patients. A green straight line indicates the same rank according to the assessment of healthcare professionals and consumers & patients.

Healthcare professionals and consumers & patients have the same number of reimbursement policy measures among the top three and last three positions of the ranking lists. Again, two measures – 'generic substitution' and 'pharmaco-economic evaluation' – are found among the top three ranks of both stakeholder groups. However, 'value-based pricing', which is ranked first by consumers and patients, holds rank 10 in the list of healthcare professionals.

Looking for an indicator of the similarities and differences among aggregated stakeholder groups, the sum of the number of equal positions and the number of common reimbursement policies among top three and last three positions in the ranking lists minus the number of policies assessed totally contradictory (in the ranking list of one stakeholder group one specific measure can be found among the top three measures, whereas the same measure is among the last measures in a ranking list of another stakeholder group) can be taken.

Figure 4.19: Comparison of the rankings of policy measures by aggregated stakeholder groups – degree of similarity



Legend: Results are achieved by counting the number of equal positions in ranking results plus the number of common policy measures among the top three and last three ranking positions – minus number of totally contradictory ranking results

Authorities & payers ranked the policy measures in a similar way as did the healthcare professionals and the consumers & patients, whereas industry and healthcare professionals showed dissimilar ranking results.

4.3.2 Ranking by geographical regions and income level

Analysis of the stakeholders' assessment of the policy measures per countries in terms of the geographical regions and the income level of the countries are presented in Table 4.7.

Table 4.7: Ranking of policy measures by geographical regions or income level

Geographical regions or income level/Policy measures	EU level	Eastern European countries	Nordic countries	Medi-terranean countries	Western and Central European countries	Higher income countries	Lower income countries
Number of completed questionnaires	*2*	*27*	*11*	*17*	*24*	*42*	*37*
Pharmaco-economic evaluation	5	3	2	1	1	1	1
Value-based pricing	7	1	2	3	4	2	2
Reimburse-ment process	8	4	2	2	2	1	2
Managed-entry agreements	6	2	4	6	3	2	3
Reimburse-ment review	10	7	5	4	5	3	4
Positive list	1	5	3	5	7	4	4
Reimburse-ment rates	2	4	6	3	6	5	3
Generic substitution	3	6	1	6	2	2	5
Reference price system	6	8	6	9	9	7	6
Pharma-ceutical budgets	11	5	8	9	10	7	5
Differential pricing	4	5	10	10	14	9	7
INN prescribing	4	10	11	8	8	6	8
Co-payment	9	8	10	7	11	8	6
Discounts / rebates / price negotiations / clawback	12	11	8	11	13	9	10
Tendering	13	9	7	12	12	10	9
External Price Referencing	14	12	9	12	14	11	11

Legend: n = number of answers by stakeholders; 'Eastern European countries' (11 countries) = Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovak Republic, Slovenia; 'Nordic countries' (3 countries) = Denmark, Finland, Sweden; 'Mediterranean countries' (6 countries) = Cyprus, Greece, Italy, Malta, Portugal, Spain; 'Western and Central European countries' (8 countries) = Austria, Belgium, Germany, France, Ireland, Luxemburg, Netherlands, UK; 'higher income countries' (14 countries) = countries with GDP/capita in Euro above the median of the 28 EU Member States, based on Eurostat figures as of November 21, 2013, i.e. Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Spain, Sweden, UK; 'lower income countries' (14 countries) = countries with GDP/capita in Euro above the median of the 28 EU Member States, based on Eurostat figures as of November 21, 2013, i.e. Bulgaria, Croatia, Czech Republic, Estonia, Greece, Hungary, Latvia, Lithuania, Malta, Poland, Portugal, Romania, Slovenia, Slovak Republic; No answers from Luxembourg and France.

Stakeholders of the Eastern European countries consider 'value-based pricing' (rank 1), 'managed-entry agreements' (rank 2) and 'pharmaco-economic evaluation' (rank 3) as the measures contributing the most to achieving the selected policy objectives. Stakeholders of the Nordic countries tend to value more 'generic substitution' (rank 1), 'pharmaco-economic evaluation', 'reimbursement process', 'value-based pricing' (each rank 2) and 'positive list' (rank 3). 'Pharmaco-economic evaluation' (rank 1), 'reimbursement process' (rank 2), 'reimbursement rates' (rank 3) and 'value-based pricing' (rank 3) are on top ranking positions in the assessment expressed by the stakeholders of the Mediterranean countries. 'Pharmaco-economic evaluation' is also ranked high in the Western and Central European countries, followed by 'reimbursement process', 'generic substitution' (both rank 2) and 'managed-entry agreements' (rank 3). No major differences are observed between the ranking results of higher and lower income countries.

As already shown for the preferred policy objectives (cf. Figure 4.9, ranking results can also be displayed at country level (cf. Annex 11 for detailed ranking results per country).

4.3.3 Ranking by policy objectives

The results presented so far display the assessment of the policy measures in the light of the underlying preference for one of all the policy objectives defined. If the measures are analysed in relation to each policy objective individually (the other policy objectives being disregarded), we learn which measures stakeholders consider appropriate for specific policy objectives (cf. Table 4.8).

Table 4.8: Ranking results per policy objective

Reimbursement policies	Policy objectives (assessment criteria)							
	Timely access to medicines	Equitable access to medicines	Reward for innovation	Cost-containment / control of PE/ budget	Long-term sustainability	Promotion of a more rational use of medicines	Increased competition	Overall ranking
Weights (scale 0 'no priority' to 50 'high priority')	42	46	32	36	43	39	32	
Pharmaco-economic evaluation	2	4	1	3	2	1	3	1
Value-based pricing	4	5	1	5	5	2	4	2
Reimbursement process	1	2	3	3	3	2	5	3
Managed-entry agreements	2	4	2	3	5	4	5	4
Reimbursement review	5	5	6	3	4	2	3	5
Positive list	2	4	5	3	5	2	5	5
Reimbursement rates	3	3	4	3	5	2	5	5
Generic substitution	2	1	10	1	1	2	1	5
Reference price system	6	6	8	3	5	4	3	6
Pharmaceutical budgets	6	6	8	2	5	3	5	6
Differential pricing	6	4	7	5	6	5	5	7
INN prescribing	6	5	11	3	5	2	2	7
Co-payment	9	7	9	3	5	2	6	8
Discounts / rebates / p.n./c.	6	7	8	3	7	6	5	8
Tendering	7	9	11	3	8	5	2	9
External Price Referencing	8	8	9	4	9	7	7	10

Legend: PE = pharmaceutical expenditure, p.n. / c. = price negotiations, clawback

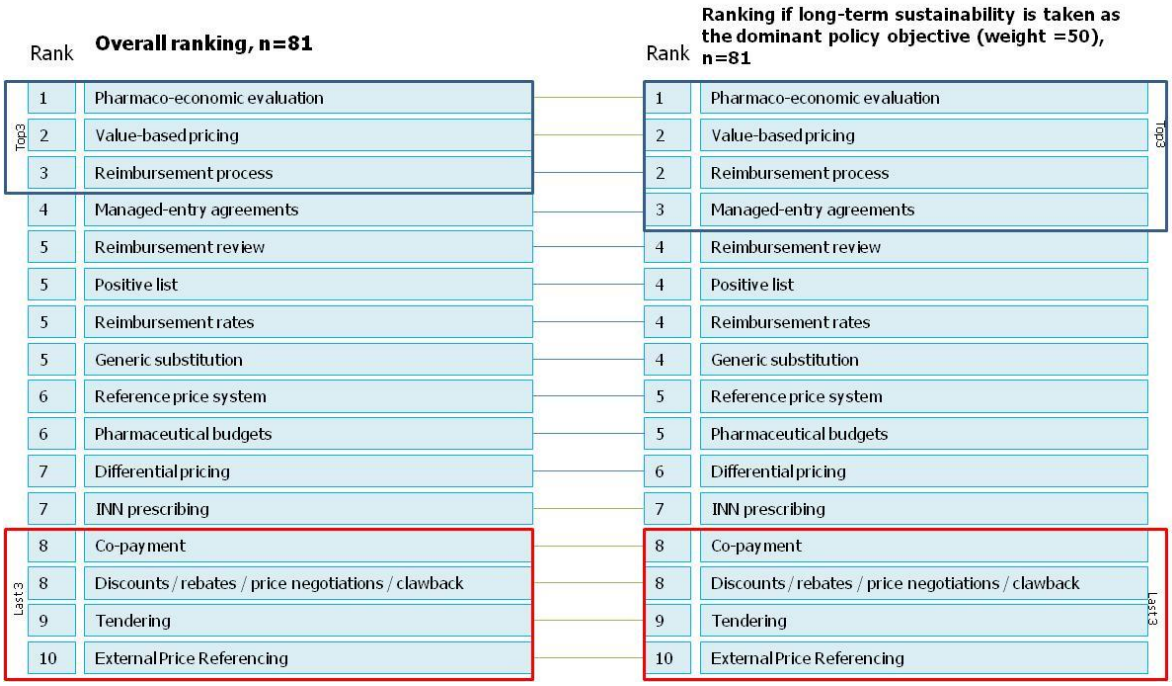
Six measures are found among the top three ranking positions as regards achieving 'timely access to medicines': the 'reimbursement process' is indicated by stakeholders as contributing the most to achieving this objective. Four policy measures (generic substitution, pharmaco-economic evaluation, managed-entry agreements, positive list) share the second rank and 'reimbursement rates' is ranked third. 'Equitable access' is considered to be achieved best by 'generic substitution' (rank 1), 'reimbursement process' (rank 2) and 'reimbursement rates'. When looking at the policy objective 'reward for innovation', stakeholders gave 'pharmaco-economic evaluation' and 'value-based pricing' (both rank 1), 'managed-entry agreements' (rank 2) and 'reimbursement process (rank 3) the highest preference values. The ranking results for policy measures supporting 'cost-containment and control of pharmaceutical expenditure' are balanced: 13 of the 16 selected policy measures are found among the top three positions indicating that each policy contributes almost equally to achieving this objective. 'Generic substitution' (rank 1), 'pharmaco-economic evaluation' (rank 2) and 'reimbursement process' (rank 3) help to ensure 'long-term sustainability' of the pharmaceutical system according to stakeholders'

opinion. For this policy objective, the middle field of the ranking list encompasses many policy measures (eight policy measures share rank 5). Ten policy measures take the top three positions as regards their contribution to achieving the policy objective of 'promotion of a more rational use of medicines', headed by 'pharmaco-economic evaluation' (rank 1). 'Increased competition is supported by 'generic substitution' (rank 1), 'tendering' (rank 2), 'reference price system', 'reimbursement review' and 'pharmaco-economic evaluation' (each rank 3).

According to all stakeholders, 'generic substitution' is best for achieving four of the seven policy objectives. However in the overall ranking 'generic substitution' is on the fifth place taking into account the weights each policy objective got from stakeholders in the selected MCDA algorithm.

In line with the reflection process on sustainable health systems, an additional ranking result was produced with the help of the MCDA tool whereby the policy objective of 'long-term sustainability' is taken as the dominant one.

Figure 4.20: Comparison of the rankings of policy measures if long-term sustainability is the dominant policy objective



Legend: The blue dotted line signals a lower rank of the respective reimbursement policy if long-term sustainability is taken as the dominant policy objective. The blue straight line signals a higher rank of the respective reimbursement policy if long-term sustainability is taken as the dominant policy objective. A green straight line indicates the same rank according to the overall ranking and if long-term sustainability is taken as the dominant policy objective.

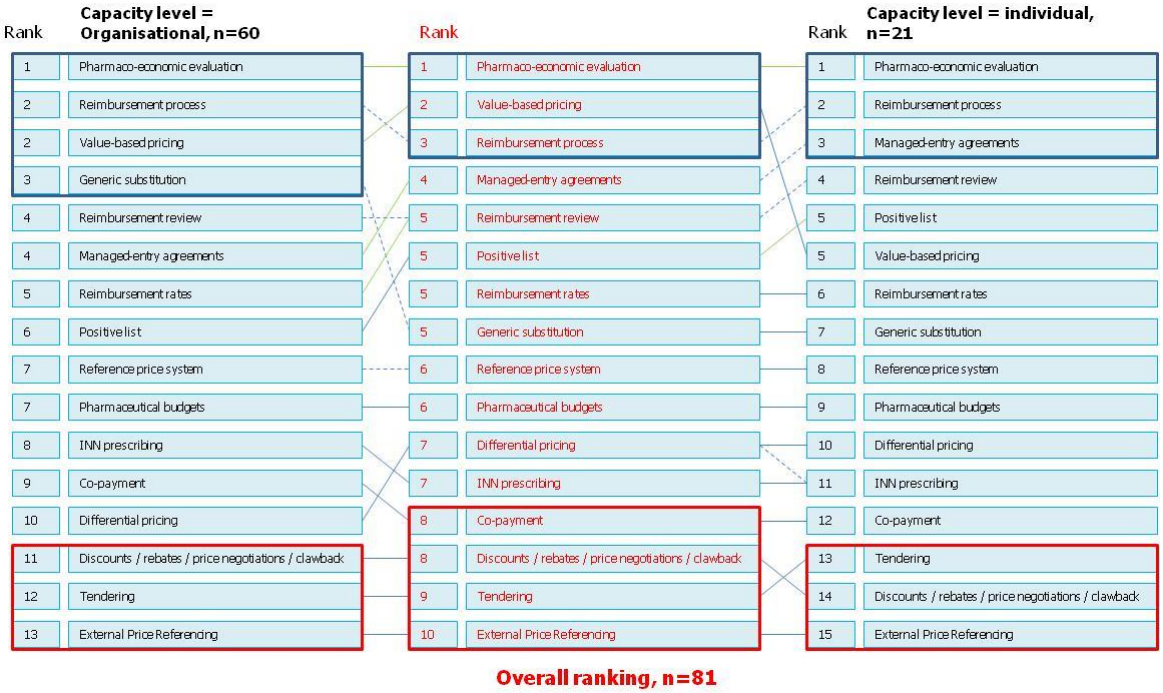
As displayed in the figure above, only minor differences between the rankings were observed when the policy objective of 'long-term sustainability' was taken as the dominant objective. 'Reimbursement process' and 'managed-entry agreements' were more important and the last positions remained the same.

4.3.4 Ranking by capacity level

In the results shown in the previous sections, all opinions of stakeholders were taken into account regardless of the level of capacity. In the survey, stakeholders were asked to reply at organisational level, however some experts could only complete questionnaires based on individual opinions.

The differences between the results at all the levels, and of stakeholders replying at organisational level and at individual level are analysed in Figure 4.21.

Figure 4.21: Comparison of the rankings of policy measures at institutional and individual level



Legend: The blue dotted line signals a lower rank of the respective reimbursement policy in the overall ranking. The blue straight line signals a higher rank of the respective reimbursement policy in the overall ranking. A green straight line indicates the same rank according to the assessments at organisational or individual level and the overall ranking.

Comparing the top three positions in the ranking lists, it can be observed that the top three results at organisational level ('pharmaco-economic evaluation', 'reimbursement process', 'value-based pricing' and 'generic substitution') are almost the same as in the overall ranking. Only 'generic substitution' falls by two in the overall ranking since it is not as positively assessed by stakeholders replying at individual level. 'Managed-entry agreements' which are ranked third by individuals are placed on the fourth place in the overall ranking list and in the list at organisational level. The last three positions in all lists contain 'discounts', 'tendering' and 'external price referencing'. Briefly said, no major differences between ranking lists of these three groups can be observed.

4.3.5 Ranking by product group

We tried to classify reimbursement policies according to the scope of the product groups covered (cf. section 3.2.2). Taking only four specific measures which are considered to be targeting new and cost-intensive medicines into account for the MCDA, the ranking looks as follows:

Table 4.9: Ranking of reimbursement policy measures targeted at new and cost-intensive medicines

	Rank
Value-based pricing	1
Managed-entry agreements	2
Discounts / rebates / price negotiations / clawback	3
Differential pricing	3

'Value-based pricing' is considered as the most suitable reimbursement policy for new and cost-intensive medicines to help in achieving the selected policy objectives.

For a second analysis on the basis of product groups, only 'generic' reimbursement policies are selected.

Table 4.10: Ranking of reimbursement policy measures targeted at generics

	Rank
Generic substitution	1
Reference price system	2
INN prescribing	2
Tendering	3

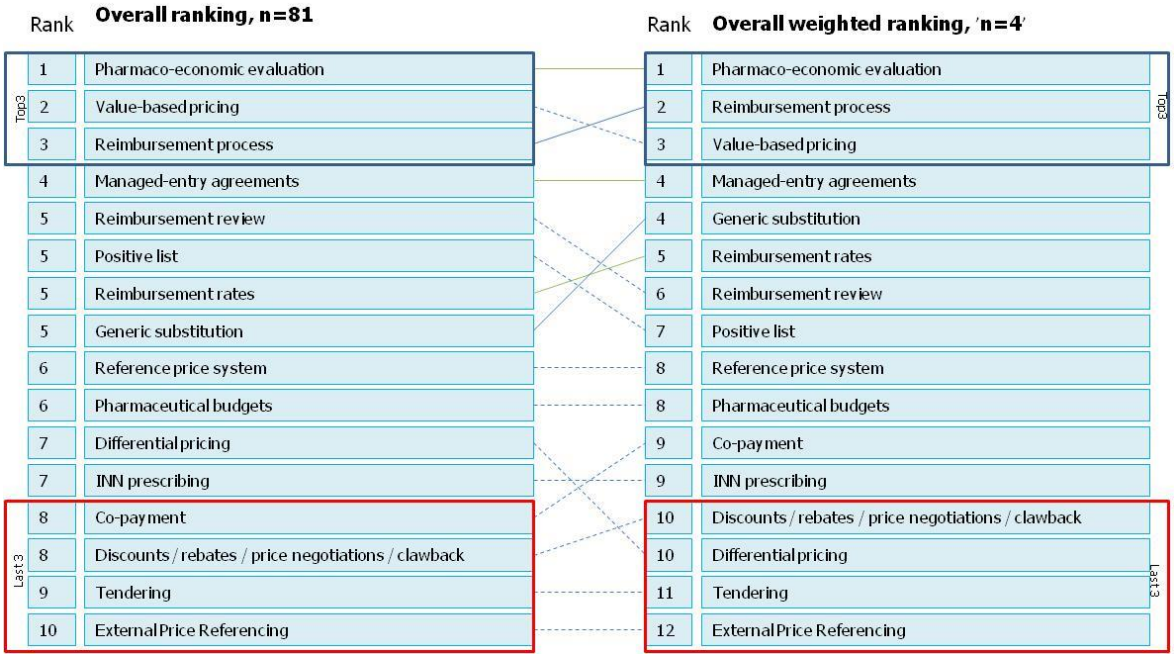
Unsurprisingly and in accordance with the overall ranking results, 'generic substitution' is assessed as the most suitable reimbursement measure in this context.

4.3.6 Weighted rankings

Since the participation in the stakeholder survey varied among stakeholder groups (some stakeholders are represented by a low number of participants while other stakeholders are represented by several organisations), it was requested to perform the MCDA also on a weighted basis: every stakeholder group has the same influence on the outcome of the ranking.

For this purpose, for every stakeholder group, mean values of weights, assessments and thresholds were calculated. For the MCDA, four performance matrices of the aggregated stakeholder groups (n=4) were taken into account whereby the less represented stakeholder groups obtain the same weight and influence on the results as the higher represented stakeholder groups.

Figure 4.22: Comparison of weighted and unweighted ranking results



Legend: The blue dotted line signals a lower rank of the respective reimbursement policy in the overall weighted ranking. The blue straight line signals a higher rank of the respective reimbursement policy in the overall weighted ranking. A green straight line indicates the same rank according to overall ranking and the overall weighted ranking.

Within the first four positions of both ranking lists, only the ranking changes whereas the reimbursement policies remain the same. 'Differential pricing' looses importance when weighting the assessments of the stakeholder groups.

The similar results between the two groups (unweighted, weighted) seem to confirm also the validity of the chosen MCDA approach, achieving a good balanced ranking result.

4.4 Discussion

4.4.1 Stakeholder representation

More than 370 persons were invited through personalised e-mails to participate in the stakeholder survey. In total, 81 completely filled questionnaires were included in the MCDA, which represents about 30 % of the 266 contacted institutions. The response rate to the invitation to participate was satisfactory and the results of the MCDA are seen as representative for all key stakeholder groups (competent authorities, public payers, research-based and generic medicines industry). Taking into account also the answers of organisations which did not complete the survey for various reasons (cf. section 4.1.1), an overall response rate of about 41% of the contacted institutions was achieved. Discussions with representatives from stakeholder organisations at European level (e.g. PGEU, PPRI) confirmed that the number of completed questionnaires is fully in line with the response rates which can be expected of surveys of such a dimension.

We originally envisaged having one respondent per Member State and stakeholder group. Despite the use of several strategies (cf. section 3.10) to motivate stakeholders to participate in the survey, this ambitious goal could not be reached.

As displayed in Annex 11 showing the ranking results per country, in 38% of the cases only one or two national stakeholders per country completed the survey. No responses were obtained from France and Luxembourg. This should be taken into account when analysing the country results of the rankings based on the MCDA.

Four stakeholder groups (consumers, patients, pharmacists and doctors) remained underrepresented in the stakeholder survey – mainly due to the fact that these stakeholder groups reported schedule problems and also said that they did not feel sufficiently competent in the field of pricing and reimbursement to assess the selected policy objectives or measures. Only one reply by a national doctors' association was included in the MCDA. The perspective of doctors on policy objectives of medicines and reimbursement policies is not appropriately reflected in this study. Therefore, an analysis for the stakeholder group of doctors was not performed.

In particular, patient or consumer organisations reported problems in completing the survey as they did not feel sufficiently competent to comment on or assess reimbursement policies of medicines. In some cases, they were confronted with this policy area for the first time. Selected comments of stakeholders who did not participate in the survey:

- *'I have tried to answer your survey but it is far too difficult. It requires an intimate knowledge of pricing systems/policies for a huge range of medicines which only a bureaucrat in the health department could answer. There is no way a simple patient organisation has this information or can properly comment.'*

- *'Sorry, I've tried to answer the questions but the subject is definitely too complicated for my experience. I'm involved in consumer protection, but the items discussed are really too specific.'*

However, even the few answers of these stakeholder groups contribute to increasing the quality of the results of this survey, though the assessment of well represented stakeholder groups (e.g. payers or pharmaceutical industry) may influence more the results of the MCDA in an unweighted approach. To account for the unequal distribution of the stakeholders in the survey, we conducted further analyses: we did a weighted analysis in which the mean results of every stakeholder group were interpreted as one data set to be entered in the MCDA tool. Thus, underrepresented stakeholder groups were assumed to have the same influence on the MCDA results as the better represented groups. An additional analysis of ranking positions (cf. section 4.3.6) showed that only minor changes in the ranking of reimbursement policies occur. This confirms the methodology that the chosen MCDA approach is a sound and balanced instrument of delivering valid and representative results.

4.4.2 Selected policy objectives

The policy objectives were selected for the stakeholder consultation based on a sound and transparent methodology which considered key existing evidence (cf. section 3.2.1). The seven selected policy objectives represent, in general, those goals which were considered as relevant by the stakeholders. A few stakeholders (27%) took the opportunity, which the questionnaire allowed, to indicate additional policy objectives which could also be considered (cf. Annex 14) – e.g.

- Stated by patient organisations:
  - EU standards for the timing of reimbursement and the minimum level of reimbursement of medicines for chronic conditions
- Stated by consumer organisations:
  - Consumer education and information
- Stated by public payers:
  - Ensuring a reliable supply of safe medicines
  - Public health and health promotion
- Stated by competent authorities:
  - Value for money
  - Improving public health and health outcomes
  - Health promotion and prevention
- Stated by pharmacists:
  - Professional/public educational programmes for prevention
  - Explicit and sustainable remuneration systems of pharmacies and wholesalers
  - National drug policy concept and sustainable use of medicines based on pharmacists' skills and competencies

- Stated by research-based industry:
  - Patient orientation
  - Access to & reward for innovative medicines
- Stated by generic medicines industry:
  - Sustainability for the generic medicines industry in order to continue availability of affordable medicines to patients
  - Increasing patients access to generic medicines and providing information to patients about the generic medicines
  - Sustainability of pharmaceutical supply.

Many of the policy objectives mentioned above and in Annex 14 were related to the reimbursement of medicines, whereas other comments suggested objectives in the broader public health areas, e.g. health promotion and prevention.

Stakeholders were also asked whether the provided definitions of the objectives matched their own understanding. Few stakeholders took the opportunity to offer additional comments to their understanding of the selected policy objectives (cf. Annex 14) – e.g., that policy objectives are interdependent or that both the static and dynamic efficiency have to be acknowledged within policy objectives.

The feedback shows that it was difficult for some stakeholders to independently assess the dimensions of each policy objective separately. The given weights / preferences for specific policy objectives should be interpreted as trends in the full context rather than as definite indicators for the decision-making processes.

It should also be acknowledged that the seven policy objectives might not fully represent the decision-making context for reimbursement practices since a few further factors (e.g. political context) might come into play when decisions on the implementation of reimbursement policies are taken.

4.4.3 Selected policy measures

Sixteen policy measures were selected for the stakeholder consultation (cf. section 3.2.2). Further measures which stakeholders proposed to include in the survey were:

- Suggestions of the generic medicines industry:
  - Prescription quotas for generics and/or biosimilars may increase the rational use of medicines under the conditions of tight healthcare budgets
- Suggestions of public healthcare payers and competent authorities:
  - Annual revision of prices of medicines (no traditional reimbursement measure)
  - Price adjustments over time, in particular, following the end of IP protection to allow room for new medicines
- Suggestions of pharmacists:
  - Although explicit and sustainable remuneration systems of pharmacies and wholesalers do not constitute a reimbursement policy for medicines, it is the reimbursement of the services rendered by the distribution chain that affects timely access.

All of the measures brought forward by the stakeholders were either considered in the long list of reimbursement policy measures (cf. section 3.2.2) or were excluded from the beginning of the survey since their focus was on the pricing of medicines (e.g. price revisions, remuneration for distribution actors).

Within the national pharmaceutical systems, pricing and reimbursement processes are strongly interlinked (cf. section 2.5) and the exclusion of some pricing policies might be considered as somewhat arbitrary. Upon the recommendation of and in consultation with the EAHC/EC, it was decided to include into the stakeholder consultation 'external price referencing' (cf. section 3.2.2), which is a major pricing policy. The key reason for doing this was that 'differential pricing', again a pricing policy but with a strong link to reimbursement since it considers the ability of a country to pay (cf. section 2.5), was also included. Since 'differential pricing' and 'external price referencing' are frequently discussed as alternatives, there was the opinion that the inclusion of 'differential pricing' required also the inclusion of 'external price referencing' in the survey. However, the low ranking results of these two policy measures (in the overall ranking: rank 7 for 'differential pricing' and rank 10 and last position for 'external price referencing) could also indicate in this context that stakeholders did not consider these policies as relevant for reimbursement. Furthermore, we believe that the concept of 'differential pricing' might not be well known with all stakeholders, which might be another explanation for this.

Generic medicines industry suggested considering a differentiation between policies targeting generics and those targeting on-patent medicines. This proposal apparently confirms the hypothesis that different policies are likely to be needed for different product groups. In the preparatory work for the stakeholder consultation, we assigned the sixteen selected policy measures to specific product groups to account for the possible need for market differentiation in terms of policy options (section 3.2.2).

4.4.4 Limitations

4.4.4.1 Terminology and concept of reimbursement policies

We are aware of the fact that stakeholders assess the selected reimbursement policies according to their (personal) understanding and expertise. It has to be acknowledged that some of the reimbursement policies are very specific and sometimes only known to a few stakeholders (i.e. authorities, payers and industry). Other stakeholders might be less familiar with some reimbursement policies and other elements of their national reimbursement system, which is likely to limit their assessments. Some stakeholders reported limited knowledge of the set up of the reimbursement system in their country. However, we tried to reduce this limiting factor by providing a number of supporting tools (i.e. providing exact definitions and also audio and video guides, fact sheets on the key elements of national reimbursement systems). An additional limitation to the interpretation of the results is that reimbursement policy measures may be implemented in different ways in the different countries, thus yielding different outcomes (cf. section 3.2.2). We tried to tackle this limitation by providing examples of reimbursement policies and asking stakeholders to assess the policies based on the examples and not on the national implementations. As shown in Annex 10 (performance matrices by stakeholder groups) not every stakeholder assessed each measure for each policy objective; some were deliberately disregarded (e.g. due to the lack of knowledge/understanding of the specific policy).

It should also be noted that stakeholders predominantly represented the national level, and thus they had a national perspective. To provide an example: 'equitable access to medicines' was understood, and was also meant to be understood, as fair and affordable access for all population groups within a country, and not between countries.

Though developed to support the stakeholders in the survey, the fact sheets led to some irritation in a few cases since respondents were asked to assess the measures in the light of their broadest interpretation, and the fact sheets, providing the real life situation, somewhat distorted their interpretation. Furthermore, reimbursement systems are dynamic, and during the course of the survey, some information on the country fact sheets (prepared well in advance of the roll-out) got outdated.

4.4.4.2 Selection of method for the stakeholder survey and of the MCDA approach

We critically reflected whether we chose the right methodology for the stakeholder consultation. According to the tender specifications, stakeholders were to be asked in the form of written consultation (e.g. electronically), that is why we decided to have an online survey.

For the selected MCDA approach, the outranking model using ELECTRE III (for details cf. Annex 5 – MCDA methodology), certain thresholds (indifference, preference and veto threshold) had to be indicated. The retrieval of the values for the thresholds via an online survey was a challenging task in this project due to limited interaction possibilities with the participants in the survey. The selection of the values for the thresholds by the participants impacts, to some extent, the final ranking results. The extent of the influence on the results was tested in several sensitivity analyses (cf. Annex 13 – results of the sensitivity analyses). The concept of thresholds relates to making the individual assessment results more transparent and understandable. Since personal and institutional preferences or assessments do not necessarily always follow rational patterns, the indication of these decision thresholds presented a specific challenge for the stakeholders. Many stakeholders indicated that they were not sure whether they understood the concept of the thresholds correctly. We tried to limit the uncertainties by providing practical examples and video guides; however, this could not diminish the burden on the side of stakeholders of having to express their feelings and assessments in the form of values required for the MCDA, since the assessments rely on more (subjective) opinions and cannot always be based on scientific facts.

Results of the sensitivity analyses (cf. section 3.5, Annex 5 for methodology and Annex 13 for detailed results of the sensitivity analyses) showed that the selected MCDA approach (outranking approach, ELECTRE III algorithm) proved to be a valid and stable instrument of comparing reimbursement policy measures taking into account different, sometimes maybe even conflicting, assessment criteria, based on the preferences by different decision-makers or stakeholders.

The ranking results were tested for

a) sensitivity for changes in preference and indifference thresholds

b) sensitivity for changes in weights (assessments of policy objectives)

c) sensitivity for changes in (number of) criteria (policy objectives) taken into account

d) sensitivity for changes in (number of) policy measures taken into account

The major findings of the extensive sensitivity analyses proved that the application of a multi-criteria based method is most suitable for answering the addressed research questions. The different steps of sensitivity testing led to the following conclusions:

a) The model is generally robust to changes in preference and indifference thresholds, a change in the thresholds leading to the elimination of the concept of weak preference causes an increase in the maximum rank and vice versa a decrease in ex aequo ranked policy measures. The concept of weak preference was therefore undermined to contribute to a consensus-oriented decision making process (as it generally seems to allow for more ex aequo ranked policy measures).

b) The model is very robust to changes in weights, especially the first ranked policy measures showed high robustness and a slight tendency towards three groups of policy measures (high, middle, low ranked) was found (and later on accentuated by the sensitivity analyses for changes in the (number of) policy measures taken into account).

c) The analysis for changes in criteria showed that the possibility of using fewer than the chosen criteria had to be dispelled as it would lead to a lack of information regarding the different stakeholders' preferences, which all have to be reflected for a consensus-seeking decision making process.

d) The sensitivity for changes in the (number of) policy measures taken into account led to the conclusion that three for all stakeholder groups commonly set clusters of policy measures (high, middle, low rank clusters) could be identified. The first cluster (highly ranked and therefore seemingly fulfilling most stakeholder´s preferences best) for the total data set (all countries, all stakeholders) consists of: Pharmaco-economic evaluation (rank 1), value-based pricing (rank 2), reimbursement process (rank 3), managed-entry agreements (rank 4), generic substitution, positive list, reimbursement rates and reimbursement review (all ex aequo rank 5).

Concerns raised by some of the stakeholders included: 1) the complexity (too many alternatives, too many parameters, too difficult to understand for some stakeholders, confusing structure, too detailed scale) of the online questionnaire; 2) the time-intensive survey; 3) missing opportunities to discuss first ranking results. The first two factors are likely to have led to lower participation rates than anticipated, even though we tried to reduce the limiting factors as much as possible using different compensation strategies (i.e. supporting tools and personalized contacts to stakeholders).

As a further step to allow for a more appropriate interpretation of the ranking results, this report might be used to challenge the results in discussions with stakeholder groups. However, this is not scope of the present study.

5 Conclusions and recommendations

This study aimed to explore which pharmaceutical reimbursement practices stakeholders consider as most appropriate to achieve specific policy objectives and, based on their assessments investigated through a Multi-Criteria Decision Analysis (MCDA), to develop a proposal for the best practice-based approach for such a policy mix, by reconciling the different – often conflictive – policy objectives.

Eight stakeholder groups (consumers, patients, competent authorities for pharmaceutical pricing and reimbursement, public payers, generic medicines industry, research-based pharmaceutical industry, doctors and pharmacists) were addressed to assess 16 reimbursement practices related to medicines (co-payment; differential pricing; discounts / rebates / price negotiations / clawback; external price referencing; generic substitution; INN prescribing; managed-entry agreements; pharmaceutical budgets; pharmaco-economic evaluation; positive list; reference price systems; reimbursement process, reimbursement rates; reimbursement review; tendering; and value-based pricing) in terms of their appropriateness to fulfil seven chosen policy objectives (timely access to medicines; equitable access to medicines; reward for innovation; cost-containment / control of pharmaceutical expenditure/budget, long-term sustainability; promotion of a more rational use of medicines; and increased competition).

Key findings

In spite of an intrinsic logic attributed to the relevance of the policy measures by some stakeholder groups (e.g. cost-containment being a necessity compared to 'real' public health policy goals such as equitable access to measures), the respondents considered all seven selected policy objectives as important, contributing weights of above 30 (scale of value from 0 to 50). Overall, high priority was attributed to the policy objective of equitable access to medicines, followed by the goals of long-term sustainability and timely access to medicines. Comparably lower weights were attributed to reward for innovation (considered however important by the research-based industry), cost-containment (high priority for public payers), increased competition (important for generic medicines industry) and rational use of medicines. Sensitivity analyses confirmed that the underlying set of criteria could not be reduced whilst ensuring the maintenance of all stakeholders' preferences.

Overall, stakeholders assessed pharmaco-economic evaluation as the most appropriate reimbursement policy to achieve the selected policy objectives. Value-based pricing and the reimbursement process were ranked second and third, followed by managed-entry agreements. Four measures (reimbursement review, positive list, reimbursement rates and generic substitution) were all ranked fifth. The sixth rank was attributed to reference price systems and pharmaceutical budgets, followed by differential pricing and INN prescribing (both rank 7). Co-payment and discounts / rebates / price negotiations / clawback (both rank 8), tendering (rank 9) and external

price referencing (rank 10) were considered to have the comparably lowest ability to achieve the different policy objectives.

Lessons learned related to the study methodology

Sound but complex methodology

We opted for an outranking approach (MCDA methodology of ELECTRE III) which allowed for the concept of weak preferences and thus reflected real world decision-processes. The chosen methodology was a robust one, as confirmed by large sensitivity analyses.

But it required from the stakeholders to openly express their preferences, including the relationship among different preferences, and to understand a rather complex methodology.

Sensitivity analyses confirmed and emphasized the need for such a multi-criteria based approach, which allows for ex-aequo ranked policy measures in the light of a consensus-seeking decision-making process.

Such an approach requires a good description and communication of the methodological concept. In addition to the written documentation, sufficient investment into the guidance of the potential respondents was required. Should such a survey be repeated, e.g. in another setting (see below), appropriate resources and time-lines will need to be planned.

Need for common understanding and clear terminology

One challenge of the survey was the fact that the selected policy measures can be designed differently and are, in fact, implemented in different ways by the individual EU Member States. Thus, we needed to define how the policy measures should be interpreted by the respondents. To ensure a common understanding, we decided that the policy measures should be related to 'in the light of the broadest possible interpretation', and examples were given. Any study of the assessment of policy measures in the field of pharmaceutical reimbursement is recommended to specify the measures; nevertheless, it is important to note that the practical experience with existing real-life policy measures in the countries, where the respondents are based, influenced their perception and, finally, the assessment.

The need for common understanding was vital in this project. Support measures such as definitions of the policy objectives and measures, audio and video guides, the country fact sheets as well as high responsiveness to questions for clarification proved essential: a few stakeholder groups (e.g. consumers, patients, and doctors) were less targeted and thus less familiar with some of the reimbursement measures. At the same time, very experienced respondents also needed clarity in order to know what exactly they were assessing.

Being aware of possible semantic overlaps, we had to choose a methodology which did not require 'independence' between the assessment criteria. With the selected method of ELECTRE III, this requirement was fulfilled.

High interest of the stakeholders in the topic

The study was met with keen interest by most stakeholders. All associations, which we addressed to ensure support in our survey, were very helpful in organising contacts and motivating their members to participate. Despite some reluctance to the complex questionnaire, stakeholders expressed genuine interest in the study. It is expected that the involved stakeholder groups are eager to learn about the study results as soon as the study results are made available.

Increased number of stakeholder groups ensured representativeness

A key question in the context of a stakeholder survey was which stakeholder groups should be addressed. We decided to have a broad understanding of stakeholders and extended the original proposal, as per the tender specifications, by including new groups (these were: competent authorities for pharmaceutical pricing and reimbursement, consumers, doctors and pharmacists). Some of the newly added stakeholder groups showed a high response rate, others not so much because they considered the survey as too complicated, and felt that they could not assess some of the reimbursement practices because these were less known to them. We believe that it was a good decision to include more stakeholder groups in spite of a low response rate of some groups because, even if only few representatives answered the questionnaire, they were at least made aware of the study.

While the increased number of different stakeholder groups enhanced the representativeness of the survey, the representation was limited in some countries, since the survey was designed to address national policy-makers, and it was not possible to achieve coverage of all or the majority of the EU Member States per stakeholder group. The majority of the respondents replied from national level, only few represented organisations being active on EU level.

Reimbursement practices are specific for specific products and settings

Some of the reimbursement practices were targeted at specific product groups, depending on their therapeutic value and the patent status. The analysis results need to be understood as a 'policy mix' which addresses both new medicines as well as off-patent medicines.

At the same time, the results of our study are limited to the out-patient sector; a survey which would include the in-patient setting would require listing further measures and defining the measures in accordance with their implementation in the in-patient sector. The chosen MCDA methodology allows redoing the survey for the in-patient sector, with clear terminology and careful selection of the possible

respondents. The present study has the limitation that, considering only one sector, no interface issues across the settings are addressed.

Proposal of a reimbursement policy mix considered as best practice

The survey made it clear that specific reimbursement practices are, among all stakeholders, considered highly relevant, whereas a few other policies are given low priority by the majority of all respondents.

Any policy mix proposed would need to be aligned to policy objectives which all relevant stakeholders consider as of high priority: These are particularly: equitable access to medicines, long-term sustainability and timely access to medicines. Still, other objectives, including those highlighted by the High Level Pharmaceutical Forum, i.e. cost-containment and reward for innovation, were also given preference and should therefore also be taken into account when designing a policy mix. It is likely that a country with a strong research-based industry will focus more on measures to reward innovation, whereas countries with lower income and/or those strongly hit by the financial crisis will rather explore ways to contain costs and might opt for a few savings measures.

Overall, highly ranked measures are those which are rather targeted at new medicines, whereas generic policies rank more in the middle. It should be noted that two of the top 3 measures (generally and in several analyses per stakeholder group) concern processes and supportive tools rather than specific policy measures: Most stakeholder groups ranked 'pharmaco-economic evaluations' as first or second. The analysis per country supports this high priority given to pharmaco-economic evaluations across different country clusters per geographic distribution and economic situation. Another key measure for all stakeholder groups (except for patients) was a reimbursement process with very clear rules, a transparent process, documented and reproducible decisions taken in reasonable time to allow the in-depth consideration of sound evidence.

According to the stakeholders' assessment, the best practice-based approach for a reimbursement policy mix should include both measures related to new medicines, including high-cost medicines, as well as generic medicines, though the policy options for new medicines were ranked higher. Value-based pricing, understood as joint pricing and reimbursement processes based on 'value' assessment, was considered as a policy option of high priority. Related to generic policies, stakeholders seem to have different preferences as to the various policies to promote generics uptake. Of the three generic policies listed in the survey, generic substitution was given preference over reference price systems and INN prescribing.

Though not in the very first rank, but in the (upper) middle, the reimbursement review has been considered as relevant by all stakeholder groups (except for the patients), which might be understood as recommendation to include some monitoring and/or review elements into the reimbursement system in order to make it easier to learn about changes and have the opportunity to react to them. Also, measures which

support prioritization such as a positive list, and, to some extent, also different reimbursement rates, were usually ranked in the middle; this suggests that stakeholders see them as a standard tool of a policy mix.

A policy mix which the stakeholders consider as 'ideal' is likely not to include high co-payments, arrangements such as discounts, rebates, price negotiations or clawbacks, tendering applied in the out-patient sector, and external price referencing. We assume that high co-payments are seen as contradictory to fair and equitable access to medicines, a policy objective which was given high priority by most stakeholders. The opposition to tendering in the out-patient sector is assumed to be based on experiences with this practice in some countries, e.g. the Netherlands, as a possible cause for medicine shortages (cf. section 2.7). Given the indications of the possible impact on availability and limited transparency (cf. also section 2.7), it might be speculated that the confidential character of discounts and rebates, which also influences the practice of external price referencing, might be an explanation for the low preference of discounts and rebates as well as of external price referencing. Another reason for the overall low preference for external price referencing could be that this practice is not considered as a reimbursement policy, but rather as a pricing measure. Differential pricing, which has been proposed as an alternative to external price referencing, is not rated very high either.

The study allows understanding which policy options could be included in the best-practice approach of a policy mix, and which measures were considered as less favourable. However, despite a few qualitative answers, we do not have a comprehensive picture of the reasons for this choice. The rationale for giving higher preferences to some policy measures, and less to others, would need to be further explored.

Policy recommendations

Based on the stakeholders' assessments of the reimbursement practices, we propose the following policy recommendations:

- The design of the best practice-based mix of reimbursement policies is likely to require a different approach depending on the policy goals which a country aims to give highest priority to.
- A policy mix considered as 'ideal' should take into account different approaches to different groups of medicines (particularly the two groups of new, high-cost medicines and off-patent medicines).
- Sound evidence, gained through pharmaco-economic evaluations, for instance, appears to be a major prerequisite in policy decisions. Ways of how to further develop and implement pharmaco-economics should be explored.
- Good processes, characterized by very clear rules, transparency, consideration of sound evidence, documentation and reproducible decisions taken in reasonable time, seem to be another major element in pharmaceutical reimbursement. Investment in improving reimbursement processes should be made.

- Reviews are another key element whose implementation should be further explored as part of an 'ideal' policy mix.
- It is recommended that stakeholders explore confidentiality issues which might negatively impact outcomes of defined policy goals.
- In order to achieve equitable access to medicines, a highly prioritized policy objective across all stakeholder groups, reimbursement policy measures should be designed in a way to avoid financial burden for the patients.

Suggestions for future research and practice

It is advisable to further explore the following issues:

- The study is limited to the out-patient sector. We suggest considering a similar study for the in-patient sector. The chosen MCDA methodology would support such a study; however, differentiations for the selected measures and stakeholders would be required.
- The present study was focused on reimbursement practices related to medicines. Pricing policies were only considered when linked to reimbursement but 'pure' pricing options (e.g. distribution remuneration) were not part of the survey. It might be of interest to learn about stakeholders' assessment of the pharmaceutical pricing policies.
- Further evidence gained in such studies on pricing policies and/or on the in-patient setting would allow drawing further conclusions, particularly related to interface issues. Furthermore, it might be worthwhile to consider developing a study design to assess possible approaches to the current challenges, such as the role of medical devices in personalized medicine, for instance.
- Related to the framework of this study (i.e. reimbursement practices in the out-patient sector), we recommend exploring the reasons for the preferences which the stakeholders attributed to the different policy measures. This could, for instance, be done in focus groups. A research of the rationale for the preferences was not scope of this study.
- Given the great interest of the stakeholders in this survey, appropriate dissemination of the results to the involved stakeholders and beyond is suggested.
- The study results may build a basis for further discussion and dialogue with the stakeholders.
- Apart from the communication with the stakeholders, we suggest also involving groups less targeted by some of the measures in order to support associations in raising awareness on this topic among their members.
- Stakeholder associations at EU level might be stronger encouraged not only to support by building contacts on their national associations but also to contribute by replying in their capacity as EU-wide association.

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7 Annexes

Annex 1: Tender Specifications

Annex 2: Literature review outline

Annex 3: List of included references in WP1

Annex 4: Definition of policy objectives and policy measures considered for the stakeholder consultation

Annex 5: MCDA methodology – peer reviewed

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Annex 13: MCDA – Results of the sensitivity analyses

Annex 14: Comments by stakeholders