Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
KCE

Drug reimbursement systems: international comparison and policy recommendations

KCE reports 147C

Belgian Health Care Knowledge Centre
Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
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Disclaimer: **- The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.
- Finally, this report has been approved by a majority of votes by the Executive Board.
- Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE.

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Executive summary

BACKGROUND AND OBJECTIVES

All health care systems have three objectives in common: system sustainability, equity and quality of care. Health care resources are limited. Therefore, all health care systems need to make choices regarding services and products that can be covered out of public resources, i.e. they have to set reimbursement priorities, taking all health system objectives into account. Policy measures, such as drug reimbursement systems, are developed to find a publicly acceptable balance between these objectives.

The aim of this study was to describe and critically evaluate drug reimbursement decision processes, to identify strengths and weaknesses of the drug reimbursement processes and to formulate general policy recommendations. We performed our analysis in the current supply-driven context, where the pharmaceutical industry decides what to launch, when to launch and at what price. It was beyond the scope of this study to fully explore the opportunities to move towards a demand-driven system, where the societal needs drive the industry's strategic plan.

METHODS AND CONCEPTS

We performed an in-depth study and comparison of the drug reimbursement systems in five European countries: Austria, Belgium, France, the Netherlands and Sweden. The choice of the countries was inspired by their history of using HTA for reimbursement decision making (the Netherlands and Sweden), the particular types of outcome of reimbursement decision procedures (Austria) and the explicit exclusion of cost-effectiveness as a decision criterion (France). Finally, given our aim of formulating recommendations for Belgium, it was obvious to include Belgium in the comparison. The main consideration was to get insight into how different systems work, without wanting to be exhaustive.

For the description of the drug reimbursement decision processes, we used the Hutton framework. This framework provides a basic structure for systematically describing so called 'fourth hurdle systems' in a detailed and comprehensive manner. The framework makes a distinction between the policy implementation level –system level– and the technology decision level –drug level– of reimbursement systems. The country descriptions were based on the review of scientific literature and policy documents and on the consultations of stakeholders in all countries by means of interviews.

For the evaluation of the systems, we used the accountability for reasonableness framework, developed by Daniels and Sabin. Accountability for reasonableness presumes that four conditions are fulfilled:

1. Transparency: the process must be fully transparent about the grounds for/rationales behind a decision.
2. Relevance: the decision must rest on reasons that all those affected by the decision can accept as relevant to meeting health needs fairly, given the resource constraints.
3. Revisability: decisions should be revisable in light of new evidence and arguments.
4. Enforcement/regulation: there must be some kind of regulation guaranteeing the three conditions described above.

Whilst the second requirement mainly relates to the content of the decision-making process, the other requirements relate to the procedural requirements for accountability for reasonableness. Why this approach for evaluating drug reimbursement systems? Decision making is not a mechanistic rational process. It is a process of weighing and considering all relevant decision criteria. Within a society there is disagreement about which ethical principles should guide priority setting. Therefore, the legitimacy of priority setting should not be assessed based on the content of decisions but on the fairness of the priority-setting *procedure*.

Based on the conceptual framework for accountability for reasonableness and the description of different drug reimbursement decision procedures, we developed a tool to increase the transparency of the decision making procedures as well as the consistency in the criteria used during the process. We analysed for each country the decision criteria used and their operationalisation. We also considered whether we could appraise their relative weight in the decision process. We did not intend to give any value judgement on the performance of each country's reimbursement system.

RESULTS

THE THREE PHASES OF DRUG REIMBURSEMENT PROCESS

The similarities and differences between the five reimbursement systems are described in Chapter 2. All systems have a positive drug reimbursement list and a manufacturer-initiated drug reimbursement process. The successive phases systems implement prior the reimbursement decision are similar across countries. All established a centralised reimbursement agency and an expert committee responsible for the assessment and appraisal of a drug reimbursement request.

The first phase is the **assessment phase. This phase is** purely descriptive and aims at quantifying the clinical, pharmacotherapeutic and pharmacoeconomic outcomes of the drug as compared with its alternative(s). The assessment report is prepared by what we call the "technical department" of the drug reimbursement agency (the RIZIV/INAMI experts in Belgium).

The second phase, the **appraisal phase**, seeks to evaluate the societal value of the drug by weighing all relevant decision criteria, including the assessment criteria and other societal considerations. In Belgium, the Commissie voor Tegemoetkoming Geneesmiddelen/Commission de Remboursement des Médicaments (CTG/CRM) (the expert committee) evaluates the drug reimbursement request file from the company, leading to an advice for the minister. The composition of the expert committee varies between countries. We identified two main models: the deliberation-driven model (Austria, Belgium) and the assessment-driven model (France, the Netherlands and Sweden). The basic difference between these models is that in the former model stakeholders are members of the expert committee, whereas in the latter model the expert committee mainly consists of scientific experts. Balanced representation of societal preferences is of utmost importance. This can be obtained either by a balanced composition of stakeholders in the expert committee or by systematically consulting stakeholders. In Belgium and France, industry representatives are non-voting members of the expert committees, participating in the appraisal discussions. They are present during the voting on an advice by a show of hands.

In the final phase, the **decision-making phase**, the final drug reimbursement decision is made, either by the responsible minister (Belgium, France and the Netherlands) or the (expert board of) the centralised reimbursement agency (Austria and Sweden). Countries allocating final decision power to the minister embed discretionary power within the reimbursement process. In Belgium, the minister is allowed to deviate from a reimbursement proposal of the CTG/CRM for social or budgetary reasons, albeit only on the basis of the same appraisal criteria that have been taken into account by the CTG/CRM in formulating its proposal.

THE FOUR CONDITIONS FOR "ACCOUNTABILITY FOR REASONABLESSNESS"

Transparency

Transparency of the reimbursement process requires that the assessment reports, and the documented appraisal and decision processes are published. All countries but Austria publish assessment reports, although the extensiveness of the publications vary. Austria only publishes the decision. Appraisal processes, i.e. the weighing of all relevant decision criteria leading to the advice and/or the decision, are rarely documented in any country and therefore rarely public. France publishes the results of the voting procedure and key issues discussed at the expert committee. The Netherlands publishes the information in several reports including key issues discussed and the reimbursement advice. Sweden publishes online the state of the process as well as a summary of the final decision and its rationale. A manufacturer can withdraw an application before the final decision is made in Sweden, guaranteeing confidentiality at the cost of transparency. In Belgium, the INAMI/RIZIV currently publishes the assessment report approved by the CRM/CTG (the so-called "day-60 report"), questions asked to the applicant and CRM/CTG replies to the applicant's answers. The final CRM/CTG proposal is not published. The final reimbursement decision by the minister is published, be it not systematically with a detailed motivation, especially in case of a deviation from the reimbursement proposal of the CRM/CTG.

Transparency also presumes clear definitions of the roles and responsibilities of each of the actors in the decision making process. In all countries assessment and appraisal are intertwined processes. In Belgium, the initial assessment report prepared by the technical department sometimes contains a critical reflection on the reimbursement proposal formulated by the company. The proposal of the company, and its critical evaluation by the technical department, although not binding for the CTG/CRM, might influence the appraisal process.

Relevance of the decision rationales and criteria

Relevance requires that all those who are affected by the decision (i.e. the "stakeholders") understand the decision problem and recognise that choices have to be made to meet the different health care system objectives. Only then, ethically acceptable rationales for drug reimbursement can be defined *and* accepted by the general public. Involvement of all stakeholders -provided that these involved stakeholders are fair-minded and understand and accept the decision problem- is considered to facilitate accountability for reasonableness, because it increases the likelihood that the rationales that are adopted will be considered as relevant and acceptable. In this report the term "stakeholders" refers to all those affected by a decision. It should be noted that the term is currently increasingly used to refer to parties with a specific, often strong own interest, which is a rather narrow interpretation of a stakeholder.

To meet both the transparency and the relevance criterion for accountability for reasonableness, decision makers should use a decision tool specifying the decisions that need to be made and the considerations and criteria to be taken into account when making the decisions.

We propose a tool, consisting of five questions to be answered during an appraisal process and for each question a set of possible criteria (see Table). There is no scientifically right or wrong set of criteria. Policy makers should make sure that the decision criteria used are socially accepted. A full discussion on each of the questions and criteria can be found in Chapter 3 of the report.

Table: Key questions and possible criteria for a drug reimbursement appraisal process and examples of their operationalisation

Decision	Question	Possible criteria	Examples of operationalisation
Medical, therapeutic and societal need	Does the product target a medical, therapeutic and societal need?	**Medical need**: - Life-threatening / non-life threatening condition - Severe / mild symptoms - Poor initial health state **Therapeutic need:** - Effective alternative treatments available / not available **Societal need:** - High / Low prevalence - Health inequality - Baseline health level	- Medical need is operationalised and used in the decision process in the Netherlands and Sweden. Belgium in principle uses therapeutic need to define the cost sharing category, although in practice it seems that disease severity (independent from therapeutic alternatives) is the main consideration. - Only France and Sweden assess(ed) the extent to which general needs criteria continue to apply over time by means of revisions of all reimbursed drugs.
Preparedness to pay out of public resources for *a* treatment	Are we, as a society, in principle, prepared to pay for a treatment that will improve this indication out of public resources?	- Own responsibility - Life-style related condition	- Only the Netherlands uses own risk and responsibility as formal appraisal criteria. All other countries apply the same criteria as for medical needs, indicating that these societies consider that treatments for high medical needs should be able to rely on public funding, independently from, for instance, patients' life-style.
Preparedness to pay out of public resources for the treatment under consideration	Are we, as a society, prepared to pay for *this* particular treatment, given that we in general would be prepared to pay for *a* treatment for this indication?	- Safety and efficacy of the treatment compared to the alternative treatment(s) - Curative, symptomatic, preventive - Therapeutic value - Significance of health gains	- All countries explicitly evaluate the safety, efficacy and therapeutic value of drugs. - Significance of health gains is a consideration for conditional reimbursement.
Preparedness to pay *more*	Given that we, as a society, are prepared to pay for this treatment out of public resources, are we prepared to pay *more* for this treatment than for the best alternative treatment?	- Added therapeutic value - Potentially induced savings elsewhere in the health care sector - Quality and uncertainty of the evidence - Acceptability of co-payments and/or supplements - Rarity of disease	- All countries consider added therapeutic value to be crucial for the preparedness to pay *more* for a drug than for its comparator. - All countries use internal reference pricing to determine the reimbursement price of products with equivalent therapeutic value. Drugs classified as having added therapeutic value are more likely to obtain a higher reimbursement price (or -basis) in all countries
Willingness to pay	How much more are we willing	- Added therapeutic value	- **(Added) therapeutic value** is the most prominent decision

(price and reimbursement basis)	to pay out of public resources for this particular treatment?	- Budget impact / ability to pay - Cost-effectiveness ratio - Medical, therapeutic and societal need - Quality and uncertainty of evidence - Limits to cost sharing	criterion in all countries. The main focus is on safety, efficacy and effectiveness. France and Austria define several categories according to the degree of added therapeutic value; Belgium and the Netherlands only distinguish between added and equivalent therapeutic value. Sweden uses a 'continuous' scale by directly linking the price to the level of added value. - **Budget impact** is considered in all countries. International price referencing is used in all countries but Sweden. This limits the effectiveness of countries' price negotiations. - All countries but France consider the **incremental cost-effectiveness ratio** of a product but none defines an explicit threshold value (range). - Countries are often unclear about how they handle **uncertainty**: it might affect either the value of the assessment elements, the reimbursement modalities or the final (conditional) reimbursement decision. - **Cost sharing** policies are implemented in all countries alongside social protection mechanisms. However, the accepted level of cost-sharing varies across countries. Belgium and France use the needs criterion to determine the level of cost-sharing for drugs; the other countries fully reimburse drugs but apply other cost-sharing policies.

The tool provides a structure for justifying decisions and for defining and making explicit the societal choices during the decision process. Some criteria may be considered at different levels and at each question the answer can be a conditional "yes". This fits with the aim of finding a socially acceptable balance between the three health care system objectives: sustainability, equity and quality of care. The weighing of the criteria should reflect societal preferences.

No formal hierarchy is defined in assessment and appraisal criteria in any of the countries. Moreover, it is rarely documented how the criteria are judged. As a consequence, their relative importance for the final decision is often unclear. In Belgium, individual expert committee members do not have to justify their voting behaviour. Lack of transparency in the appraisal process can reduce accountability of systems.

Revisability

Accountability for reasonableness presumes revisability of decisions in the light of new evidence. Revisability is especially important in cases of uncertainty.

Case-by-case revisions are embedded in most countries. They are systematic for specific drugs in Belgium and the Netherlands and for all drugs in France; in Austria and Sweden revisions occur on an ad hoc basis. Group-wise revisions are performed on an ad hoc basis in all countries. None of the countries imbedded revisions of the entire reimbursement package systematically in their system; France and Sweden, however, did perform such a revision of the full package once. In all countries, revisions can have consequences such as delisting and/or a change in the reimbursement level. Sweden successfully delisted drugs based on revisions, whereas in Belgium, it has been proven difficult to change an earlier decision once the product is used in routine practice. Moreover, in the absence of clear guidance on the evidence expected at revision and making explicit the consequences of not satisfying the pre-defined conditions, it becomes more difficult to justify a change in the reimbursement modalities.

Enforcement

Accountability of reasonableness requires enforcement of the transparency, relevance and revisability requirements.

The critical evaluation of the **outcomes** of the reimbursement processes is in all countries mainly done by monitoring pharmaceutical expenditure, as an indicator for impact on system sustainability. Evaluation on other health system objectives (equity and quality of care) mainly focuses on general outcome measures such as overall health and socio-economic differences in overall health. However, these indicators cannot attribute the outcomes to the drug reimbursement policy. The critical evaluation of the **procedures** is performed by external (parliamentary) committees on an ad hoc basis. All systems formally implemented appeal options for stakeholders. All agencies fall under ministerial responsibility.

CONCLUSIONS

All countries address the five key questions defined in our framework for drug reimbursement decision making. However, the degree to which the questions are answered explicitly and the relevant criteria are operationalised and implemented varies across countries. In order to ensure acceptability of the decision criteria, it is essential to be transparent about societal choices.

The confrontation of the Belgian system with the framework of 'accountability for reasonableness' identified a number of characteristics potentially amenable to improvement, as is the case in all countries. The recommendations in the next section highlight the reforms that would be needed to reach an ideal world in which all conditions for accountability for reasonableness are fulfilled. They are formulated in generic terms. Any judgment with regard to the extent to which they can or should be translated into concrete reforms and the ways to do so will depend on political choices, which lie beyond the scope of this report.

RECOMMENDATIONS

The recommendations are formulated from the perspective of a 'best practice' for drug reimbursement systems regarding 'accountability for reasonableness'. The implementation of the recommendations is essentially the result of a political process, with political considerations potentially hindering the realisation of the best practice.

REGARDING TRANSPARENCY

- **Assessment of a product and appraisal of its value should be disentangled and performed in different phases in the reimbursement process. The roles and responsibilities of different actors should be clearly defined.**

ASSESSMENT PHASE

- **An assessment report should include a critical assessment of all the available evidence and uncertainty, assign a level of evidence and highlight where evidence is missing. Experts should obtain a declaration from companies that all relevant evidence is presented in their drug reimbursement request file, including information from ongoing studies.**
- **The preliminary conclusions in the assessment report written by the technical department should be neutral with respect to the clinical, therapeutic and societal significance of the benefits of the drug.**

APPRAISAL PHASE

- **The expert committee should advise (or make a decision) independently from the proposal in the reimbursement request of the manufacturer.**
- **The appraisal process should make use of an explicit framework specifying, for each advice (or decision), the social choices and decisions made during the process as well as the relevant criteria on which these choices and decisions are based. The five key questions mentioned in the table included in this summary should be addressed explicitly and documented.**

- **The appraisal and decision making process should become more transparent, revealing societal decision criteria and valuation of each of these criteria during the process, to increase coherence and justification of decisions.**

REGARDING RELEVANCE OF DECISION CRITERIA

- **There should be a balanced representation of societal preferences in the appraisal process.**
- **Added therapeutic value should be a necessary but not sufficient condition for a higher price or reimbursement basis. Insufficient or lack of added therapeutic value should lead to an equal or lower reimbursement basis compared to that of the best therapeutic and reimbursable alternative.**
- **Disease severity should always be considered in the light of already existing treatment alternatives.**
- **To guarantee system sustainability, value for money (evaluating the reasonableness of –extra– cost for –extra– effects) should be discussed during the expert committee meetings and be part of the considerations underpinning the reimbursement advice (or decision).**
- **In case of uncertainty, the expert committee might consider reducing the estimated level of added therapeutic value, reimbursing at a lower price, making a risk sharing agreement, or advising temporary reimbursement with clear guidance on the kind of evidence to be presented at revision and with the enforcement of clear consequences.**

REGARDING REVISABILITY

- **Decisions should be revisable, especially in case of much uncertainty around the evidence.**
- **Reasons for revisions should be: new treatment opportunities (including non-pharmaceutical) becoming available, lower effectiveness and/or higher costs than predicted , and a changing economic and/or societal context.**
- **Revision should include the possibility of delisting of products, possibly limited to delisting for specific indications only in case of multiple indications for the same product.**
- **Large across-group revisions should be performed to ensure prioritising the highest medical, therapeutic and societal needs.**

REGARDING ENFORCEMENT

- **Performance of the system in terms of transparency, relevance of decision criteria and revisability of decisions should be systematically monitored.**
- **Follow-up indicators of drug reimbursement decision-related outcomes may need to be developed or refined through future research.**

Scientific summary

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	Country	English / *Local language*
AU	INT	Austria
ACP	NL	Appraisal committee/ *Advies Commissie Pakket*
AGES	AU	Austrian Agency for Health and Food Safety / *Agentur für Gesundheit und Ernährungssicherheit*
Art.	INT	Article
ATC	INT	Anatomic Therapeutic Chemical
ASMR	FR	Improvement in medical service rendered / *Amélioration du service médical rendu*
ASVG	AU	General Social Insurance Act / *Allgemeines Sozialversicherungsgesetz*
AWBZ	NL	Act for Exceptional Medical Expenses/ *Algemene Wet Bijzondere Ziektekosten verzekering*
BAK	AU	Federal Chamber of Labour / *Bundesarbeiterkammer*
BE	INT	Belgium
BMG	AU	Federal Ministry of Health / *Bundesministerium für Gesundheit*
CBG	NL	Medicines Evaluation Board/ *College ter Beoordeling van Geneesmiddelen*
CEESP	FR	Economic and public health committee/ *Commission évaluation économique et de santé publique*
CEPS	FR	Economic Committee for Health Products/ *Comité Economique des Produits de Santé*
CFH	NL	Expert Pharmaceutical Advisory Committee/ *Commissie Farmaceutische Hulp*
CRM/ CTG	BE	Drug Reimbursement Committee / *Commission de Remboursement des Médicaments / Commissie voor Tegemoetkoming Geneesmiddelen*
CT	FR	Transparency Committee/ Commission de la Transparence
CTG/ CRM	BE	Drug Reimbursement Committee / Commissie voor Tegemoetkoming Geneesmissdelen / Commission de remboursement des médicaments
CVZ	NL	Health Care Insurance Board/ *College voor Zorgverzekeringen*
DAM	FR	National Health Insurance representatives/ *Délégués de l'assurance maladie*
DBC	NL	Diagnosis related Treatment Combination/ *Diagnose Behandel Combinatie*
DRC	BE	Drug Reimbursement Committee
DRG	INT	Diagnosis related groups
DTC	SW	Drug and Therapeutic Committee
EKO	AU	The Reimbursement Code / *Erstattungskodex*
EMA	INT	European Medicines Agency
EU	INT	European Union
FR	INT	France
GDP	INT	Gross domestic product
GIP	NL	Drug Information System of the Health Care Insurance Board/ *Geneesmiddelen Informatie Project*
GVS	NL	Drug Reimbursement System/ *Geneesmiddelen Vergoedingssysteem*
HAS	FR	National Authority for Health/ *Haute Autorité de Santé*
HEK	AU	Pharmaceutical Evaluation Board/ *Heilmittel-Evaluierungskommission*
HTA	NT	Health Technology Assessment
HVB	AU	Main Association of Austrian Social Security Institutions / *Hauptverband der Österreichischen Sozialversicherungsträger*

INAMI/ RIZIV		National Institute for Health and Disability Insurance/ *Institut National d'Assurance Maladie-Invalidité* *Rijksinstituut voor Ziekte- en Invaliditeitsverzekering*
INN	INT	International Non-proprietary Name
INT	INT	International
LFN	SW	Pharmaceutical Benefit Board/ *Läkemedelsförmånsnämnden*
MoH	INT	Minister of Health
MPA	SW	Medical Product Agency/ *Läkemedelsverket*
NBHW	SW	National Board of Health and Welfare/ *Socialstyrelsen*
NFU	NL	Dutch Federation of Universal Hospitals/ *Nederlandse Federatie van Universitair Medische Centra*
NICE	UK	National Institute for Health and Clinical Excellence
NL	INT	The Netherlands
NVZ	NL	Dutch Hospitals Association/ *Nederlandse vereniging van ziekenhuizen*
NZa	NL	Dutch Health Care Authority/ *Nederlandse Zorgautoriteit*
ÖAK	AU	Austrian Chamber of Pharmacists / *Österreichische Apothekerkammer*
ÖäK	AU	Austrian Medical Chamber / *Österreichische Ärztekammer*
OECD	INT	Organisation for Economic Cooperation and Development
OMS	NL	Medical Specialists Association/ *Orde van Medisch specialisten*
OTC	INT	Over The Counter drugs
PK	AU	Pricing Committee / *Preiskommission*
RCT	INT	Randomized Controlled Trial
R&D	INT	Research and Development
RöV	AU	Guidelines on Economic Prescribing / *Richtlinien über die ökonomische Verschreibweise von Heilmitteln und Heilbehelfen*
SALAR/ SKL	SW	Swedish Association of Local Authorities and Regions/ *Sveriges Kommuner och Landsting*
SBU	SW	Swedish Council on Technology Assessment in Health Care/ *Statens Beredning för medicinsk Utvärdering*
SEK	SW	Swedish Crowns/ *Svenska kronor*
SFK	NL	Foundation for Pharmaceutical Figures/ *Stichting Farmaceutische Kengetallen*
SMR	FR	Medical service rendered / *Service médical rendu*
SW	INT	Sweden
TLV	SW	Dental and Pharmaceutical Benefits Agency/ *Tandvårds- och läkemedelsförmånsverket*
UHK	AU	Independent Pharmaceutical Commission/ *Unabhängige Heilmittelkommission*
UK	INT	United Kingdom
UNCAM	FR	National Union of Health Insurance Funds/ *Union nationale des caisses d'assurance maladie*
VAT	INT	Value added tax
VWS	NL	Healthcare, Welfare and Sports/ *Volksgezondheid, Welzijn en Sport*
WGP	NL	Act on Pharmaceutical Prices/ *Wet Geneesmiddelenprijzen*
WKÖ	AU	Economic Chamber / *Wirtschaftskammer*
WOG	NL	Act of provision of pharmaceuticals/ *Wet op de geneesmiddelenvoorziening*
WTG	NL	Health Care Tariffs Act/ *Wet Tarieven Gezondheidszorg*
ZN	NL	Dutch Health Insurance Organisation/ *Zorgverzekaars Nederland*
ZVW	NL	Health Insurance Act 2006/ *Zorgverzekeringswet*

1 INTRODUCTION

1.1 BACKGROUND

In a context of continuously increasing public expenditure on health care in general and pharmaceuticals in particular, questions with respect to the efficiency and sustainability of the drug reimbursement policy are increasingly raised. KCE was asked to study options for an effective and structured drug reimbursement policy in Belgium.

A study on the opportunities for improving a system starts with an analysis of the strengths and weaknesses of the current system, given its objectives. A comparison between systems in European countries with similar objectives may help identifying the areas where systems perform well, where they could be improved and how they could be improved.

Previous studies often only studied the use of health technology assessment (HTA) in general health care coverage and reimbursement decision making,[16-21] specific drug policies[22] or parts of the drug reimbursement system from a broad perspective,[23-26] such as drug pricing policies,[27, 28] the link between pricing and reimbursement,[29, 30] stakeholder involvement in the decision making process[31] and the role of specific reimbursement criteria in decision making.[2, 24, 32-35] Vuorenkoski et al.[36] concluded from a literature review that most studies are descriptive.[31, 34, 35, 37] They suggest that more analytically oriented studies would enhance our understanding of how reimbursement decision making processes perform against system objectives. Several studies did analyse system processes against an ethical theoretical framework for accountability for reasonableness. They often examined, however, only one country[37, 38] or only focussed on a particular part of the process.[37, 39]

To improve upon previous research, we first provide a detailed and comprehensive description of five European drug reimbursement systems in this study. Secondly, we compare for these countries the drug reimbursement system and policy objectives, institutions, processes and criteria applied and investigate the output and implementation of the systems. Thirdly, we evaluate the five systems' organisation, structure and procedures against an ethical theoretical framework for accountability for reasonableness in order to provide insight into the legitimacy of decision making within these systems. Finally, we identify strengths and weaknesses of the five systems and, based on this, formulate general policy recommendations. As independent observers of the current drug reimbursement systems, we cannot pretend to be able to provide a solution to all potential problems of the existing systems. We might be able to look at things from a different angle, however, shedding a light on pathways that have not been fully explored yet.

1.2 OBJECTIVES

The aims of this study are:

- to describe the objectives and formal structures of the drug reimbursement systems in five European countries and to identify formal criteria used in the respective reimbursement decisions processes;
- to describe the implementation of drug reimbursement procedures in real life;
- to analyse, based on these descriptions, the similarities and differences between systems;
- to draw general conclusions with respect to the strengths and weaknesses of drug reimbursement systems in terms of their procedure and their content and outcomes;
- to formulate general recommendations for drug reimbursement systems.

The main focus of this study is on drug reimbursement systems and their implementation. A study of drug pricing or other pharmaceutical and non-pharmaceutical policy instruments used in countries to reach the health system objectives is beyond the scope of this study.

1.3 METHODS AND ANALYTICAL FRAMEWORKS

1.3.1 The description of the drug reimbursement systems

The analytical Hutton Framework (Hutton et al. 2006) was used to describe, analyse and compare the Belgian, Austrian, Dutch, French and Swedish drug reimbursement systems. We selected these countries because they were either our home country for which we wanted to formulate specific recommendations (Belgium and the Netherlands) or because they have a long history of use of HTA for reimbursement decision making (Sweden and the Netherlands). The choice of France was partly opportunistic (no language barrier for the Belgian researchers) and partly because of its explicit exclusion of the cost-effectiveness ratio as a reimbursement decision criterion, which contrasts with the other countries. Austria was selected because it was considered – based on conversations with international experts – to provide an interesting example of a drug reimbursement decision process with different types of outcomes compared to the other countries. Thus, we selected five systems representing a) various historical contextual backgrounds such as having a Beveridge-type (Sweden), Bismarck-type (Austria, Belgium, France, and the Netherlands), and managed competition (the Netherlands) health care system, b) various types of final decision makers, i.e. either the reimbursement agency (Austria and Sweden) or the minister of health (Belgium, France and the Netherlands), and c) various decision implementation levels (national in Austria, Belgium, France and the Netherlands and regional in Sweden). The United Kingdom was not included in our study because we did not want to replicate previously performed research but rather wanted to provide new insights from other countries.

We investigated policy documents, explored literature and conducted interviews with stakeholders involved in the drug reimbursement procedure. We did not analyse specific reimbursement dossiers. The selection of relevant interviewees was based on their specific involvement in the drug reimbursement procedure. Interviewees encompassed policy makers, patients (if involved in the process), and the pharmaceutical industry. A complete list of interviewees is provided in the colophon of this report. Interviews were performed by mail questionnaire (1), phone (2) or face-to-face using a semi-structured interview (34). In total 54 persons participated in the interviews/ consultation rounds: 3, 24, 5, 14 and 11 in Austria, Belgium, France, the Netherlands and Sweden respectively.

The Hutton framework is a descriptive framework. It provides a basic structure for describing the so called 'fourth hurdle' systems in a detailed and comprehensive manner. The term 'fourth hurdle' was invented by the pharmaceutical industry and refers to the fact that most countries impose specific requirements to justify the reimbursement of drugs in addition to the criteria imposed for market access (i.e. quality, efficacy and safety). These additional requirements are often an additional barrier to widespread implementation of a new drug and are therefore called the 'fourth hurdle'. Hutton and colleagues developed the framework to improve our general understanding of reimbursement systems and to achieve a better understanding of how systems use HTA in their decision making processes.[40]

The framework makes a distinction between the policy implementation level and the technology decision level. The **policy implementation level** describes how the drug reimbursement system is embedded in the broader political system. It encompasses a description of:

- the (legal) establishment of the system, i.e. the organisations and actors involved, relationship to the health ministry;
- the objectives of the system in broad terms, i.e. societal, industrial and health system objectives;
- the implementation of the system, directly by the health ministry, independent from or dependent on other health system organisations and
- the accountability of the system, i.e. managerial, political and legal accountability, obligations to consult stakeholders.

The **technology decision level** describes the process of an individual drug reimbursement application. This level distinguishes three different stages in the reimbursement process:

- the assessment
- the decision-making and
- the outputs and implementation.

Based on the descriptions of both levels, information on the characteristics of the reimbursement systems can be grouped into four sets, related to different areas:

- the constitution and governance
- the methods and processes
- the use of evidence and
- accountability and transparency.

Hutton et al.[40] developed a questionnaire to facilitate data collection in order to obtain a full overview of a reimbursement system. The collected information can be summarised in a matrix for each country. Table 1 presents the generic format of the matrix used in this study to describe each country's drug reimbursement system (see country descriptions in the appendices).

Table 1: Elements of the Hutton framework

	Elements of the system			
1. Policy level	Establishment	Objectives	Implementation	Accountability
2. Technology decision level	Constitution and governance	Methods and processes	Use of evidence	Transparency, accountability
a) Assessment	Consultation and involvement of stakeholders	Methodology	Evidence-base for assessment	Presentation and communication of assessment results
b) Decision	Who makes the decision	Decision making process	Evidence-base and additional influences	Content and documentation of the decision
c) Outputs and implementation	Appeal and dissent	Implementation and communication	Monitoring and reappraisal	Evidence of the impact of the decision

Source: Hutton et al. 2006[40]

1.3.2 Assessing accountability for reasonableness

The Hutton framework is a descriptive framework and therefore does not assign a normative value to the structure of a system. The framework can enhance our understanding of how different policies function in relation to specific requirements, related to the outcomes of the system as well as to the process of coming to these outcomes. First, reimbursement systems have clear health system objectives (quality of care, sustainability and equity), rooted in common societal values (see chapter 2). However, judging the performance of drug reimbursement systems on the outcomes of these objectives is difficult. Second, in a democratic system health care policy making should be a legitimate process for society. In this report, we operationalise legitimacy as accountability for reasonableness. To assess systems on their strengths and weaknesses relative to their accountability for reasonableness, we use a theoretical framework developed by Daniels & Sabin, defining the conditions for achieving legitimate and fair coverage decisions for new treatments.[41]

The central idea behind "accountability for reasonableness" is that, in the absence of consensus regarding the relevance of ethical principles, priority setting is legitimate if everyone agrees on a fair priority-setting procedure.[41] In other words, it is recognised that moral disagreements exist within a community about the ethical principles that should guide priority setting, but that despite this, consensus might be found about the fairness of a procedure. When translated to drug reimbursement procedures, this implies that there should not necessarily be consensus about the weight given to each of the drug reimbursement criteria (e.g. added therapeutic value, improvement in applicability as part of the added therapeutic value, severity of disease, budget impact) but there should be agreement about the fairness of the decision making process and the relevance of the criteria considered during the process.

According to Daniels and Sabin, a fair and legitimate priority setting procedure satisfies four conditions:

1. Transparency: the process must be fully transparent about the grounds for/rationales behind a decision
2. Relevance: the decision must rest on reasons that all stakeholders can accept as relevant to meeting health needs fairly given the resource constraints
3. Revisability: decisions should be revisable in light of new evidence and arguments
4. Enforcement/regulation: there must be some kind of regulation guaranteeing the three conditions described above.

1.4 KEY CONCEPTS

The term **drug reimbursement system** is used in this report for the policy system that determines whether or not a drug is entitled to reimbursement and under what conditions. It encompasses the entire process from the submission of a reimbursement request to the final decision.

We use the umbrella term **technical department** for the responsible department (also called "the secretariat") of the reimbursement agency that prepares the assessment, accumulates evidence and draws up draft reports. We use the term **expert committee** for the responsible committee of external experts evaluating the reimbursement file and formulating the reimbursement advice (or decision). Unless specified otherwise, **minister of health** is used to refer to the minister responsible for the drug reimbursement system.

The Hutton framework distinguishes between "assessment" and "decision making" at the technology decision level. We add the concept of appraisal at this level. The National Institute of Health and Clinical Excellence (NICE) in the United Kingdom was one of the first institutions that formalised the distinction between assessment and appraisal.[21]

In the **assessment phase**, the clinical, pharmacotherapeutic and pharmacoeconomic outcomes of a drug are quantified and compared to available reimbursed drugs. The assessment thus determines the (incremental) clinical efficacy and effectiveness, the (incremental) pharmacotherapeutic value and the (incremental) cost-effectiveness ratio of a drug. In principle, the elements considered in the assessment phase can be broader, including also a description of ethical and organisational issues. The assessment phase is purely descriptive in nature, meaning that it does not include a value judgement. It describes the evidence, the level of the evidence (taking into account the methodological quality of the studies presented) and the uncertainty about the outcomes.

The societal value of a drug is evaluated in the **appraisal phase**. Appraisal is context-specific and implies evaluating the societal *value* of a drug by weighing the assessment outcomes and other (societal) criteria. These criteria mainly reflect health system objectives such as equity, quality of health care and system sustainability. It seeks to gauge the societal willingness to pay for a drug with a particular outcome on each of the criteria. Some of the criteria are difficult to measure objectively. For clarity of the further analysis, we limit the criteria considered during the assessment and appraisal phase to health(care sector)-related criteria. Impact of a positive reimbursement decision on e.g. the national economy or employment is not taken into account in the appraisal phase according to our definition.

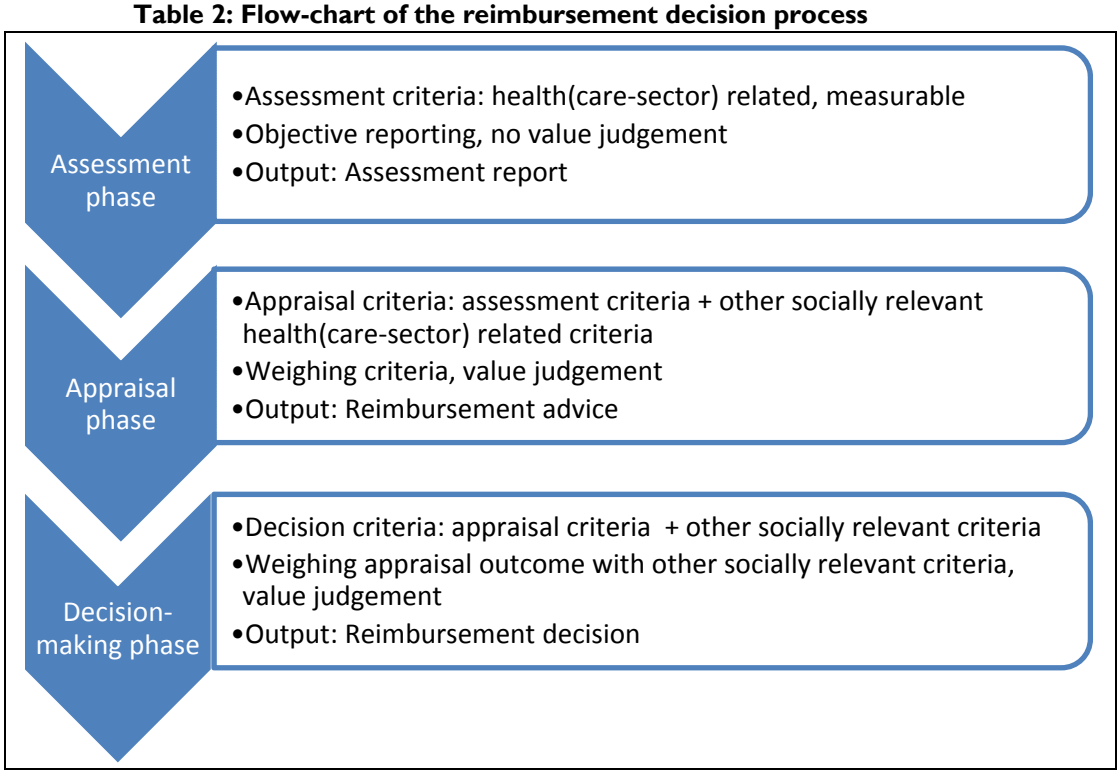
The final reimbursement decision is made in the **decision-making phase**. The decision is based on a value judgement (i.e. an appraisal) of pharmaceutical interventions from a broader societal point of view. This implies including the above mentioned health system objectives as well as other non-health care-related outcomes. As stated by the World Health Organisation "It is the role of ministries and ministers, as the stewards of the health of their people, to take responsibility […] and to be accountable for the health sector and for action – across sectors – that influences health."[42] Better health is a means to obtain a bigger and more productive economy as well as higher levels of wellbeing – two societal objectives the decision maker is supposed to take into account when making decisions. Health system sustainability is not necessarily obtained by reducing health spending or limiting its increase. Health can be regarded as an asset, helping to address sustainability challenges.[42] At the same time, the decision maker has to ensure that health spending does not crowd out expenditures on other goods and services that provide welfare gain.[43] This is the broad societal responsibility decision makers have to take.

The additional distinction we make between appraisal and decision-making compared to the Hutton framework is important, as there is not necessarily a one to one relationship between the outcomes of the assessment and appraisal process and the final decision.

The required strength of the relationship between the advice and the decision is a political decision. Countries can choose to consider *all* socially relevant criteria in the appraisal process, including the health care sector related and the non-health care sector related criteria, in which case there is no reason to make a distinction between the appraisal and decision making phase. Countries can also choose to give discretionary power to the minister responsible for drug reimbursement decisions.

A graphical presentation of the different phases in a drug reimbursement decision process, with for each phase our operational definition, is given in Table 2.

Table 2: Flow-chart of the reimbursement decision process



1.5 STRUCTURE OF THE REPORT

Chapter two describes our findings regarding similarities and differences between the Austrian, Belgian, Dutch, French, and Swedish drug reimbursement systems. The chapter starts with setting the scene for the Hutton framework comparison (paragraph 2.1). It briefly describes the five health care systems and pharmaceutical policies to define the context of each drug reimbursement system. Subsequently, we start using the Hutton framework to compare the five drug reimbursement systems (paragraphs 2.2 and 2.3). In these sections we compare the reimbursement policies, the assessment, appraisal and decision-making processes and the outputs and implementation of decisions. For each of these framework elements, we evaluate how the systems are governed, who are the involved key actors and what are the methods and processes used. A summary of findings is presented in Table 5 to Table 9. More detailed descriptions of the reimbursement systems in each country are provided in the appendices, following the structure of the Hutton framework. The third chapter moves beyond the descriptive Hutton framework and discusses the possible strengths and weaknesses of reimbursement systems in terms of "accountability for reasonableness". This chapter also provides the final conclusions and general recommendations. In the final chapter, we reflect on the issues in the current Belgian drug reimbursement system as identified during the consultation rounds with the members of the Drug Reimbursement Committee (CTG/CRM).

Key messages

In this report, we compare five European drug reimbursement systems (Austria, Belgium, France, the Netherlands and Sweden) regarding their

- **system institutions and reimbursement policies,**
- **assessment, appraisal and decision making processes,**
- **reimbursement criteria applied and**
- **outputs and implementation.**

We discuss potential strengths and weaknesses in terms of the procedural requirements for accountability for reasonableness of drug reimbursement decisions in a democratic system.

Our premise is that in a democratic system a health care decision maker can only be held accountable for the reasonableness of his/her decisions if the objectives of the health care system are clearly specified and if a number of procedural criteria and criteria with respect to the contents of the decision are satisfied.

2 COUNTRY COMPARISON

2.1 CONTEXTUAL BACKGROUND

2.1.1 Health care system characteristics

All five countries have a health care system covering almost their entire population (>99%). The systems are, however, rooted in a different historical context. The Swedish system originates from Beveridge-type national health system and has a long tradition of decentralisation, whereas the other four countries originate from Bismarck-type social insurance system. With social insurance systems increasingly relying on general taxation for health care financing, the distinction between the systems is increasingly becoming blurred. The Dutch system is the only health insurance based system in our comparison with a regulated market by means of managed competition between providers and insurers.

Although all health systems and health policies are mainly regulated at the national governmental level, policy implementation and financial responsibility can be regional or rely on actors outside the government. This is reflected by the different decision implementation levels in different countries.

2.1.2 Health care system and policy objectives

Many similarities are found between the five countries concerning their stated health care system and policy objectives, including the pharmaceutical policy objectives. The overarching and primary objective of any health care system is to improve or maintain health, within the constraints of limited resources and societal preferences with respect to equity. We identified the following health policy objectives in all countries: system sustainability, equity and quality of care. Some authors have argued that system sustainability is a policy constraint rather than a policy goal because it is not independent from other health system objectives such as health gain, efficiency, equity and quality.[43] Similarly, WHO identifies five health system objectives,[a] which do not include financial sustainability.[44] We do not argue, however, that system sustainability is an independent policy objective. Health policy in general, and drug reimbursement policy in particular, should address all three policy objectives. The objectives are often competing. For example, maximal access to high quality of pharmaceutical care would be guaranteed by full reimbursement of all drugs with therapeutic value, but such a policy would conflict with the objective of keeping the system sustainable. Similarly, giving access to all types of pharmaceutical care would not be so difficult if the patient would be held responsible for the full cost, but such a decision would conflict with the equity objective because some patients would not be able to afford specific treatments. The three policy objectives are, therefore, not independent.

All agencies responsible for drug reimbursement policy included in our study define system sustainability as one of their objectives. We therefore present sustainability as a policy objective, although we recognize it is, as such, not an independent health care system objective. It can be regarded as an intermediate objective, contributing to reaching the primary objective of improving and maintaining health.

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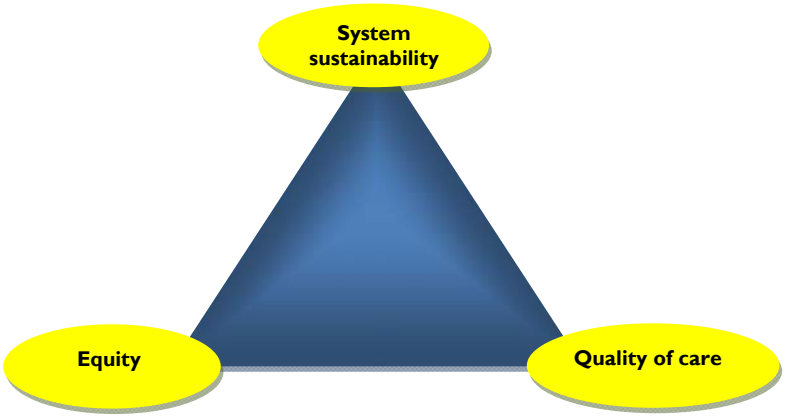
[a] The five health system goals according to the WHO are health, health equity, responsiveness, responsiveness equity, and equity in financial contribution.

One could see the three objectives as the poles of a triangle (Figure 1), where the aim of health care policy – and by implication drug reimbursement policy – is to balance the objectives and obtain a socially accepted equilibrium that reflects to the best possible extent the societal preferences. Countries might differ in how they make trade-offs between the three policy objectives and hence where they are situated within the triangle. Policy making always implies dealing with the inherent equity-efficiency trade-off of the system, where efficiency simultaneously deals with the sustainability objective and the quality of care objective.

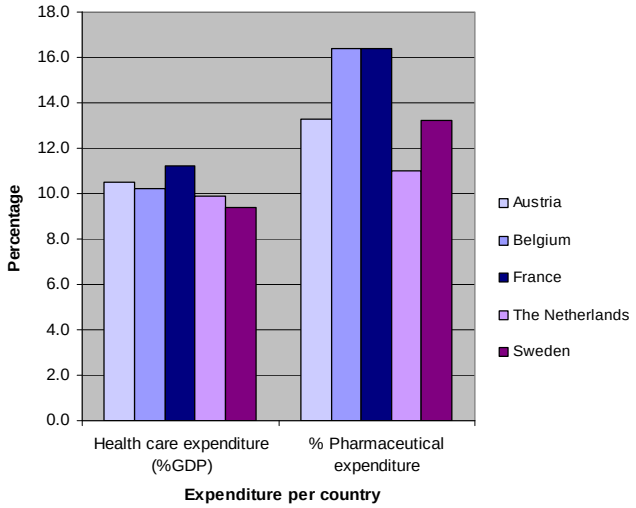
Figure 1: Competing health care policy objectives



2.1.3 Health care funding and pharmaceutical expenditure

All countries experience rising health care and pharmaceutical expenditure, which are putting an increasing pressure on health care budgets. Figure 2 displays health care expenditure as a percentage of gross domestic product (GDP) and the share of pharmaceutical expenditure in total health care expenditure for all five countries. Health care expenditure varies from 9.4% of GDP in Sweden to 11.2% of GDP in France. Larger variation is observed between countries in pharmaceutical expenditure as a share of total health care expenditure, ranging from 11.0%[a] in the Netherlands to 16.4% in Belgium and France.

Figure 2: Health care and pharmaceutical expenditure

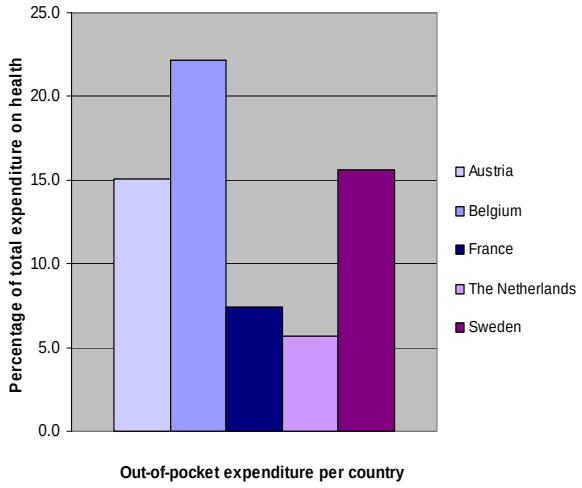


Source: OECD Health Data 2010 – Year 2008

a OECD estimate for year 2007

The largest share of total health expenditure in all countries is publicly financed (> 75%); patients are responsible for less than 25% of the expenditure. Figure 3 shows the share of out-of-pocket expenditure in total health expenditure per country. The percentage of out-of-pocket expenditure is lower in the Netherlands (5.7%[a]) and in France (7.4%) than in Austria (15.1%), Sweden (15.6%) and Belgium (22.2%[b]). It should be noted that although the estimates for all countries originate from the same source (OECD), there may be variations in the composition of these figures between the countries. The figures should therefore be interpreted with caution.

Figure 3: Out-of pocket expenditure on health



Source: OECD Health Data 2010 – Year 2008

Similarly, prescription drugs are largely financed from public sources. Although inpatient and outpatient drugs are reimbursed by national compulsory insurance or the national health system, the way they are reimbursed differs. Drugs delivered in the hospital sector are financed by means of diagnosis related group (DRG) system, by means of a lump sum per hospitalisation day, or by decentralising budget responsibility. All countries but Sweden have a specific and/or supplementary financing scheme for highly expensive inpatient drugs. However, in Sweden total health care budget responsibility is often decentralised to hospitals.

All five countries have an open-ended budget for pharmaceuticals although this is moderated by setting annual goals for pharmaceutical expenses, which are closely monitored. Budget control mechanisms exist in all countries: a priori if there is a presumed budgetary risk and/or ex-post when the budget has effectively been exceeded. Budged control mechanisms are implemented on an ad hoc basis. In Belgium, drug budget control mechanisms exist, such as maximum prices, reference pricing, risk-sharing agreements and turnover taxes imposed on the pharmaceutical industry to cover the budget excess up to €100 million.[c] In France, most companies make agreements with the national pricing authority (CEPS) that define the annual rebates to be made to the national insurance if the growth rate objective is exceeded. The few companies that do not enter the framework agreement are subject to another regulatory mechanism known as the safeguard clause.[d] In the Netherlands several policies are applied to control the pharmaceutical expenditure such as maximum prices, price reductions, claw-back agreements and preferential policies.

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a OECD estimate

b OECD estimate

c Programme -Law of 22 December 2008[45]

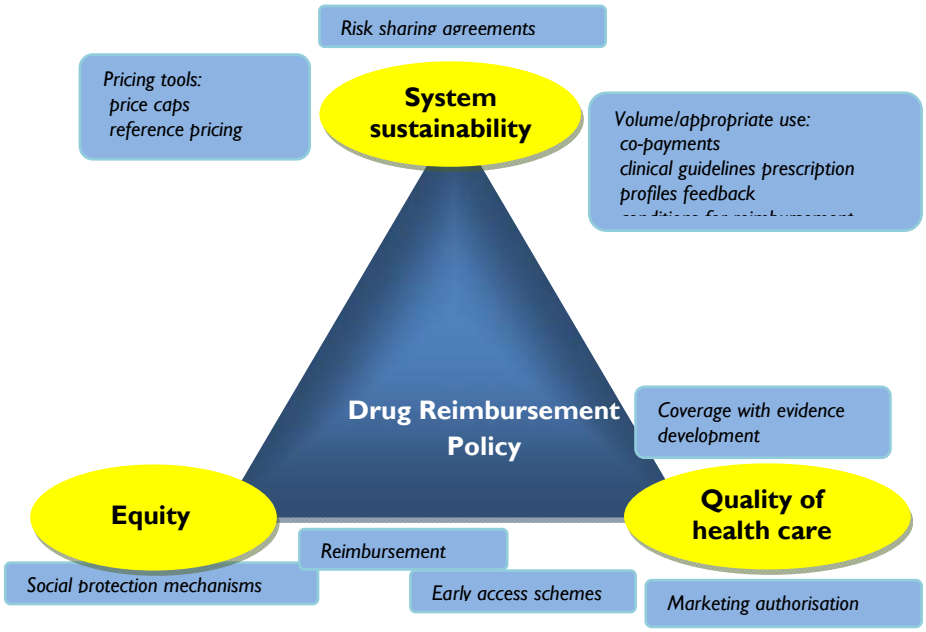
d The safeguard clause consists of a contribution to be paid by a pharmaceutical company when its pre-tax volume of sales of reimbursable drugs in France exceeds the growth rate objective. The amount of the rebates paid by each company is not publicly known.

In Sweden, county councils receive an annual governmental grant for outpatient pharmaceutical expenditure which is negotiated based on the content of the positive outpatient drug list. However, the county councils´ pharmaceutical budgets remain a part of their total budget and can thus also be classified as an 'open-ended' budget.

2.1.4 Pharmaceutical policies

The five countries not only differ in how they balance the three health policy objectives but also in the tools they use to meet these objectives. Figure 4 presents some of the applied tools (blue rectangles). System sustainability can, for example, be enhanced by supply- and/or demand oriented policy tools. Supply-oriented tools include pricing policies and risk sharing agreements; demand-oriented tools target the key-drivers of the demand, being the patients, providers and pharmacists. It is important to note that the same tool can serve different objectives.

Figure 4: Pharmaceutical policy tools



2.1.4.1 Pricing policies

All countries adopt price regulations. France, Sweden and Austria have no centralised price regulations for inpatient drugs, meaning that hospitals, county councils and hospital pharmaceutical commissions, respectively, directly make price agreements with manufactures. Although the Netherlands has drug price regulations, hospitals can directly make price agreements with manufactures.

Although pricing and reimbursement responsibilities may belong to separate ministries or agencies (as in Belgium, France and the Netherlands) pricing and reimbursement are strongly linked. In all countries, the final price and/or reimbursement basis at least partially depend on the drug reimbursement evaluation. For example, the price allowed for a drug with similar therapeutic value compared to the available reimbursable alternative(s), is strongly related to the price of the alternatives (internal reference pricing), while a drug with a recognised added therapeutic value can usually obtain a price premium.

Price regulation occurs at the national level, but noteworthy is that all countries but Sweden use external price referencing. This means that comparison with prices in other EU countries is used to determine the national price of a new pharmaceutical product. It should be noted that even though Sweden does not use external price referencing, it is the only country in which the price and reimbursement decision is made as one combined decision by one agency, taking cost-effectiveness into account as direct price criterion.

The use of external price referencing, combined with national pricing and reimbursement regulations, influence manufacturers' decisions and timeframes for applying for reimbursement in a particular country and, as a result, the time of access to drugs in countries.

Additional pricing tools such as price freezes and/or cuts are applied in all countries except Austria and Sweden. Moreover, all countries but Austria use internal reference pricing. This system limits the reimbursement of drugs by establishing a maximum price or reimbursement level for a group of pharmaceutical products. The Netherlands applies clusters with therapeutically equivalent drugs whereas in Belgium and France the internal reference pricing scheme only clusters drugs with same active chemical ingredients. In Sweden the accepted price of drugs is based on the price of therapeutically similar drugs.

2.1.4.2 Risk sharing agreements

Risk sharing agreements are another tool to control the budget impact. Different types of risk sharing agreements exist, ranging from price-volume agreements on the aggregate level to pay for performance on the individual patient level. France is the only country that frequently uses financial based risk sharing agreements by means of price-volume contracts. In Belgium financial based risk sharing agreement with a company are also possible. So far only a few agreements have been made but revisions in the procedure in 2010 may lead to an increase in these arrangements in the coming years. Such agreements can only be negotiated for drugs with a recognised added therapeutic value but for which the expert committee formulated no or a negative reimbursement advice. Although the Swedish central reimbursement agency does not use financial risk sharing agreements, county councils are allowed to make these agreements. This, however, rarely occurs.

2.1.4.3 Stimulating appropriate use

Besides price regulations, several tools are used to encourage appropriate use of pharmaceuticals. All countries publish to various extents prescription guidelines (HVB´s prescribing guidelines in Austria, INAMI/RIZIV guidelines in Belgium, HAS guidelines in France, CFH guidelines in the Netherlands and DTC guidelines from county councils in Sweden). In France, the national health insurer also sends representatives to prescribing physicians to increase the impact of guidelines (Délégués Assurance Maladie). Policies can also target prescribers by monitoring prescription behaviour (e.g. feedbacks) possibly combined with financial incentives.

2.1.4.4 Co-payments and deductibles

All countries use co-payments and/or deductibles for pharmaceuticals. Table 3 summarises the cost-sharing arrangements. In the Netherlands outpatient drugs on the positive list are fully reimbursed but patients pay a general compulsory deductible, irrespective of the type of health care consumed. In France the reimbursement rates vary depending on disease severity and the level of medical service rendered (SMR), but the majority of the remaining out-of-pocket costs are borne by the complementary health insurance, which covers almost the entire population. Since 2008, a deductible per package is applied for outpatient drugs. Similarly, Austria applies prescription fees for outpatient drugs, meaning that patients have to pay a deductible per drug package. In Sweden, patients are fully reimbursed for outpatient drugs once they have reached a drug specific co-payment limit. In Belgium, patients pay a co-insurance for pharmaceuticals (i.e. a percentage of the reimbursement basis). There are five reimbursement categories defining the level of co-insurance. The reimbursement categories are meant to reflect the therapeutic necessity of the drug. The co-insurance is capped per drug package.

Moreover, Belgium implemented an income-dependent ceiling for total out-of-pocket expenditures (excluding supplements) for all partially reimbursed health care, including pharmaceuticals.

As a consequence of the various reference pricing schemes implemented in Belgium, France and The Netherlands (the reference reimbursement system, the tariff basis for reimbursement (TFR) and internal referencing price scheme, respectively), patients are responsible for the extra expenses if they consume a more costly drug than the average cluster or reference price. This means that any price difference is added to initial co-payment(s). Sweden uses a system of obligatory generic substitution in which substitutable pharmaceuticals are clustered, patients only pay the price difference when they refuse the generic substitute.

All five countries apply cost-sharing mechanisms for hospital care which includes drug use. Austria, Belgium, and Sweden apply fees per hospitalisation day whereas France applies two type of fixed fees, one if the patient stays over 24 hours and one if treatment costs exceed a certain threshold. The Netherlands has a general deductible including costs for hospital care.

Table 3: Cost sharing arrangements for drugs

	Austria	Belgium	France	The Netherlands	Sweden
Cost-sharing arrangements					
Outpatient drugs	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
- Mechanism	Prescription fees	Product-specific capped co-insurance	Prescription fees	General health care deductible	Drug-specific co-payment with total co-payment limit
- Cost sharing for generics / reference pricing / cluster pricing	n/a*	Co-pay above reference price for drugs included in the RPS	Co-pay above cluster price for drugs included in the TFR	Co-pay above max cluster price (for all drugs)	Co-pay above generic substitute
Inpatient drugs (or as part of hospital use)	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
- Mechanism	Co-payment per hospitalisation day	Co-payment per hospitalisation day	Co-payment per admission	General health care deductible	Co-payment per hospitalisation day
Reimbursement levels and cost-sharing for outpatient drugs					
Level(s) of reimbursement	100%	100%; 75%; 50%; 40%; 30%	100%; 65%; 35%; 15%	100%	100% after-co-payment limit
Criteria for reimbursement level	n/a	Drug categories: A; B; C; Cx and Cs (based on treatment necessity)	Disease severity and level of clinical benefit (SMR)	n/a	n/a

*In Austria a drug with similar therapeutic value cannot to be priced higher than the reference price.

2.1.4.5 *Stimulating demand for less costly drugs*

Pharmaceutical policies also seek to increase the share of low-priced drugs such as generics. Physicians are encouraged to prescribe using the international non proprietary name (INN) in all countries but Austria and Sweden. In Sweden such a prescription is invalid. However, this is balanced by the obligatory generic substitution by pharmacists. Belgium and Austria are the only countries where generic substitution has not been implemented (yet[a]), whereas in France and the Netherlands it is encouraged through (financial) incentives. In Belgium, only when physicians prescribe using INN, pharmacists should first try to deliver the lowest-priced drug and, if not available, move to a higher-priced drug.

2.1.4.6 *Social protection mechanisms*

The five countries use preferential policies to protect vulnerable groups against high out-of-pocket expenses or unequal access to health care. Countries differ in the criteria they use to define vulnerable groups. This can be based on societal, health and/or economic considerations (e.g. elderly, chronically ill and low income patients). Social protection mechanisms can be designed for health care in general – in which case they also apply to pharmaceutical expenses – or for pharmaceutical expenses in particular.

[a] In Belgium, generic substitution is provided for by the law (Art. 34 of the Law of 6 August 1993) but this law has not been put into practice yet because the Royal Decree is still lacking.

2.1.4.7 Marketing authorisation and (early) access schemes

Access to high quality pharmaceutical care is mainly ensured by marketing authorisation policies. All five countries control market access on the basis of efficacy, safety and quality criteria. To guarantee access to necessary drugs that are not (yet) assessed by the reimbursement agency, some countries have implemented early access schemes. In Austria, drugs being considered for reimbursement can already be reimbursed during the evaluation period (180 days) under specific conditions. Moreover, there is a list of non-reimbursed drugs which, under the ex-ante approval of a physician of the health insurance funds, may be reimbursed on an individual basis. The treatment must be essential and no other reimbursable medication should exist. In Belgium the publicly funded Special Solidarity Fund reimburses expensive and non-reimbursed drugs on an individual basis. In France, new innovative drugs against serious or rare diseases, which are still under development but for which there is believed to be clear evidence, can be granted a temporary use authorisation (ATU, Autorisation Temporaire d'Utilisation) in a hospital setting. Authorisation can be given either for a cohort of patients or on an individual basis and is granted for one year, renewable until market authorisation is granted. Sweden has no specific policy for ensuring early access before a reimbursement decision is taken. However, county councils are allowed to provide and reimburse any drug without an assessment by TLV. In the Netherlands there is no scheme that offers reimbursement before a drug is assessed by CVZ.

2.2 POLICY IMPLEMENTATION LEVEL

This section compares the five drug reimbursement systems at the first level of the Hutton Framework, i.e. the policy implementation level (see Table 1). This level considers the main objectives of the drug reimbursement systems, their establishment, their implementation, and their accountability. Our findings are summarised in Table 5 (page 25).

2.2.1 Objectives of the drug reimbursement system

As mentioned above, similarities were found between the countries in their health care policy objectives. All systems explicitly state to seek equitable and affordable access to high quality health care in a sustainable manner. In Austria, Belgium, France and the Netherlands, financial sustainability is expressed in the overall drug policy objectives in terms of monitoring the pharmaceutical budget. All countries strive towards both sustainability and quality of care by increasing efficiency in pharmaceutical care.

Besides the common general health care policy objectives, some objectives are specific to the drug reimbursement system. First, transparency towards the pharmaceutical company is a shared objective. Triggered by the EU Transparency Directive 89/105/EEC, all systems seek to ensure transparency in their reimbursement processes towards the applicant. Improving transparency was central in recent reforms of the systems. Second, rewarding innovation and private investments in pharmaceutical R&D is also an objective shared by all systems. This is mostly achieved by granting higher prices to pharmaceuticals with added therapeutic value. None of the systems is clear about the actual place of these "non-health" objectives, but they allow the minister (Belgium, France and the Netherlands) or the drug expert committee level (Sweden) to take them into account in their reimbursement decision.

2.2.2 Establishment of the system

2.2.2.1 A wave of reforms

In the last decade, all countries have quite intensively reformed their reimbursement system's legal basis. Seeking to improve efficient decision-making in the context of increasing health care expenditure and complying with the Transparency Directive were key motives for the changes. With regard to the former objective, all countries but France added the requirement of pharmacoeconomic evidence in the reimbursement application. With regard to the latter objective, most reforms sought to improve the involvement of the applicant in the procedure and transparency in terms of reimbursement criteria. Independent advisory committees were set up in all countries and made responsible for the critical assessment of the reimbursement request. In the Netherlands, the reimbursement agency was established in the early 80s, changed to an assessment agency with a more independent role in 1999 and was again revised in 2006. In Belgium, the procedure was deeply revised and the transparency commission in charge of the evaluation of reimbursement requests was replaced by a new expert committee (CRM/CTG). In Sweden the reimbursement procedures were intensively modified in 2002 and a new agency (TLV) was established accordingly. In France, the existing expert committee was modified to integrate the National Authority for Health (HAS) set up in 2004. In Austria not only the expert committee (HEK) was established in 2004 but the overall drug reimbursement system was revised and implemented in 2005.

2.2.2.2 Scope of the system

In all five countries drugs have to be enlisted on a positive reimbursement list in order to be entitled to reimbursement. The reimbursement eligibility of each individual drug is thus assessed in all countries. All centralised drug reimbursement systems consider outpatient drugs. The systems vary for inpatient drugs. In the Netherlands only expensive inpatient drugs are part of the system, whereas in Belgium and France inpatient drugs are part of the system. In Sweden and Austria inpatient drugs are not assessed by the central drug reimbursement agencies but are the responsibility of county councils in Sweden and the hospitals and the Länder in Austria.

2.2.2.3 Manufacturers initiated process

In all five systems, the reimbursement process is initiated by manufacturers by submitting a reimbursement request, including supporting evidence. An exception is a reimbursement application for expensive inpatient drugs in the Netherlands, this process ought to be initiated by (university) hospitals federations, the medical specialists association or the Dutch Health Insurance Organisation. Nevertheless, in most cases the manufacturer is the one who prepares the reimbursement request. In Austria, the HVB is legally entitled to initiate a reimbursement procedure in the absence of a reimbursement request from the company, although in practice it rarely occurs.

2.2.2.4 Centralised reimbursement procedure

a) Organisational structure

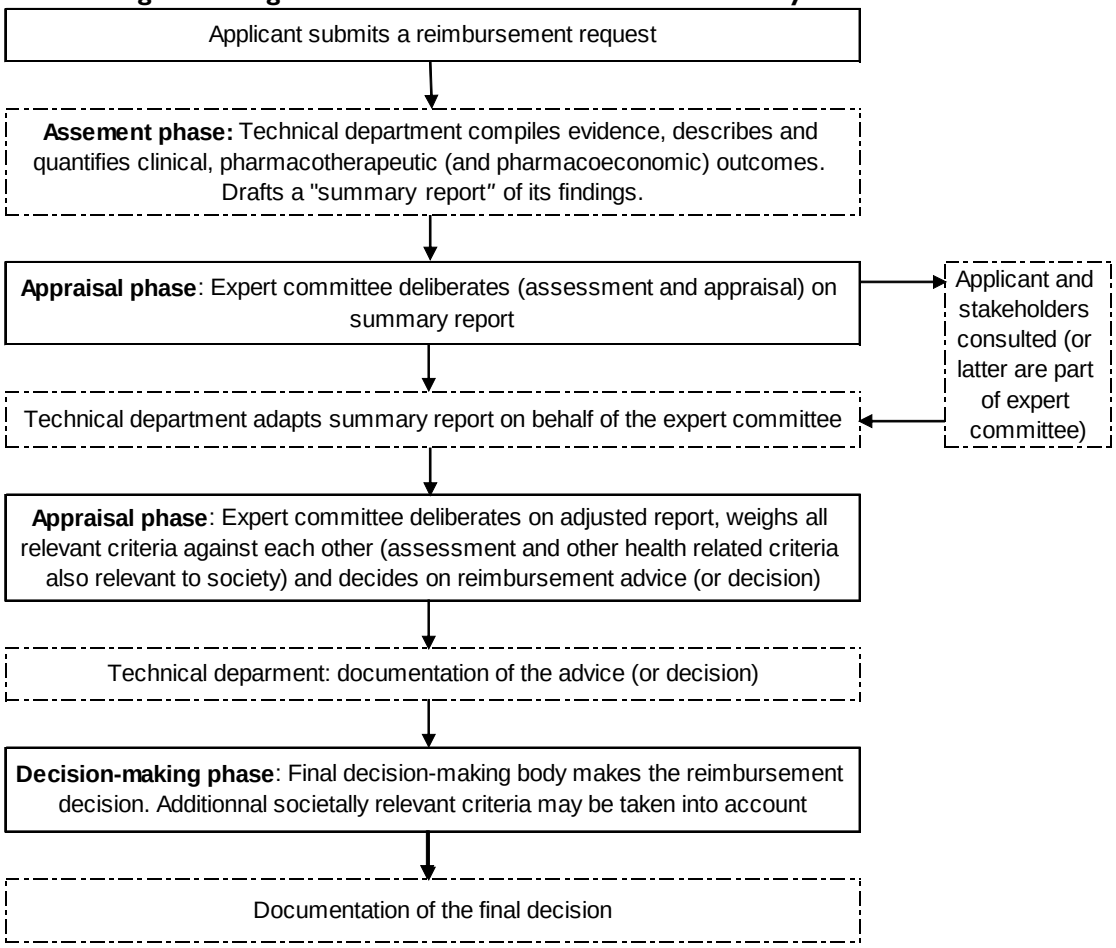
A shared characteristic of the five reimbursement systems is the existence of a centralised reimbursement agency: HVB in Austria, INAMI/RIZIV in Belgium, HAS in France, CVZ in the Netherlands and TLV in Sweden. Within these reimbursement agencies a drug reimbursement expert committee is responsible for advising the final reimbursement decision-maker (except in Sweden). Expert committees are considered independent because committee members are appointed for their scientific skills, personal capacities and expertise; and members have to disclose any conflicts of interest. In Austria, France and the Netherlands, the reimbursement agency appoints the expert committee members whereas in Belgium and Sweden the minister of health appoints these members, who are nominated by the stakeholders they represent. Members with conflicts of interest for a specific case might be excluded from the voting procedure and/or the meeting. In France and Belgium the expert committees meet once every two weeks.

In Austria, the Netherlands and Sweden they meet once a month. Noteworthy is that only the Netherlands has a separate appraisal committee (ACP) besides the expert (assessment) committee (CFH).

A second common feature is the existence of a specific technical department – or secretariat – within the centralized reimbursement agency responsible for compiling scientific evidence, both from the manufacturers' file and from the additional evidence found in scientific literature and/or from expert opinions. This technical department prepares the critical assessment of the reimbursement request and drafts the preliminary summary report and/or reimbursement proposal.

Figure 5 provides a general overview of the organisational structure of reimbursement systems and present a general flow-chart. Country-specific more detailed flow-charts are provided in the respective appendices.

Figure 5: Organisational structure of reimbursement systems and flow-chart



b) Composition of the expert committees

A closer look at the composition of these agencies and their responsibilities in the reimbursement process unveils divergences across the countries. Table 4 shows the expertise of the various committee members in detail. Belgium has the largest expert committee, consisting of 31 members, 23 of which have voting rights, and Sweden has the smallest expert committee.

Table 4: Composition of the expert committee

	Austria	Belgium	France	The Netherlands	Sweden
Expert committee	**HEK**	**CRM/CTG**	**CT**	**CFH (ACP)**	**TLV expert board**
Voting members	**20** - 3 academics - 10 sickness funds - 2 physicians - 1 pharmacist - 2 employees/ consumers - 2 pharmaceutical industry	**23** - 1 chairperson - 7 academics - 8 sickness funds - 4 physicians - 3 pharmacists	**20** - 1 chairperson from HAS board - 19 members with medical of pharmacological expertise	**CFH: (max) 24** - 1chairperson from CVZ - members with expertise in pharmacological, medical, health sciences and economics **(ACP): 9** - 3 CVZ board of directors - 6 members with societal expertise (e.g. patient, ethicist, economist)	**7** - 1 chairperson - 1 pharmacologist - 1 (health) economist - 1 patient -3 health care planners
Permanent consultative members	**1** - 1 from federal government	**8** - 4 from ministries - 3 pharmaceutical industry - 2 from INAMI/RIZIV	**8** - 4 from public institutions - 1 pharmaceutical industry representative - 3 sickness funds representatives	n/a - 2 ministerial observers	n/a
Total	**21**	**31**	**28**	**24 (9)**	**7**

We could distinguish two main models for the composition of these committees. The Belgian and Austrian committees mainly consist of representatives of all relevant stakeholders (e.g. medical, pharmacological and/or health economics academics and representatives from prescribers, pharmacists, sickness funds and the pharmaceutical industry). Experts entitled with a voting right are allowed to appraise the reimbursement request in the light of their stakeholders' preference values. One may argue that decision making incorporates societal preferences as long as the weight given to each stakeholders' opinion reflects societal preferences.

In contrast to the first model the composition of the committee more heavily relies on academic and other scientific experts in Sweden, the Netherlands and France. Stakeholders can be consulted but are not entitled to participate in the deliberation. In the Netherlands, the CFH (and/or the CVZ) can decide to appoint relevant stakeholders (e.g. physicians, physician associations, patient associations and hospital associations), who receive one or two weeks to put forward their comments. Sweden recently reduced the number of expert members and changed the composition of the expert committee in such that previous scientific experts were replaced by members with health care planning expertise. As a result, besides the chairperson, three of the six voting members are health care planners from county councils.

Noteworthy is that the Belgian and French expert committees include members from the pharmaceutical industry. They only have a consultative task and do not have voting rights. However, they are present during the voting procedure that occurs by showing of hands. The Austrian committee has two representatives of employees and consumers with voting rights. The Dutch appraisal committee (ACP) and the Swedish expert committee have a patient representative.

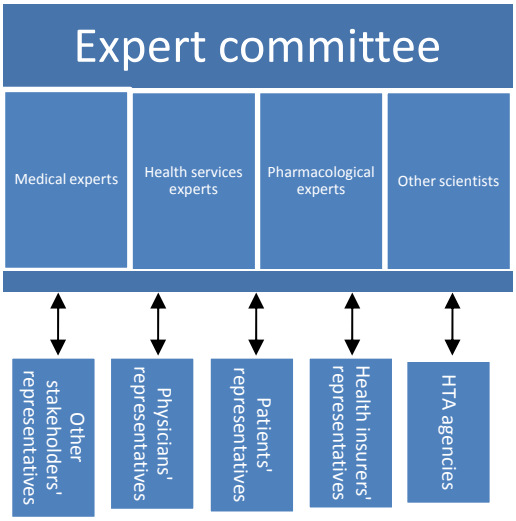
c) Deliberation-driven and assessment-driven model

The two implementation models can be classified as: (1) deliberation-driven models and (2) assessment-driven models. In the deliberation-driven model, the expert committee consists of representatives of all relevant stakeholders. In the assessment-driven model the expert committee mainly consists of academic/scientific and other experts. The latter consults relevant stakeholders on a case-by-case basis. Figure 6 gives a graphic presentation of the relationships between the stakeholders and the expert committee in the two models.

Figure 6: Deliberation-driven versus assessment-driven drug reimbursement systems

Deliberation-driven model

Assessment-driven model



Deliberation-driven models, such as in Belgium and Austria, aim to formulate advices which incorporate societal preferences by having all relevant stakeholders represented in the expert committee. Stakeholders are appointed as committee members for a specific period of time and hence involved in the appraisal process of every individual product. As such there is room for discussion about the rationale and reason for each new advice. The crucial and challenging task in this model is to select appropriate representatives, who are reasonable and fair-minded, understand the basic objectives and challenges of drug reimbursement decision making and are willing to look for mutually justifiable decisions. Lobbyists who are insensitive to reasonable and fair argumentation and only defend their personal interest, tend to block the system and should therefore not be appointed as expert members.

Assessment-driven models, such as in the Netherlands, Sweden and France, more heavily rely on academic and other scientific experts from different disciplines. These experts should reasonably adopt societal preferences to individual dossiers. This model is generally less subject to the influence of lobbyists during the appraisal phase, although such influence cannot be ruled out. Also in assessment-driven models deliberation with respect to weighing several decision criteria needs to take place. This weighing might be influenced by the public opinion about a specific product, as exposed in the media, and by direct formal or informal contacts between experts and individual patient organisations or industry.[38]

It should be noted that the distinction between assessment-driven and deliberation-driven models does not suggest anything about the objectivity and transparency of the process. A deliberation process is *per definition* never neutral or value-free. Therefore, it is of utmost importance that either committee members use societal preferences independently from their personal preferences or the committee is composed in such a way that societal preferences are represented in a balanced way.

d) Deliberation process within the expert committee

Another divergence concerns the rules around the deliberation process, e.g. consensus, quorum of presence, mode of voting. The Netherlands is the only country where members base their advice on consensus. If no consensus is reached, the advice is based on majority voting. In Sweden, France and Austria majority allows to approve an advice (decision). Belgium is unique in that a two-third majority is required to accept or reject an advice. This rule implies that the committee may end up with no advice. In that situation, the final decision-maker, the minister of social affairs receives no guidance for his/her decision from the expert committee and can only rely on the report of his/her representative at the expert committee.

e) Discretionary power of the minister of health

In all countries, the minister of health is responsible for defining the overall drug reimbursement policy and steering the system. However, divergences were found concerning the minister's responsibility in final decision-making. In Belgium, the Netherlands and France, the minister is responsible for making the final drug reimbursement decision. But even at that level, differences were found in the level of discretionary power allotted to the minister.

In France, the minister rarely deviates from the advice of the expert committee. The only notable exception occurred after a group revision which took place between 1999 and 2001, 835 drugs were no longer deemed to have a sufficient level of medical service rendered (SMR) to justify reimbursement. Facing criticism from the industry and a number of patients and providers, the minister decided not to delist these drugs all at once, but rather to progressively de-list drugs in three waves.

In Belgium, the minister is allowed to deviate from the advice for "social or budgetary reasons", be it within limits specified by law. The limits are that the deviation from the advice can only be based on one or more of the assessment elements which have already been appraised by the expert committee. Deviation from the advice –most often for budgetary reasons– sometimes occurs.

In contrast to outpatient drugs, the reimbursement decision for expensive inpatient drugs in the Netherlands is made by the Health Care Authority (NZa). Nevertheless, the minister is not only allowed to deviate from the reimbursement advice for outpatient drugs but also allowed to overrule the reimbursement decision for expensive inpatient drugs. Both deviations rarely occur.

Noteworthy is that in Austria and Sweden the minister has neither a decision right nor discretionary power with respect to individual reimbursement decisions.

2.2.2.5 From clinical effectiveness to health technology assessment (HTA)

Many European countries use HTA to support coverage and reimbursement decisions.[20] The extent of using HTA differs amongst countries. Sweden and the Netherlands have a long tradition of using HTA to inform health care policy making, amongst others through the research of independent agencies such as iMTA (the Netherlands) and SBU (Sweden). Cost-effectiveness is an explicit drug reimbursement criterion since 2002 and 2005 in Sweden and the Netherlands, respectively. Use of HTA is relatively more recent in Austria, Belgium and France. Since 2000, assessments of costs and health outcomes are used on a regular basis to inform Austrian reimbursement decisions. Moreover in 2006 the independent Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA) was established. Similarly, in 2001 cost-effectiveness was formally introduced as a reimbursement criterion in the Belgian drug reimbursement procedure and in 2004 the Belgian Health Care Knowledge (KCE) was established. While the expert committees have a legal obligation for assessing and appraising drug reimbursement requests, HTA agencies very often work on an ad hoc basis or at the specific request of policy makers. In 2008, the French National Authority for Health (HAS) was encouraged by legislation to consider cost-effectiveness information. The Economic and Public Health specialised Committee (CEESP), a specific advisory committee was set up accordingly.

Nevertheless, it is still not clear whether this new committee will effectively influence reimbursement decisions in the future or whether its role will be restricted to advise on the use of cost-effective drugs within the HAS clinical guidelines.

2.2.3 Implementation: a positive reimbursement list

In all systems, the final reimbursement decision is binding and implemented by means of a positive reimbursement list. The positive list may contain information on possible conditions for reimbursement (e.g. specialist prescription only). All systems have a positive list for outpatient drugs. Belgium has one positive list for inpatient and outpatient drugs although some drugs may be restricted to the hospital setting, whereas France applies one reimbursement process and two lists (an outpatient and an inpatient list). The Netherlands has a second positive list only for expensive inpatient drugs. In contrast, in Sweden and Austria, inpatient drugs do not fall under the centralised drug reimbursement system.

2.2.4 Accountability: impact assessment

All systems fall under ministerial responsibility and are therefore audited on an ad-hoc basis by (parliamentary) committees. There is a shared policy trend towards increasing transparency of decision-making and reimbursement procedures. However, all countries only systematically assess the impact of the reimbursement system by monitoring drug expenditure and not against other system objectives. None of the countries systematically evaluates the impact of the reimbursement system on points such as (equal) access of patients to drugs or the impact on non-drug-related health care costs. Furthermore, all countries seem to experience difficulties in evaluating the actual long-term performance of the drug reimbursement system in terms of achieving value for money. It seems unfeasible to assess the extent to which the different drug reimbursement systems reach the stated objectives as no full set of clear performance indicators for each of the objectives are available. Countries evaluate other system objectives on points such as healthy life expectancy by socio-economic status. However, it would be difficult to attribute an effect on quality of health care or on system sustainability to the drug reimbursement system or pharmaceutical policy only, as pharmaceutical policy is part of a larger political system. For example, social protection mechanisms may be in place to ensure equitable and affordable access to good quality of health care in general. These protection mechanisms do not necessarily make a distinction between pharmaceutical care and other types of health care. All countries state equal access as one of their main objectives. Nevertheless, decentralisation might result in variations in accessibility. For example, regional financial responsibility in Sweden, and hospital pharmaceutical formularies responsibility for Länder and hospitals in Austria, may lead to accessibility variations.

Table 5: Policy implementation level of drug reimbursement systems

	Austria	Belgium	France	The Netherlands	Sweden
Establishment					
- Process initiator	Manufacturer (or HVB)	Manufacturer	Manufacturer	Manufacturer (outpatient drugs)	Manufacturer (outpatient drugs)
- Decision procedure	Centralised for outpatient drugs. Decentralised for inpatient drugs	Centralised for outpatient and inpatient drugs	Centralised for outpatient and inpatient drugs	Centralised outpatient and expensive inpatient drugs	Centralised for outpatient drugs Decentralised for inpatient drugs
- Role of Minister	Policy setting, steering and overview	Policy setting, steering and overview	Policy setting, steering and overview	Policy setting, steering and overview	Policy setting, steering and overview
- Decision mandatory	Yes	Yes	Yes	Yes	Yes
System objectives	Guarantee affordable care, access to quality care and financial sustainability	Sustainability, equity, accessibility, efficiency and quality of care	Sustainability of a high quality and equitable health care system	Guarantee safe, efficient and affordable care according to individual's need	Protect individuals against high costs; value for money
Implementation	Positive list	Positive list	Positive list	Positive list	Positive list
Accountability	Parliamentary audit committee, and minister overviews	Parliamentary audit committee and minister overviews	Parliamentary audit committee and minister overviews	Audit, check & balances and minister overviews	Parliamentary audit committee and minister overviews
Impact assessment	Drug expenditure (HVB and Court of Audit)	Drug expenditure	Drug expenditure	Drug expenditure	Drug expenditure

2.3 TECHNOLOGY DECISION LEVEL

This section compares the five drug reimbursement systems at the second level of the Hutton framework, the technology decision level. This level considers the assessment and appraisal phase, the decision making phase and the implementation of the decisions (see Table 1). We evaluate similarities and differences regarding the key actors, the applied reimbursement criteria, methods and processes. Table 7, Table 8 and Table 9 provide a summary of findings on the technology decision level regarding the reimbursement advice, the final reimbursement decision and the output and implementation of the system, respectively.

2.3.1 Assessment and appraisal phase

As mentioned above, the authorities responsible for making the final reimbursement decision mainly rely on the reimbursement advice from the independent advisory bodies – except in Sweden where the independent expert committee makes the final decision. The reimbursement advice is the result of an assessment and appraisal process. Table 7 (page 30) summarises our findings on the reimbursement advice procedure: the actors and stakeholders involved in the assessment and appraisal phase and the criteria used.

2.3.1.1 Key actors

Assessment and appraisal are often found to be intertwined processes and this translates into more or less hybrid phases in which assessment informs appraisal. As a result, the division of responsibilities for the assessment and appraisal are not always clear-cut. The Netherlands is the only country with an assessment committee (CFH) and a separate appraisal committee (ACP). Although the main appraisal task is assigned to the appraisal committee, appraisal also occurs alongside the assessment, and during the final advice phase by CVZ's Board of Directors. Reimbursement advices are not appraised by the ACP on a case-by-case basis. In Sweden, only one actor (TLV) is responsible for the entire process from assessment to final decision making, there is no advice phase. In Sweden, France, Belgium and Austria, the separation between assessment and appraisal is not clear-cut. The technical department starts the assessment and informs the expert committee. The latter is *in fine* responsible for the assessment and the appraisal. This means that the expert committee discusses the assessment and appraises the reimbursement request in the light of the assessment. The expert committees, except the Swedish, advise the final decision bodies. It should be noted that the assessment reports prepared by the technical departments may contain elements of appraisal (e.g. estimating the likelihood of the accuracy of the budget impact).

2.3.1.2 Therapeutic value

We stated earlier that the objective of an assessment is to measure and present outcomes objectively. A common key characteristic in the assessment phase is the evaluation of the therapeutic value of the drug. Although all countries assess a drug's therapeutic value, the assessment itself remains country specific. Efficacy, effectiveness, safety and side-effects are formal criteria shared by all countries in the therapeutic value assessment. Moreover, interviewees in all countries acknowledged that these four criteria were the most important criteria in assessing the added therapeutic value. Although these criteria appear to be relatively similar, they are subject to different interpretations between countries and even between experts. None of the countries expresses an explicit hierarchy between these criteria.

The outcome of the therapeutic value assessment differs between countries. In Austria and France, the level of therapeutic value is rated in one of the multiple categories.[a]

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[a] Note that assigning a drug to a category defining its (level of) added therapeutic value involves a value judgement and hence an appraisal. All countries make such judgements when defining the added therapeutic value of a drug. It is therefore difficult to separate the assessment of the added therapeutic value (e.g. number of life years gained) from the appraisal of the added therapeutic value (e.g. relevance of this number of life years gained).

Austria applies six categories ranging from '*no added benefit*' to '*important benefit for the majority of patients*'. France distinguishes five levels of improvement in the medical service rendered (the ASMR): no or inadequate, minor, modest, significant, and major improvement.

The Netherlands uses three different outcomes, referring to added therapeutic value. A drug is assessed as having either '*less therapeutic value*' (no reimbursement), '*similar value*' (Annex 1A) or '*added therapeutic value*' (Annex 1B). Finally, in Belgium the assessment results in a binary outcome for added therapeutic value. The drug is either granted Class 1, i.e. recognition of an added therapeutic value, or Class 2, i.e. similar/ analogous therapeutic value. Generics are directly assigned a Class 3. No distinction is thus made in Belgium or the Netherlands in the degree of added value. In contrast, Sweden uses a sliding scale for added therapeutic value in such that the price depends on the incremental cost-effectiveness of the drug.

The implication of the therapeutic value assessment appears to be similar in all countries, at least to some extent. In all countries drugs with an added therapeutic value can obtain a higher reimbursement price. However, for drugs with no *added* but rather a similar therapeutic value, countries apply different rules. In France, drugs attributed an ASMR V, i.e. 'no major improvement', should be reimbursed if and only if *savings* are generated for the compulsory health insurance. In the Netherlands drugs with therapeutically equivalent value are grouped within a therapeutic class or cluster in which all drugs are reimbursed equally. In Belgium, the reimbursement basis of therapeutically equivalent drugs equals the reimbursement basis of their comparators. In Austria, drugs with similar or analogous therapeutic value should have a lower consumer price than the price of the best therapeutic reimbursable alternative.

Table 6 summarises our findings concerning the appraisal of the therapeutic value.

Table 6: Therapeutic value

Austria	Belgium	France	The Netherlands	Sweden
Formal criteria				
Clinically-relevant benefit to the patient	- efficacy - effectiveness - safety - comfort - applicability	- efficacy - applicability - side effects - compliance - the therapeutic maintenance level	- effectiveness - efficacy - side effects - experience - applicability - ease of use	All effects on a person's health and quality of life: - efficacy - effectiveness - safety/ side-effects - ease of use
Outcome				
1. no added benefit (generics) 2. analogous or similar therapeutic benefit 3. added therapeutic benefit for a subgroup of patients; 4. added therapeutic benefit for the majority of patients; 5. important added benefit for a subgroup of patients; 6. important added benefit for the majority of patients	Class 1: added therapeutic value Class 2: analogous or similar therapeutic value Class 3: generics/ copies (=same active ingredient)	ASMR V: No major improvement ASMR IV: Minor improvement ASMR III: Modest improvement ASMR II: Significant improvement ASMR I: Major improvement	Annex 1A: similar therapeutic value Annex 1B: added therapeutic value	Sliding scale
Implication				
Categories 5 and 6 are entitled to negotiate a price above the EU average price	Class 1 drugs are entitled to negotiate a price above the comparator's price	ASMR I to III are entitled to a price premium compared to the comparators (close to free pricing)	Annex 1B drugs are entitled to a price premium (evidence on pharmacoeconomics and budget impact required)	Price (premium) based on cost-effectiveness ratio

2.3.1.3 *Cost-effectiveness assessment*

All countries but France have cost-effectiveness as formal reimbursement criterion. Although the French reimbursement agency was explicitly encouraged to use cost-effectiveness information for decision making, the expert committee has until now been reluctant to take cost-effectiveness into account for reimbursement decisions. A new Economic Evaluation and Public Health Committee (CEESP) was set up in 2008 to conduct cost-effectiveness evaluations but it is still unclear whether it will effectively influence reimbursement decisions. In Belgium and the Netherlands, cost-effectiveness is taken into account only for drugs with recognised added therapeutic value. Similarly, in Sweden and Austria cost-effectiveness evidence requirements are most important for drugs claiming added therapeutic value. Allowing price negotiation reflects that countries do not take the price (and thus the ICER) as given.

However, further exploring the assessment of cost-effectiveness evidence reveals divergence in how countries deal with the assessment. In Austria, a separate health economics team assesses the quality of the cost-effectiveness evidence and its level of uncertainty. In Sweden, the expert committee assesses the actual cost-effectiveness ratio itself. In Belgium, the technical department assesses the quality of the cost-effectiveness evidence as well as the actual cost-effectiveness ratio. In contrast, the Dutch expert committee (CFH) formally only evaluates the robustness of the cost-effectiveness evidence. The outcome of this assessment is either sufficiently or insufficiently founded evidence, no relative degrees in robustness are applied.

2.3.1.4 *Appraisal*

Appraisal implies weighing assessment criteria against each other and against other socially relevant criteria. Appraisal occurs when expert committee members need to reach a conclusion about the societal value and the societal willingness to pay for a drug. Compared to assessment, appraisal criteria as well as the weighing process are less transparent in all countries. Austria is the only country with explicit appraisal criteria. In Belgium, besides therapeutic value four additional criteria are used to appraise the reimbursement request: price demanded by the company, budget impact, cost-effectiveness and therapeutic importance in the light of unmet medical and societal needs. As a result, a drug with a recognised added therapeutic value may end up with a negative proposal, for example, because the requested price was deemed excessive.

In France, the medical service rendered (SMR) evaluation is supposed to answer the question whether the drug is worth to be covered by the social security and solidarity system. Besides the level of efficacy relative to side-effects, four other criteria are used, i.e. severity of disease, properties of treatment (preventive, curative, symptomatic), place of the drug in the therapeutic strategy, and the public health benefit. Public health benefit is a function of severity of disease, relative impact on mortality, morbidity and quality of life, unmet medical need, level of confidence in the extrapolation and external validity of the evidence, impact on heath care organisation and impact on access to other treatments. The outcome of the public health benefit criterion is difficult to objectify.

In the Netherlands, the appraisal committee (ACP) was only recently established and its actual influence on the reimbursement process is not clear yet but the committee has developed formal appraisal criteria such as medical need, disease severity and rarity, public health, accessibility, affordability for patient and/or society, and life-style.

In Sweden, one could suggest that the three principles of human value, need and solidarity, and cost-effectiveness, which are legally imposed by the government, put forward formal appraisal criteria. Sweden promotes a value for money system and, at the national level, budget impact is explicitly not a formal reimbursement criterion.

Although four countries have cost-effectiveness as reimbursement criterion, none of the countries applies a strictly defined or transparent cost-effectiveness threshold (range). In 2009, the Dutch advisory body (CVZ) published an indication for a threshold range but the actual status of this threshold range remains unclear, as the minister has neither confirmed this range nor endorsed a threshold.

Interviewees in most countries acknowledged that if there would be an implicit threshold, it would be an increasing threshold depending on factors such as disease severity and medical need. Interviewees also acknowledged to be relatively lenient towards orphan drugs and drugs for severe and life-threatening diseases.

All things considered, it seems that besides formal assessment and/or appraisal criteria, additional criteria often remain implicit. These informal criteria are often derived from the system objectives (system sustainability, equity and quality of care). But as mentioned before, these primary objectives are often competing. Therefore, the relative importance or the hierarchy between these objectives might be assessed differently by different countries and expert committee members.

Furthermore, in all countries the relative importance of assessment versus appraisal criteria remains unclear. Consequently, it is not always transparent to what extent evidence of the assessment is actually used in relation to, most often, more informal appraisal criteria.

2.3.1.5 Stakeholder participation

Stakeholder participation in the assessment and appraisal phase can influence the societal value judgment of the drug. The five systems differ in the arrangements they use to ensure stakeholder participation. First, stakeholders can be represented in the expert committees, especially in deliberation-driven models. Furthermore, stakeholder participation is formally arranged in all countries. In all countries medical doctors can be consulted for their expertise in a specific medical field. In the Netherlands and Sweden, patient associations are commonly consulted stakeholders. Additionally, in Sweden county councils' representatives of SALAR have insight in the draft assessment report and can put forward their point of view in writing and are entitled to deliberate with the expert committee (the latter only occurred four times in the last eight years).

In Sweden, Belgium and France, applicants have the opportunity to put forward their point of view or refute factual errors once during the reimbursement process, in a deliberation (or 'hearing') with the expert committee, before a final reimbursement advice (or decision) if formulated. In contrast, in Austria, the expert committee can invite the applicant to clarify information in a hearing. In the Netherlands, applicants can put forward their response on the draft reimbursement advice during the last phase of the advice process. In Belgium, the applicant can first send written comments after receiving the first evaluation report regarding the added therapeutic value assessment and after receiving the provisional advice on reimbursement and reimbursement modalities if these differ from the application.

Furthermore, in Sweden applicants can request a joint scientific advice meeting with the reimbursement agency and the market authorisation authority during phase II and III studies in an ongoing pilot project.

2.3.1.6 Documentation of the reimbursement advice

All countries publish their reimbursement advice (decision) reports. The decision-making process, however, is often not documented. Especially the weighing process of the appraisal is less transparent. In France, the minutes of the meeting are published on the HAS website. These include the main points of discussion on a drug reimbursement request and the voting results. Also published on the HAS website are the results of the assessment and the motivated advice. The Belgian system publishes the initial assessment report, the responses from the applicant, and the reaction of the committee to the applicant's responses whereas the (provisional) advice is not published. In Belgium and France, confidential information is concealed if requested by the applicant and judged justified by the expert committee. In the Netherlands, the assessment and appraisal reports are available online. Sweden publishes the final report online after deliberation with the manufacturer; confidentiality issues stated by the latter are concealed. It should be noted that manufacturers can withdraw their application up until a final decision has been made. This might guarantee confidentiality, however, at the cost of transparency.

Table 7: Technology decision level: Reimbursement advice

	Austria	Belgium	France	The Netherlands	Sweden
ASSESSMENT					
Main actor(s) - Preparation, processing and reporting - Responsible advisory committee	HVB HEK	INAMI/RIZIV CRM/CTG	HAS CT	CVZ CFH	TLV TLV Expert Board
Represented stakeholders/expertise in expert committee	Academics Physicians Pharmacists Sickness funds Employees/ consumers Employers/industry	Academics Physicians Pharmacists Sickness funds	Medical and pharmacological experts	Academic, medical, pharmacological and (health-) economic experts	Pharmacological and health economic experts Health care planners Patient representative
Consultative stakeholders/experts present in expert committee (no voting rights)	A representative from the federal government	Representatives from ministries (Health, Economy, Budget and Social Affairs), pharmaceutical industry	Representatives from public institutions, pharmaceutical industry and sickness funds	Ministerial observers	n/a
Consultation other stakeholders/ experts	Physicians	Physicians	Physicians	Physicians, physician- and patient associations	Physician and patient associations and county councils
Assessment criteria - Efficacy - Effectiveness - Safety & Side-effects - Ease of use/comfort - Added therapeutic value - Cost-effectiveness - Other(s):	 Yes Yes Yes Yes Yes Yes Exhaustive list of assessment elements available in the annex of the VO-EKO	 Yes Yes Yes Yes Yes Yes Therapeutic and social needs	 Yes Yes Yes Yes Yes No Public health, treatment properties	 Yes Yes Yes Yes Yes Yes* Applicability, feasibility *robustness of evidence	 Yes Yes Yes Yes Yes Yes
APPRAISAL					

Main actor	HEK	CRM/CTG	CT	ACP (CVZ + CFH)	TLV Expert Board
Explicit appraisal criteria	No	Yes	Yes	Yes	Yes
Appraisal criteria	No additional criteria but the system objectives	Added therapeutic value, clinical effectiveness, budget impact, cost effectiveness and price/reimbursement basis	SMR evaluation criteria: efficacy vs side effects, place of the drug with regard to alternatives, severity of disease, treatment properties, public health benefit	Added therapeutic value, cost-effectiveness, medical need, disease severity & rarity, public health, accessibility, own responsibility, societal affordability	Human value, need and solidarity and cost-effectiveness
Threshold (range) for cost/QALY	No	No	No	No	No
Expert committee report publicly available	No	Yes	Yes	Yes	Yes No, if applicant withdraws case
Expert committee deliberation basis	Majority voting	Two-third majority voting	Majority voting	Consensus (if no consensus: majority voting)	Majority voting
Expert committee advice binding	No	No	No	No	Yes
Time frame for the advice (target)	90 days	150 (legal)	90 days	Outpatient: 90 Exp. inpatient: 60	n/a

2.3.2 Decision making phase

In Belgium, France and the Netherlands[a] the final reimbursement decision is made by the minister of health whereas in Austria and Sweden the minister has no decision making capacity at the individual reimbursement decision level. These differences in decision making responsibilities mainly reflect diverging institutional contexts.

In Sweden, having a longstanding tradition of decentralisation, the final decision is made by the Expert Board of TLV based on majority voting. This expert committee is thus responsible and accountable for the assessment, appraisal and final decision.

Austria has two decision processes. First, the expert committee makes a decision based on majority voting on the reimbursement advice. Second, one of the four deputy general directors association of Austrian Social Security Institutions (HVB) makes the final reimbursement decision based on this advice. There is no set rule stipulating under what circumstances the recommendation from HEK can be overruled. Nevertheless, HVB is allowed to deviate, but in practice it rarely occurs.

In France, Belgium and the Netherlands[b], decision making also occurs in two phases. First, the expert committee comes to a reimbursement advice based on a voting procedure (Belgium and France) or consensus (the Netherlands). Second, the minister of health makes the final reimbursement decision based on this reimbursement advice. It should be emphasised that the final decision can deviate from the reimbursement advice based on additional concerns. These concerns, such as equity, accessibility to good quality of care, and other societal relevant criteria, are often not clearly defined and thus remain implicit.

The reimbursement advice is hence binding in none of the countries, but differences are found in *how* the minister can deviate and how frequently he or she deviates in practice. In Belgium, the law stipulates that the minister may deviate based on societal and/or budgetary reasons. The decision criteria cannot be different, however, from the appraisal criteria used by the expert committee, being therapeutic value, price of the product, importance of the product in medical practice in function of therapeutic and societal needs, budget impact and cost-effectiveness. The minister of budget can still advise the minister of social affairs *not* to reimburse a product even in the case of a positive reimbursement advice. Moreover, when there is no two-third majority reached on a positive or negative proposal, there is formally no reimbursement advice from the expert committee and hence the minister makes the decision autonomously. As a representative of the minister has been present during the discussions at the expert committee, this decision is an informed decision, be it with more possibilities for direct negotiation between the company and the minister. In France and the Netherlands, the minister is allowed to deviate from the advice, but this rarely occurs in practice. Table 8 (page 35) provides a summary on our findings regarding the reimbursement decision.

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[a] The Dutch Health Care Authority (NZa) formally makes the reimbursement decision for expensive inpatient drugs, but the minister can overrule this decision.

[b] Three phases in case of expensive inpatient drugs.

2.3.2.1 *Documentation of the decision*

Similar to the documentation of the reimbursement advice, the decision is publicly available in all countries. However, the decision-making process is often not documented. Even in countries where the decision can deviate from the advice, the documentation on the actual role of additional criteria often remains limited. Especially appraisal criteria and the weighing process are often not transparent. This may be partly due to the historical developments of the systems. Previously, most drugs were reimbursed and it was generally accepted that deciding on using a specific drug was the responsibility of physician. In the last decade, all countries, faced with increasing health care expenditure, intensively reformed their reimbursement systems. Drug reimbursement became a tool for rationing health care. The societal criteria for deciding on drug reimbursement are still under development, however, and need further refinement. Gradually they might become more transparent. Meanwhile, it needs to be borne in mind that the deliberation process and relative weights of various criteria can vary across reimbursement decisions and depend on the characteristics of the drug, the disease and the context.

2.3.2.2 *Conditional reimbursement*

The outcomes of reimbursement decisions are similar in all countries. The possible outcomes are: *reimbursement*, *no reimbursement*, or *conditional reimbursement*. All countries apply reimbursement restrictions, for example only reimbursement for specific indications, specific population groups, or access restrictions (e.g. consent requirement, specialist only prescription). Conditional reimbursement may be used for health concerns and/or budgetary purpose.

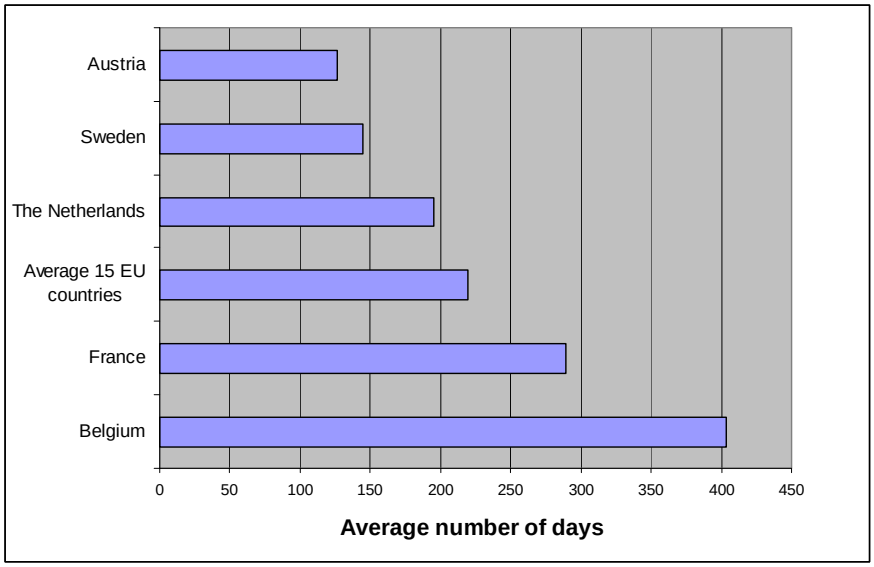
2.3.2.3 *Temporary decisions*

The use of temporary decisions is more diverging across countries. In France, all positive decisions are temporary, all drugs are re-assessed every five years. In contrast, only decisions on drugs with recognised added therapeutic value in Belgium and expensive inpatient drugs in the Netherlands are temporary. In Sweden, the reimbursement agency decides case-by-case to approve the drug temporarily. In contrast, none of the decisions in Austria are temporary.

2.3.2.4 *Timelines*

All European countries are required by the European Transparency Directive to make a final reimbursement decision within 180 days (excluding clock stops). However, all countries can set shorter target time frames for their national system. Austria, France and Belgium apply strict timelines for the reimbursement advice (90 days, 90 days and 150 days, respectively) and the final reimbursement decision (180 days). These target time frames are not always met. Figure 7 shows average time intervals between market authorisation and patient access to drugs from January 2006 to December 2008. EPFIA reports an average time interval of 219 days for fifteen European countries with a positive list.[46] Austria, Sweden and the Netherlands require less time compared to this average whereas France and Belgium use more time. Clock-stops and time lags between the decision and publication in the Official Journal are included in these time intervals.

Figure 7: Average time intervals between market authorisation and patient access from 1 January 2006 to 31 December 2008



Numbers obtained from The European Federation of Pharmaceutical Industries and Associations.[46]

Not meeting the target time frame only has consequences in Belgium. In the absence of a formal decision on the reimbursement modalities at day 180, the applicant's proposal is automatically approved. The Netherlands aims to finalise an application for outpatient drugs within 90 days and an application for expensive inpatient drugs within 60 days. However, these target time frames are often not met, the reimbursement advice often takes an additional four to six weeks and the final decision by the minister another three to four weeks. The Swedish government previously stressed that the reimbursement agency should make a final decision within 120 days, but has recently taken away this goals since applications were in 2009 finalised on average within 101 days.[47]

Table 8: Technology decision level: Final reimbursement decision

	Austria	Belgium	France	The Netherlands	Sweden
Decision-making body	HVB	Minister	Minister	Minister[a]	TLV
Discretionary power final decision maker	Yes, deviation rarely occurs	Yes, deviation sometimes occurs	Yes, deviation rarely occurs	Yes, deviation rarely occurs	n/a
Stakeholders involvement Additional evidence/ criteria	No No	Yes Yes	Yes Yes	Yes Yes	n/a n/a
Motivation of decision publicly available	Yes	Yes	Yes	Yes	Yes
Restricted reimbursement (e.g. specific indications; prior permission)	Yes (Yellow box)	Yes (Chapter IV)	Yes	Yes (Annex 2)	Yes
Temporary decision	No	Yes (Class 1)	Yes (all drugs)	Outpatient: No Expensive inpatient: Yes	Yes (case-by-case)
Risk sharing agreements	No	Yes, financial based (Class 1 with negative/no proposal from CRM/CTG)	Yes, financial based (price volume agreements)	No	TLV: No County councils: Yes (but rarely)
Time frame for decision (target)	180 days	180 days If no decision: automatically approved	180 days	180 days	180 days (actual: 101 days)

[a] In case of expensive inpatient drugs: Dutch Health Care Authority (NZa)

2.3.3 Output and Implementation

2.3.3.1 Appeal

Appeal options differ between the countries. As mentioned before, applicants have formal opportunities to put forward their point of view or express disagreements during the reimbursement process; but they are also entitled to appeal to the final decision. In all countries but Austria, applicants can appeal to an administrative court and these appeals are based on procedural issues. In Belgium, France and the Netherlands, any stakeholder can appeal to the administrative court, although in practice, given the procedural basis of the appeal, stakeholders other than the applicant rarely introduce a case. In contrast, the Independent Pharmaceutical Commission in the Austrian system acts as an appeal court for procedural and content issues. Noteworthy is that in the Netherlands it is possible to request for an Expert Review based on the evidence and content of the application. This Expert Review often precedes a court case to examine the feasibility to put forward the case to the court system.

2.3.3.2 Implementation of the decision

All countries have mechanisms to support the implementation of the reimbursement decision by disseminating scientific evidence and improving appropriate drugs use by means of drug formularies and prescription guidelines. Austria, Belgium, France and the Netherlands have national drug formularies (issued by the national reimbursement advisory bodies or the national health payer). In contrast, in Sweden every county council has its own drug therapeutic committee and thus its own guidelines. Consequently, even though national decisions are compulsory in Sweden, there is local variation in drug use. Although the national reimbursement agency does not use budget impact as a reimbursement criterion, county councils bear budget responsibility and might be inclined to consider budgetary reasons within prescription guidelines.

2.3.3.3 Reappraisals

We found diverging policies regarding the reappraisal of enlisted drugs. Reappraisals can be either ad hoc or systematic; and can affect a single drug or multiple drugs (i.e. group reappraisals). Reappraisals may result in changes in reimbursement conditions or delisting. Ad hoc re-assessments can be initiated in all countries by the reimbursement agency, the drug expert committee and/or the final decision maker. However, policies for systematically reviewing enlisted drugs differ across countries. The Austrian system does not have a policy requiring systematic reappraisal of drugs. The HVB is entitled to request an ad hoc reappraisal of a drug from HEK, e.g. when new pharmacological, medical and health economic evidence becomes available. In Belgium, all innovative drugs (i.e. Class 1) are systematically reviewed after 18 to 36 months. Delisting from the benefit scheme rarely occurs, in contrast to changes in the reimbursement conditions. In the Netherlands, outpatient drugs are not systematically reviewed. Since 2006, expensive inpatient drugs ought to be reassessed four years after the initial positive reimbursement decision. However, so far no reassessment has been conducted and thus the actual consequences are not clear yet. In France all reimbursement decisions are temporary. Drugs are systematically reassessed every five years. This can lead to change in the assigned level of (improvement of) medical service rendered (i.e. (A)SMR) and thus result in a different reimbursement level or drug price. Delisting is also a possible and real outcome of the reappraisal. In Sweden all drugs included in the old reimbursement scheme (i.e. enlisted before 2002) are currently being reviewed according to therapeutic classes. This process has already resulted in changes in guidelines but also in delisting of drugs from the reimbursement scheme.

2.3.3.4 Impact assessment

Finally, impact assessments of reimbursement decisions are often restricted to monitoring prescription volumes or drug expenditure. Nevertheless, policies for systematic reviews of reimbursement decisions seem to get increasing attention within most systems. Such policies provide the opportunity to evaluate actual health effects alongside costs of reimbursement decisions. Table 9 summarises our findings on the output and implementation of decisions.

Table 9: Technology decision level: Output and implementation

	Austria	Belgium	France	The Netherlands	Sweden
Appeal and dissent - Grounds for appeal - Initiator - Appeal options	Yes Procedural and substantive grounds Applicant UHK (Independent Pharma Commission)	Yes Procedural grounds Any stakeholder State Council	Yes Procedural grounds Any stakeholder State Council	Yes Procedural grounds Any stakeholder Expert Review + Administrative Court	Yes Procedural grounds Applicant Administrative Court
Implementation decisions - Mechanism - Prescription guidelines - Local variations	 National drug formulary Yes No	 National drug formulary Yes No	 National drug formulary Yes No	 National drug formulary; Pharmaco-therapeutic groups. Yes No	 County councils & Drug Therapeutic Committees Yes Moderate - major
Re-appraisal - Systematic - Ad hoc - Consequences re-appraisal	 No Yes Changes in conditions, delisting	 Yes, for Class 1 and orphan drugs Yes Changes in reimbursement modalities; de-listing (rarely occurs)	 Yes, for all drugs and every 5 years Yes Delisting	 Outpatient: No Expensive inpatient: Yes Yes Outpatient: delisting (rarely occurs) Inpatient: awaiting	 Yes (drugs enlisted < 2002) Yes Delisting
Impact assessment of the reimbursement decision	Drug expenditure	Drug expenditure	Drug expenditure	Drug expenditure, prescription volumes	Drug expenditure

Key messages

- **System sustainability, equity and quality of care are the three main health policy objectives. They are interdependent and can be competing.**
- **All systems have a national drug reimbursement system for outpatient drugs, the system for inpatient drugs varies.**
- **The minister makes the final decision in BE, FR and NL, whereas the reimbursement agency makes the final decision in AU and SW.**
- **All systems implemented formal stakeholder involvement.**
- **Expert (advisory) committees are based on an assessment-driven model (FR, NL, SW) or a deliberation-driven model (AU, BE).**
- **None of the systems applies a formal hierarchy in the appraisal criteria. Nevertheless, therapeutic value appears the most prominent appraisal criterion in all countries.**
- **All countries, but France, use the cost-effectiveness ratio as a formal reimbursement criterion but none of the countries uses a cost-effectiveness threshold (range).**
- **Appraisal criteria are often not transparent and only NL has a separate appraisal committee.**
- **Documentation of the reimbursement decision is publicly available; however, the decision making process is often not transparent.**
- **The reimbursement decision is made at the national level but the implementation is regional in AU and SW.**
- **Systematic reappraisals are conducted in BE (Class I and orphan drugs), FR (all drugs) and NL (expensive inpatient drugs).**
- **FR and SW launched a large revision of all reimbursed drugs. This revision is still ongoing in SW.**
- **Only FR and BE use financial risk-sharing agreements.**
- **All systems only evaluate the impact of the drug reimbursement system on drug expenditure (i.e. sustainability) and not on the other system objectives (i.e. quality of care and equity).**

3 DISCUSSION

Our study revealed that the Austrian, Belgian, Dutch, French and Swedish decision-making processes converge in some and diverge in other respects. Moreover, we observed that system characteristics that seem to be quite similar between countries often have different practical implications.

All systems have the same objectives:

- Sustainability of the system
- Equity
- Quality of care

As explained in chapter 2, a trade-off has to be made between these objectives. How this trade-off is made is basically a normative choice: countries aim to find a socially acceptable equilibrium between reaching the different health system objectives. However, judging the performance of drug reimbursement systems on these desired outcomes is difficult.

Any democratic health system should have a legitimate policy making process that facilitates decisions to be taken in line with public values. In this report, we operationalise legitimacy as accountability for reasonableness. We use the theoretical ethical framework developed by Daniels and Sabin to discuss whether and how drug reimbursement systems satisfy the requirements for accountability for reasonableness in the light of the system objectives and the societal values. The framework basically focuses on procedural requirements, although the "relevance" requirement strongly relates to the content of policy decisions.[41]

The framework of Daniels and Sabin describes the conditions for a priority setting system in health care that entails "accountability for reasonableness" in general.[41] Drug reimbursement procedures are by their very nature priority setting procedures: they determine how choices about the allocation of scarce (pharmaceutical) health care resources are made.

Based on our analysis, we identify opportunities for improvement of drug reimbursement systems in general at the end of this chapter. The policy recommendations formulated at the end of this chapter are generic, i.e. to a certain extent applicable to all systems. The reflections made here are largely based upon the comparison of the different systems but also on the information obtained from the interviews with policy makers and other stakeholders in the different countries. These reflections are, however, strictly ours and do not necessarily reflect the views of the people interviewed.

3.1 ACCOUNTABILITY FOR REASONABLENESS

As explained in Chapter 1 a fair and legitimate priority setting procedure satisfies four conditions according to Daniels and Sabin:

- Transparency of the process
- Relevance of the reasons used to make a decision
- Revisability of decisions in light of new evidence
- Enforcement/regulation of the three previous conditions.

The relevance criterion makes the link between the procedural requirements for accountability for reasonableness and the requirements related to the content. We extended the Daniels & Sabin framework with an analysis of the actual criteria used in the decision making process and their relationship with the objectives of the health care system and integrated this into the framework. A discussion about the theoretical strengths and weaknesses of the framework itself is beyond the scope of this study.

3.1.1 Transparency

All drug reimbursement systems included in our study underwent major reforms as response to rapidly increasing pharmaceutical expenditures and addressing the requirements of the European Transparency Directive in 1989.[481] The Directive was issued on the initiative of Directorate General Enterprise and Industry out of concern over potential distortions of intra-Community trade in medicinal products which may be caused by national measures controlling public health expenditure. The objective of the Directive was to enable interested parties to verify that national pricing and reimbursement decisions do not impinge on pharmaceutical trade within the European Union.[49] This should be obtained by ensuring transparency of the national procedures for drug pricing and reimbursement towards the pharmaceutical industry. Besides defining the timeframe within which decisions about pricing and reimbursement must be taken, the Directive states that:

- Negative decisions must be communicated to the applicant and contain a statement of reasons based on objective and verifiable criteria;
- decisions must be open to judicial appeal at national level.

One might think that the transparency requested is closely related to the transparency requested by the accountability for reasonableness framework, but this is incorrect. The type of transparency imposed by the Transparency Directive is largely insufficient to ensure accountability for reasonableness.

- Firstly, the Directive only requires that motivations for the *negative* decisions are communicated *to the applicant* (i.e. the manufacturer asking for reimbursement), not for the positive decisions and not to the general public. This implies that only the agreement between the applicant and the decision maker seems to matter, while for accountability for reasonableness the vision of all relevant stakeholders matters.
- Secondly, the decisions should be based on "objective and verifiable criteria". However, criteria used in a drug reimbursement request –even if explicit– are rarely fully objective and verifiable, nor is their relationship with the actual decision. For example, the added therapeutic value of a drug can be measured in terms of an objective outcome parameter (e.g. number of life years gained compared to the alternative). The *value* and the *weight* given to this element in the final decision is, however, neither objective nor verifiable. Although this is a general issue, applying to the entire drug reimbursement decision process and thus to this entire report, we highlight it here because it is a requirement imposed by the Transparency Directive that cannot be sufficiently satisfied.

In conclusion, although the European Transparency Directive has increased the transparency of the drug reimbursement decision process to some extent, it cannot ensure the kind of transparency required for accountability for reasonableness because of the main focus on the transparency towards the applicant only and not towards the general public.

Our comparison showed that all countries but Austria publish at least the assessment reports. However, the extensiveness of information on the assessment varies between countries. The appraisal process, leading to the advice, and/or the decision process, is rarely made public, although variations were found between countries. Noteworthy is that in Sweden manufacturers can withdraw their case before the final reimbursement decision has been made in which case no report is published. Although this might guarantee confidentiality, it is at the cost of transparency.

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1 Council Directive 89/105/EEC of 21 December 1989 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion within the scope of national health insurance systems. (http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/pricing-reimbursement/transparency/index_en.htm)

Proper justification of an advice or decision, with a sufficiently differentiated reflection on the multiple considerations taken into account during the appraisal and decision making process and with a clear statement on the final position taken, should be provided in order to be fully transparent and enhance trust in the system. This does not mean that the weights given to each of the decision criteria should be quantified – this would not be feasible – but the rationales and justifications should be explicit.

The next paragraph elaborates on the ethical acceptability of rationales for decisions. This discussion will eventually give clues about how increased transparency can be obtained.

3.1.2 Relevance of the decision rationales

The relevance criterion requires that all stakeholders understand the decision problem and recognise the choices that have to be made to meet the different health care system objectives, i.e. people must be aware that resources are limited and fair choices have to be made within this resource-constrained context. These three objectives (sustainability, equity and quality of care) are the leitmotiv throughout the drug reimbursement decision process. Only if this awareness exists within the general population, ethically acceptable rationales for drug reimbursement can be defined *and* accepted by the general public.[50] Involvement of all those who are affected by a decision in the decision process is considered to facilitate the accountability for reasonableness, because it increases the likelihood that the rationales that are adopted will be considered as relevant and acceptable.[38, 50] This applies to both the assessment-driven and the deliberation-driven systems. Both models require members of the expert committees to disclose potential conflicts of interest. However, even without conflicts of interest, people will have their personal reference set of values and might use these – consciously or subconsciously – during the appraisal process. A conflict of interest statement is therefore a necessary but insufficient condition to ensure acceptability of the rationales used during the appraisal process. An appraisal is *per definition* never neutral or value-free.

As deliberation-driven models, in contrast to assessment-driven models, include all stakeholders directly in the expert committees, the risk of personal preferences creeping into the appraisal process might be higher. The main issue is that diverging preferences within the expert committee should be balanced by appointing appropriate committee members.

3.1.3 Relevance of the decision criteria

To meet both the transparency criterion and the relevance criterion for accountability for reasonableness, decision makers should first design a framework for the decision process, specifying:

- the decisions that need to be made,
- when in the process they should be made and
- which considerations and criteria should be taken into account when making these decisions.

We identified five key questions that need to be answered in a drug reimbursement decision process:

- Medical, therapeutic and societal need: does the product target a specific need?
- Are we prepared to pay for a treatment that will improve this indication out of public resources?
- Are we prepared to pay for this treatment out of public resources?
- Are we prepared to pay more for this treatment than for the best alternative?
- How much more are we willing to pay out of public resources for this treatment?

This decision framework tries to bring a certain logic in the order of the questions. However the order in which the questions are addressed often differs in current practice. Nevertheless, defining the health care needs upfront –as in our framework– might be important to reconcile industrial and societal objectives. It would allow producers to target R&D funds towards "high need" indications and would be a first step towards a more demand-driven pharmaceutical health care system.

Before explaining the decision framework in-depth, we would like to highlight four important points for a clear understanding of our framework:

1. The framework provides a structure for justifying decisions as well as a tool for defining and making explicit the societal choices that are made during the decision process. It should allow the reconstruction of the decision process.
2. Criteria used to answer one question can be relevant for answering other questions in the framework. Severity of disease, for instance, will be a consideration in the decision related to the medical need as well as in the decision related to the willingness to pay for the added therapeutic value.
3. The order in which the questions are presented does not mean that at some stages the decision maker might not have to return to previously answered questions, in order to reconsider whether the earlier made decisions still apply.
4. At each question, the answer can be "yes, but only under certain conditions". In this case the conditions have to be taken along further down the process.

A complete summary of the framework, including the decisions to be taken, the corresponding questions to be answered and the criteria that can be used for answering the questions is provided in Table 10.

Table 10: Key questions and corresponding criteria in the conceptual framework for the drug reimbursement appraisal process

Decision	Question	Possible criteria
Medical, therapeutic and/or societal need	Does the product target a medical, therapeutic and/or societal need?	**Medical need:** - Life-threatening / non-life threatening condition - Severe / mild symptoms - Poor initial health state **Therapeutic need:** - Effective alternative treatments available / not available **Societal need:** - High / Low prevalence - Disease leading to health inequalities - Baseline health level
Preparedness to pay out of public resources for *a* treatment	Are we, as a society, prepared to pay for *a* treatment that will improve this indication out of public resources?	- Own responsibility - Life-style related condition
Preparedness to pay out of public resources for the treatment under consideration	Are we, as a society, prepared to pay for *this* particular treatment, given that we in general would be prepared to pay for *a* treatment for this indication?	- Safety and efficacy profile of the treatment compared to the safety and efficacy profile of the alternative treatment(s) - Curative, symptomatic, preventive - Therapeutic value - Significance of health gains
Preparedness to pay *more*	Given that we, as a society, are prepared for this treatment out of public resources, are we prepared to pay *more* for this treatment than for the best alternative treatment?	- Added therapeutic value - Potentially induced savings elsewhere - Quality and uncertainty of the evidence - Acceptability of co-payments

		and/or supplements - Rarity of disease
Willingness to pay: price and reimbursement basis	How much more are we willing to pay out of public resources for this particular treatment?	- Added therapeutic value - Incremental costs - Budget impact / ability to pay - Cost-effectiveness ratio - Medical, therapeutic and societal need - Limits to cost sharing - Quality and uncertainty of evidence

Before discussing each of the questions with their possible criteria, we would like to make some comments that are important for the appropriate use of this framework.

- From the beginning the focus should be on the indication of the drug, not on the complete health condition of the patient population. For example, in case of a drug preventing nausea after chemotherapy, the indication is nausea, not cancer. The underlying condition (cancer in this example) might, however, be a consideration in the decision on the reimbursement level (e.g. although the condition is not life-threatening, full coverage might be considered because of the severity of the underlying disease). In case of preventive interventions, the condition being prevented is the indication.
- Decisions about "need" for any treatment for a condition should be separated from the price, costs and effectiveness of a product.[51] An intervention is valuable if it responds to a need.[52] The price or cost of an intervention does not determine its value. For a product to be worthwhile, its societal value should be higher than the price. For a product to be economically sustainable for the producer its price should be higher than the cost.
- Similarly, "preparedness to pay" should be strictly separated from ability to pay. Preparedness to pay refers to the concept of being *in principle* prepared to pay for something out of public resources, independent of the ability to pay. Preparedness to pay is different from "willingness to pay" in that willingness to pay refers to the amount society is willing to pay for a product. In contrast to preparedness to pay, willingness to pay *does* depend on ability to pay, as well as on the value of a product.
- Discussions about sub-populations can be performed at different phases in the process. This fits within the perspective of searching for a socially acceptable balance between the three objectives of health care systems: sustainability, equity and quality of care. It implies that the answer to each of the questions can be "yes/no, except for a specific patient population", in which case the considerations further down the process only relate to a specific population.

In the following section we discuss the relevance of the reimbursement criteria for answering each of the five key questions in Table 10. We emphasised earlier that the order in which the questions are answered in current practice often differs from the order presented in this framework. As far as our information allows, we analyse for each criterion whether these countries use them in the drug reimbursement process, if they are sufficiently operationalised and whether we can get an impression of their relative weight in the decision process.

3.1.3.1 *Question 1: Is there a medical, therapeutic and/or societal need?*

A product is valuable in as far as it meets a specific need. This may be a medical need, a therapeutic need and/or a societal need.[52] Need depends on a combination of factors, such as:

- the severity of a disease(medical need)
- the necessity of treatment(medical need)
- the availability of alternative treatments for the disease and the effectiveness of those treatments (therapeutic need)
- the prevalence of the disease (societal need)
- inequalities in health (societal need)

The more severe a disease is, and the less effective alternative treatments are or the fewer the available alternatives, the higher the *medical and therapeutic* need. The more frequent the disease and the higher the health inequalities induced by the disease, the higher the *societal* need, if society is averse to health inequalities. The evaluation of medical, therapeutic and societal need essentially happens in relative terms: what is the severity of the disease and necessity of treatment *compared to* other diseases that need to be treated.

Our concept of "need" allows the inclusion of three different principles of justice in health care rationing according to Cookson & Dolan[53]: the need principle, the egalitarian principle and the maximising principle. In this classification, the *need principle* mainly refers to what we call "medical need", based on disease severity and treatment necessity.[m] The *egalitarian principles* states that health care resources should be allocated so as to reduce inequalities in health.[53] It relates closely to what we call "societal needs". Finally, the maximising principle of justice requires that health care should be distributed so as to bring about maximum benefit, be it in terms of health, well-being or capabilities.[55, 56] This principle requires consideration of both medical and therapeutic needs as well as capacity to benefit. This principle also relates closely to "societal need" for a society wishing to maximise population health by the allocation of health care.

Furthermore, our concept of need also includes interpretations of need as described by Hasman.[51] Firstly, the *poor initial state interpretation*, as in disease severity, refers to "medical need". Secondly, the *normal functioning range interpretation* describes that everyone in society should be entitled to reach a certain threshold level of health. This interpretation reflects both the "medical need" and the "societal need" to reduce inequalities in health.

Which principles actually to apply, is a societal decision, but empirically it appears that a pluralistic approach to defining need, encompassing several principles, fits best with the general public's intuition of social justice in health care.[53]

Defining the criteria that should determine the medical, therapeutic and societal need is already difficult, but even more so is the weighing of a combination of the criteria encompassed by the concept of need. For example, should a frequent chronic disease with mild symptoms affecting especially adolescents with a less privileged socio-economic background get a higher or lower priority than a less frequent acute disease with severe symptoms affecting elderly with a more privileged background? How should the mortality of a disease weighed against severity of symptoms, prevalence and health inequality?

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[m] Also "capacity to benefit from treatment" is often included in this concept in literature.[51, 54] However, in our framework needs are considered independent from any specific treatment. Therefore, we consider capacity to benefit as something that might lead to a "yes/no, except for" answer in the question related to preparedness to pay for the treatment under consideration (question 3) rather than as a criterion determining medical need in itself. It seems more appropriate, therefore, to either take it into account when discussing the conditions and restrictions for reimbursement or when considering the preparedness to pay for the treatment under consideration. In our framework, we refer to this concept as "significance of health benefits".

Efforts have been made in capturing the criteria of quality of life and duration of life in single health outcome measures such as Health Adjusted Life Expectancy (HALE), Disability Adjusted Life Year (DALY) and Quality Adjusted Life Years (QALY). Each of these measures is limited to medical need and require additional measures to draw conclusions about therapeutic and societal needs alongside medical need.

In literature, suggestions to operationalise the need-criteria have mainly focused on specific criteria, often in isolation. For example, approaches for operationalising disease severity have been developed. It should be noted that they can only provide a partial answer to the need-question, mainly addressing medical need. By taking the available treatment alternatives into account when determining disease severity (i.e. disease severity given current treatment options), therapeutic need is addressed at the same time.

One approach for operationalising disease severity – the **"fair innings" approach** – would be to define a kind of "baseline health level" everyone is entitled to according to society.[57] As such, patient populations who are, given the state-of-the-art therapeutic options, still situated far from this level of health will be considered to have a higher medical need than patients living an acceptable live already. The fair innings approach fits within the egalitarian social justice principle.[53]

The crucial issue here is the definition of the baseline health level. This is a multidimensional concept, encompassing duration as well as quality of life, as in QALYs. Applying the fair innings approach using QALYs to define medical needs implies first defining the number of QALYs everyone is entitled to (the "fair innings") and then calculating the absolute difference between the expected number of QALYs in a specific disease, given the current treatment options, and the "fair innings". The larger the absolute difference, the higher the medical need.[n]

A second approach – the **"severity of illness approach"** – would give a higher priority to people who are worse off, given the current treatment options.[58]. If applying QALYs for this approach, it would mean calculating the number of remaining QALYs and giving the highest priority to the people with the lowest number of QALYs. The problem with this approach is that it does not distinguish between a low number of remaining QALYs due to old age or a low number of QALYs due to a severe disease.

The third approach – the **"proportional shortfall" approach** – would define the medical need of a population based on the proportion of health lost due to the disease, given the state-of-the art therapeutic options, as compared to the baseline health level.[59] The baseline health level is the expected health level of this population without the disease. If applying QALYs for this approach, a higher proportion of QALYs lost implies a higher medical need.

Besides severity of disease, however, also other "need criteria" have to be considered to determine the medical, therapeutic and societal need for a treatment. Weighing these criteria implies an appraisal of the relative importance of each of the criteria defining need, which is, as for the appraisal of the relative importance of all other criteria relevant for a drug reimbursement decision, not easy. Nevertheless, considering the medical, therapeutic and societal need for a treatment remains crucial in the decision making process and cannot be omitted. By considering explicitly each criterion accepted as relevant for answering the need-question, transparency in the judgement about need can be ensured.

An issue related to the *relative* nature of the needs evaluation is that all countries consider reimbursement requests case by case the first time they are submitted. This implies that health care needs are not prioritised in general. In other words, the drug treatment for a specific health condition is not prioritised against treatments for other conditions. France tackles this problem by means of the assessment of the SMR ("medical service rendered"). France evaluates the medical service rendered to determine the medical need.

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n Note that the QALY measure may not be the right instrument to apply for the fair innings approach if society wishes to apply a different weight for duration of life compared to quality of life. If the approach is considered appealing but not using QALYs, an alternative measure has to be sought.

Disease severity is one of the criteria to be taken into account for the appraisal of the SMR°. If the SMR is judged "insufficient", a negative reimbursement advice is sent to the minister.

Another option to tackle this problem would be to perform large group revisions, i.e. revisions across therapeutic classes. This is an approach for evaluating the consequences of the case-by-case drug reimbursement decision procedure on the medical needs served by the system. It looks critically at the entire package of reimbursed drugs and assesses whether the health care priority criteria still apply to it. A large group revision has been performed in France and Sweden for drugs that had not been reassessed before. France subsequently implemented reassessment of drugs' SMR every 5 years.

In the Netherlands, medical need is operationalised formally in the appraisal criteria by using disease severity applying the proportional shortfall approach. Sweden has medical need and solidarity as one of the three principles for priority setting in health care. This principle is further defined in various levels of disease severity. These levels distinguish life threatening diseases, prevention, and less severe acute and chronic diseases. In Belgium necessity of treatment is used to determine the category of reimbursement (level of co-insurance). It varies from necessary treatments for life-threatening diseases to symptomatic treatments.

All these countries have operationalised need in some phase in their decision making process, although in most cases it is limited to medical need. The degree of detail and comprehensiveness in which countries operationalise medical need varies. Furthermore, the relative weight of medical need remains unclear. Noteworthy is that most interviewees acknowledged that disease severity –as in medical need– was important in decision making.

Rarity of a disease was also mentioned by the interviewees as being important in decision making. At the European level, incentive mechanisms have been implemented to stimulate R&D of pharmaceuticals for rare diseases. The rationale for these incentives is that companies are less inclined to develop products for rare diseases because such products are less likely to give an adequate return on investment. As a consequence, people with rare diseases would have fewer chances for being treated. It can be questioned whether rarity *as such* determines the need or rather the fact that often no alternative treatment exists for a severe disease, that happens to be rare.[60]

3.1.3.2 Question 2: Are we, as a society, prepared to pay for a treatment that will improve this indication out of public resources?

It needs to be decided whether or not the society would want to pay for a treatment out of public resources. Before the preparedness to pay for the specific treatment under consideration is discussed, policy makers should determine whether society would be prepared to pay for *anything* that would improve the indication of the treatment under consideration. They should do this independent from the cost or effectiveness of any treatment. The decision is more fundamental and relates to defining societal choices, such as "does society want to pay for treatments for a life-style related condition?" or "can society keep the patient responsible for the covering the cost of the treatment?". The answer might be "yes, if…", for instance if it is difficult to define the causal relationship between the life-style and the disease or if a particular low-cost treatment (e.g. paracetamol) is not part of a more general best-practice treatment path of a complex disease. The preparedness to pay is in that case subject to conditions.

In contrast to "need", the criteria considered here will not directly be related to the characteristics but rather to the causes of the disease (e.g. unhealthy or risky behaviour), the characteristics of the population groups affected by the disease or the nature of the outcome. Transparency about ethical choices remains one of the most difficult issues in any drug reimbursement system.

° The other criteria are: level of efficacy relative to adverse effects; place of the drug in the therapeutic strategy (in particular with regard to the available treatment alternatives), the properties of the treatment (preventive, curative or symptomatic), the public health benefit.

Although the preparedness to pay out of public resources is not necessarily strictly linked to the medical, therapeutic and societal need (i.e. the first question), both aspects will in practice frequently be considered as one decision. This is the case if society feels that treatments for high needs should be able to rely on public funding, independently from, for instance, the life-style or personal responsibility of the patient.

If we look at the countries, we can observe that they operationalise this question similar to the needs question in such that mainly disease severity is used as criterion in several phases of the reimbursement process. In the Netherlands, own risk and responsibility is a formal appraisal criterion. In Sweden priority setting according to the medical need and solidarity principle is a way of answering the question if society is prepared to pay for a treatment for this indication. Once again, the relative weights of these criteria remain unclear in all countries.

3.1.3.3 Question 3: Do we want to pay for this product out of public resources?

It needs to be examined whether society wants to pay for the treatment under consideration, given its characteristics. Considerations at this stage are the safety and efficacy of the treatment compared to alternative treatments, whether it concerns a curative, symptomatic or preventive treatment and its therapeutic value. Preparedness to pay for a particular intervention may also relate to the *significant health gain interpretation*, as described by Hasman as the capacity to benefit, given the medical need.[51] Society might for instance be prepared to pay for an intervention if the intervention results in at least a significant improvement in patients' health.[51] In this case, significance of health gains should be defined. Moreover, as health gains can be measured in absolute and relative terms, a choice needs to be made about the most appropriate measure.

Question 3 is often considered in combination with question 2. All countries evaluate the therapeutic value of each individual drug to consider if this drug should be reimbursed and thus paid for by society.

3.1.3.4 Question 4: Do we want to pay more for the drug as compared to the comparator?

Whether or not a society wants to pay *more* for a drug than for its comparator depends on the added societal value of the product. This value depends on its added therapeutic value and on the potential savings it can induce elsewhere in the health care sector.

Other considerations will be taken into account at this stage, such as the quality and uncertainty of the evidence about the added therapeutic value and the induced cost savings.

All countries use internal reference pricing to determine the reimbursed price for products with equivalent therapeutic value. This is a way to express that society is not willing to pay more for the drug than for the other products with equivalent therapeutic value. Much less systematic is the evaluation whether or not the comparator can be *replaced* by the new product and thus be delisted.

If the drug is classified to have added therapeutic value, it is likely that the drug obtains a higher reimbursed price in all systems. This is for example implemented by granting Class 1 and Annex 1B in Belgium and the Netherlands, respectively. This is a way to express that society is willing to pay more for drugs with added therapeutic value.

When the expert committee agrees that, based on the added therapeutic value, induced cost savings and uncertainty regarding the evidence, is not worth paying for out of public resources, there are still several options for the pricing and reimbursement decision. The reimbursement basis should in principle be equal or lower than that of the comparator but the price can be higher. The argument for allowing a higher price could be that, even though the added value was not considered worth paying for out of public resources, the drug does produce an added (therapeutic) benefit that individual patients might value and be willing to pay for.p

p This approach should in principle be cost-neutral to the public health care payer. However, the higher use of the new product is not necessarily offset by an equal reduction in the use of the comparator. It has

3.1.3.5 *Question 5: How much more are we willing to pay out of public resources for this treatment?*

Probably the most difficult task of the expert committees is to determine *how much* the added societal value is worth. In practice, it is difficult to measure public values in monetary terms. Therefore, within the current context of a supply-driven system, where pharmaceutical companies decide what to launch, when to launch and at what price and policy makers have little insight into the price structure of a drug, decision-makers will in practice have to consider whether the budget impact implied by the price requested by the company is reasonable given the incremental therapeutic value of the product and *given the other concerns* they might have (e.g. equity).

All these concerns, and criteria for dealing with these concerns, need to be weighed against each other in order to determine whether the cost of the product is socially acceptable. The criteria and the relative weight given to each of them are not made explicit ahead of time for different reasons.

- Decision-makers and stakeholders might want to give different weights in different situations. For example, therapeutic value may get more weight when no alternative treatment is available than when an alternative treatment is available.
- The weight stakeholders (or their representative) involved in the decision process give to each criterion might be partially influenced by their personal preferences.

No system can define a general rule applicable to decisions in all situations,[62] but by providing an explicit answer to each of the crucial questions for drug reimbursement decision making (in Table 10) the decision making process could be reconstructed. Although this is done to different extents in different countries, all countries seem to have similar general appraisal criteria, in some countries they are more in others they are less explicit.

In the following paragraphs, we describe six possible criteria for determining the amount of (additional) willingness to pay:

- added therapeutic value,
- budget impact,
- cost-effectiveness,
- severity of disease given the available treatment options,
- cost sharing and
- uncertainty of evidence.

i. Added therapeutic value

In all countries, increased efficacy and/or effectiveness and safety get the highest weight in deciding about the added therapeutic value. Although improvement in comfort, ease of use and applicability are often mentioned as determinants of the added therapeutic value, they are in practice rarely sufficient for a product to be considered to have an added therapeutic value. As a consequence, products only with added therapeutic value on comfort are less likely to be reimbursed at a higher price (or reimbursement basis) than products with an added benefit on effectiveness, ceteris paribus. The reason for increased comfort having less weight in the added therapeutic value appraisal might be twofold:

- evidence for these kinds of outcomes is less robust and can be contested more easily
- society is not willing to pay more for increased comfort, given the other medical needs.

been observed that the mere reimbursement of an additional new drug that is equally effective than its comparator and reimbursed at the same price might increase the total use of drugs in that therapeutic class. A recent study of KCE about the use of statins confirmed this hypothesis with observational data.[61]

As mentioned before, in all countries a drug classified as having added therapeutic value is likely to obtain a higher reimbursed price. There is, however, a difference in the way countries define and use the outcome of added therapeutic value. Austria and France classify the degree of added therapeutic value in several categories whereas Belgium and the Netherlands use a binary outcome. Therefore, the Austrian and French system more explicitly reveal how much more society is willing to pay publicly for the degree of added value. Sweden is the only country that is more or less using a sliding scale by directly linking the price to the added value and thus explicating how much more the system is willing to pay for the added therapeutic value.

ii. Budget impact

The budget impact of a product should reflect both the costs induced by the new treatment as well as the induced savings, either within or outside the health-care sector. For a policy maker, it might be important to separate the aspects of costs and savings in different sectors and consider them as separate elements in the decision-making process.

If the estimated budget impact is lower than the societal value of the product, it should be reimbursed. As all other assessment elements, the budget impact estimate is always uncertain. Therefore, measures to control the budget impact are in place in all countries. These measures include:

- influencing the price and/or reimbursement basis,
- influencing utilisation (e.g. conditional reimbursement, a priori approval),
- financial risk sharing agreements.

Countries' bargaining power in price negotiations is limited by the ripple effect of international price referencing policies in most countries. International price referencing gives an incentive to companies to request a high price. Countries therefore mainly try to control the budget impact through measures that influence the utilisation of drugs (demand-side measures) although some countries, such as France and Belgium, also use price-volume agreements to control the budget impact (supply-side measures). For companies financial risk sharing agreements may be more interesting than price negotiations because in a financial risk-sharing agreement a product keeps its facial price. Only Sweden does not use international price referencing and the reimbursement agency formally does not evaluate the budget impact in decision making. However, budget impact is important at regional level, where county councils are responsible for both the financing and the implementation of the decision.

Besides conditional reimbursement, in which case a drug is reimbursed conditional on a priori approval, appropriate utilisation can be obtained by enforcing clinical guidelines. Guidelines can be enforced in several ways. For statins Belgium has defined the "first choice treatment", reimbursed without conditions, and a "second choice treatment" subject to conditions, for patients who failed to benefit from the first choice treatment.

All countries try to influence volume by the dissemination of clinical practice guidelines, but the effectiveness seems to differ between the countries. In Sweden, differences in outcomes between county councils are observed, which might be partly attributable to regional differences in the implementation of clinical guidelines. All countries also use financial disincentives for the patient to influence utilisation, for example by co-payments, co-insurance or deductibles.

In all systems budget impact plays a role in the reimbursement decision or in the implementation of the decision. Moreover, all countries only evaluate the outcome of the decision on drug expenditure and thus financial sustainability. Nevertheless, it is not transparent how budget impact is balanced against the other criteria.

iii. Cost-effectiveness

All countries but France combine the incremental costs and incremental benefits into an incremental cost-effectiveness ratio (ICER) and use the ICER as an appraisal element to decide whether the drug offers value for money, taking all relevant concerns into account. All countries deny using a cost-effectiveness threshold value or range of values explicitly. Thus the normative value of the actual cost-effectiveness ratio is not transparent in all countries. Moreover, the relative weight of cost-effectiveness compared to the other criteria remains unclear. Observational studies and interviews in Belgium have shown that the cost-effectiveness ratio has a rather limited weight in the appraisal process.[62, 63] Only Sweden uses the incremental cost-effectiveness ratio to determine the acceptable price of a product. The absence of an explicit ICER threshold value possibly indicates that the "other concerns" cannot be neglected when comparing the actual or estimated costs for the public benefits of a product with the societal value. It implies that the ICER threshold is probably not constant but a function of the other concerns. These other concerns may for instance relate to the severity of the disease given the treatment options already available. This reflects that in all countries policy makers have discretionary power in decision making.

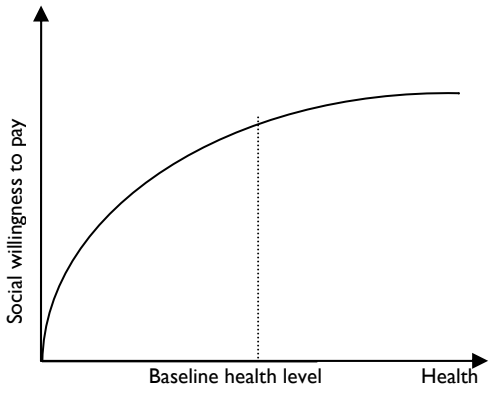
iv. Medical need

The amount a society is willing to pay extra for a drug compared to the best alternative depends, among others, on the severity of the disease. This criterion also determined the medical need. We can build further on the approaches described for determining medical need to show how severity of disease becomes relevant for the willingness to pay question.

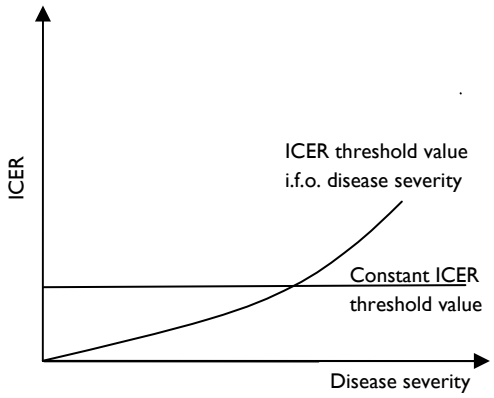
Both the fair innings and proportional shortfall approach define a target level of health: in the fair innings this is a health level everyone is entitled to, in the proportional shortfall approach this is the level of health without the disease. The closer the disease state is to the target level of health, given the current treatment options, the lower the societal willingness to pay for additional benefits will be (Figure 8). In other words, society is willing to pay *more* for a treatment for a severe disease than for a treatment of a mild disease with the same absolute added health benefit.

Figure 8: Societal willingness to pay for additional health benefits

Societal willingness to pay for added therapeutic value in function of disease severity[q]



Constant ICER threshold value versus ICER threshold value in function of disease severity



Source: Stolk et al. (2004)[59]

q The form of this function can be different. It might be the case, for instance, that the societal willingness to pay for minor improvements in very bad health states is (almost) 0. The function might also be discontinuous of s-shaped.

The increasing willingness to pay with increasing disease severity is a direct consequence of the trade-offs a society has to make with regard to the competing health care policy objectives. Besides disease severity, also age and socio-economic status may be considered relevant criteria from the equity point of view. As such, the ICER threshold becomes a complex function of different variables.

All countries are reluctant to use a constant ICER threshold value or even a range of values. During the decision making processes, it is relevant, however, to consider the different elements making up the incremental cost-effectiveness ratio separately, i.e. added therapeutic value and incremental cost, and weigh these elements against the other relevant criteria. Most interviewees acknowledged that if there would be a threshold it would be an increasing threshold mainly depending on disease severity and rarity. Rarity and availability of alternative treatments are often related. Prices of drugs for rare diseases are often high because pharmaceutical companies have to recover their costs from a small population. A society faced with a product for treating a severe rare disease for which no alternative treatment exists, might be prepared to pay the high price demanded by the pharmaceutical company, because of solidarity with patients with rare diseases. The solidarity principle increases in this case the societal value of a product far beyond its therapeutic value. A higher willingness to pay for drugs for rare diseases has been observed in all countries, showing the strength of the solidarity principle in all countries. It gives companies the opportunity to set high prices and remain rather inflexible in price negotiations.

As previously described, in the Netherlands disease severity is operationalised by using the proportional shortfall approach in formal appraisal criteria. However, it should be mentioned that the Dutch appraisal committee only recently drew up this appraisal criterion and that so far it is unclear to which extent this is used for individual drug decisions. The Dutch reimbursement agency recently brought up an indication for a threshold range depending on disease severity, however, the minister has neither confirmed this range nor endorsed a threshold. In Sweden the main priority setting principles imply that persons in greatest need have the highest priority. The Swedish committee explicitly considers "marginal utility" which is further defined by TLV as "if no alternative treatment exists, cost should be reasonable". However, the implication of the term reasonable is not further defined. This might indicate that TLV does not want to endorse a range because they do not want to encourage strategic behaviour.

Belgium uses "necessity of treatment" to define the level of cost sharing. Interestingly, a negative correlation has been observed between the level of cost sharing and the added therapeutic value of drugs.[63] This indicates that products for more severe diseases are more likely to be considered of added therapeutic value in Belgium. In France, medical need is one of the criteria determining the SMR. The SMR determines the level of cost-sharing but not the price (which is determined afterwards by the CEPS). In Austria, although not explicit, medical need is considered in the evaluation of the therapeutic benefit, which in turn is strongly related to the price.

All countries take into account disease severity given available alternative treatments. Nevertheless, the actual operationalisation in explicit and comprehensive criteria covering all diseases remains limited. Even though we observed that this criterion is important, the relative weight of this consideration is not clear in any of these countries.

v. Cost sharing

All systems use cost sharing policies in health care and/or drug use in specific. Nevertheless we observed varying degrees of share of out-of-pocket expenditure (see paragraph 2.1.4.4). Thus countries accept diverging levels of cost-sharing.

The country comparison showed that some countries use the medical needs criterion to determine the level of co-insurance (France, Belgium) whereas other countries apply other cost-sharing policies and fully reimburse drugs (Austria, the Netherlands and Sweden). Cost sharing policies might be implemented to

- ensure efficiency in the use of health care and
- ensure the sustainability of the health care system.

Using cost sharing instruments to meet two of the health system objectives (sustainability and quality of care) implies dealing with the third objective (equity, including, amongst others, financial accessibility). By using the medical needs criterion to define the level of co-insurance or co-payment (Belgium and France), affordability is higher for the most necessary treatments. However, even then it is considered that there are limits to cost sharing. All countries implemented various social protection measures to ensure affordability and equity.

vi. Uncertainty of evidence

In areas where uncertainty is high, the likelihood of people disagreeing on the relative weight to be given to each of the decision criteria increases. This complicates the appraisal and decision making process. The countries included in our comparison are not often clear about how they handle uncertainty. Uncertainty basically exists for several assessment and appraisal criteria, added therapeutic value and budget impact covering most of them. Uncertainty about the added therapeutic value might lead to expert committees' lowering the estimate of the added therapeutic value, advising to restrict reimbursement or deny reimbursement. Another possibility is that the expert committee takes a temporary reimbursement decision, conditional upon additional evidence collection. Policy makers could also decide to pay a lower price than the price requested by the company for the drug based on the degree of uncertainty, until uncertainty has been reduced.[64] At revision, the new evidence is taken into account to assess whether the initial price is acceptable given the societal value of the product. Uncertainty about the budget impact might also be limited by means of price-volume agreements, which are applied in France and Belgium.

3.1.4 Relevance of decision criteria: summarising countries' achievements

In the previous section we discussed the relevance of the reimbursement criteria for answering each of the five key questions in Table 10. We analysed for all criteria whether countries use them in the drug reimbursement process, how they were operationalised and whether we have an impression of their relative weight in the decision process. We emphasise that we can only give insight into each countries' achievements based on our observations and that we do not aim to give a value judgement on the performance of each country's reimbursement system.

We observed that all countries address the five questions of our decision framework in the reimbursement decision making process. Several questions are interrelated and are reconsidered in several phases. However, the degree to which the relevant criteria are operationalised and implemented varies across countries.

Added therapeutic value seems to be the most prominent criterion in decision making in all countries, and all have operationalised this criterion quite extensively. The importance of added therapeutic value addresses the system objective of quality of care. Furthermore, the outcome of the therapeutic value assessment is often made transparent in the decision (e.g. allowing higher prices).

Also **disease severity** seems important in decision making in all countries, reflecting the equity objective of systems. This criterion is used to address all five questions of our framework. Nevertheless, the detail to which disease severity is operationalised varies across countries.

Cost-effectiveness addresses the system sustainability and quality of care objectives. It is a reimbursement criterion in all countries but France. However, none of the countries has an explicit threshold (range). Therefore in most countries the actual role of this criterion in decision making is unclear.

Budget impact, which reflects the sustainability objective of a system, is considered in all countries either at the national decision level or at the regional implementation level. All countries more or less have an open-ended pharmaceutical budget. However, allotted discretionary power enables reimbursement denial because of budgetary reasons.

Disease rarity seems an important criterion for the willingness to pay for a product. It reflects the equity objective of systems: patients with rare diseases should have equal chances of treatment and should be able to afford these treatments.

Cost sharing policies are implemented in all countries. All countries implemented policies to ensure equity in health care.

Some countries seem to use **own responsibility** as an explicit criterion for defining societal priorities in health care.

The relative importance of all criteria mentioned above often remains unclear in all countries and especially appraisal criteria often lack transparency. This can result in differences in accountability of the systems: the lower the transparency of both formal and informal criteria, the less accountable a system.

3.1.5 Revisability

Accountability for reasonableness presumes revisability of decisions in the light of new evidence.

Revisability is most important in cases where there is uncertainty about the estimates of efficacy, effectiveness, cost-effectiveness and budget impact. In areas where uncertainty is high, the likelihood of people disagreeing on the relative weight to be given to each of the decision criteria increases. This complicates the appraisal and decision making process.

Austria is the only country that did not implement any system of systematic revisions, although ad hoc revisions can be initiated. Belgium and the Netherlands have a revision procedure for positive decisions for all Class 1 and expensive inpatient drugs, respectively. The revision occurs only once, 1.5 to 3 years after the initial decision in Belgium, 4 years after the initial decision in the Netherlands. France revises all positive decisions every 5 years. Sweden currently revises all drugs previously enlisted and also decides on a case-by-case basis whether revision is needed. In all countries, revisions can have consequences such as delisting and/or a change in the reimbursement level. In the Netherlands, no revision of the expensive inpatients drugs has been performed so far, the first ones are due at the end of 2010. Therefore the actual consequences are not clear yet.

The revisability criterion demands for the revisability of decisions 'in the light of new evidence', suggesting that for some drugs revision might not be required, i.e. for drugs for which there is no or little uncertainty, at least for as long as no new alternative is introduced on the market. The cost-effectiveness of collecting more information should be considered upfront when deciding on the need for a revision.

Revisions should be possible at any time after a decision has been taken. The medical need and therapeutic value of a drug may change over time, as new treatment opportunities (also outside the pharmaceutical sector) are developed and the economic and societal context changes. This may induce the need for delisting of products, as in France and Sweden. In that sense, a reimbursement decision should always be temporary.

3.1.6 Enforcement

In the context of accountability for reasonableness, enforcement refers to the enforcement of the first three conditions: transparency of the drug reimbursement procedure, relevance of rationales and criteria used during the process, and revisability of the decisions. It relates to the possibility to enforce a system that balances the health system objectives using democratic procedures and criteria.

In all countries, not much self-evaluation of the drug reimbursement system is performed on the process and on the outcomes. All agencies fall under ministerial responsibility and are audited (and/or certified) as agency by external (parliamentary) committees. Reimbursement processes themselves or parts of the processes are only monitored on an ad hoc basis. All countries implemented formal appeal options to reimbursement decisions.

In Belgium and the Netherlands pharmacoeconomic procedures and the use of pharmacoeconomic evidence have been evaluated and recommendations formulated. Both systems seem to be rather open to public scrutiny: external parties are given the opportunity to perform ad hoc assessments of the procedures or specific elements of the procedure. In France, an ad hoc evaluation of the drug policy was performed by the parliament, leading to the recommendation to consider economic evaluations in the procedure.

Pharmaceutical expenditure as outcome of the reimbursement system is an indicator for health system sustainability. This is monitored in all countries. However, increasing pharmaceutical expenditure does not necessarily imply decreasing efficiency of health care resource use and can therefore as such only be used to assess financial sustainability. Global health outcomes are also monitored in all countries, but these are of course not necessarily drug-related. General indicators such as socio-economic differences in health can be used to evaluate the equity and quality of care objectives, but it is difficult to ascribe these outcomes specifically to the drug reimbursement system.

4 GENERAL CONCLUSIONS AND RECOMMENDATIONS

The aim of this study was to examine similarities of and differences between five European drug reimbursement systems in order to assess to what extent policy makers can be held accountable for the reasonableness of their decisions in different organisational and procedural contexts. We studied and compared the drug reimbursement systems of Austria, Belgium, France, the Netherlands and Sweden. We examined whether the four conditions for accountability for reasonableness (i.e. transparency, relevance of the rationales, revisability and enforcement) were satisfied. The ultimate aim is to make suggestions for improvement.

All five countries have three main health policy objectives in common: financial sustainability, equity and quality of care. The public payer is continuously faced with a dilemma between ensuring equitable access to high quality health care and ensuring sustainability of the health care system. The challenge of policy makers is therefore to find a publicly acceptable balance between these objectives.

All countries established expert committees responsible for the assessment and appraisal of drug reimbursement requests and involved relevant stakeholders in the process (either through representation within the expert committees or through consultation). This created room for discussion about the relevance of the rationales and criteria used in the drug reimbursement decision process, given the overall system objectives. In the composition of expert committees in a deliberation-driven system, balanced representation of societal preferences is of utmost importance. In assessment-driven systems, consultation of stakeholders should be systematic in order to ensure adequate representation of societal preferences in the appraisal process.

In both deliberation- and assessment-driven systems assessment and appraisal are intertwined processes. It is important to manage the differences between assessment and appraisal appropriately. Assessment is purely descriptive and value-free and implies quantifying the clinical, pharmacotherapeutic and pharmacoeconomic outcome with scientific rigour. Appraisal implies evaluating the societal value of a drug by weighing the assessment criteria other (societal) criteria.

To reach accountability for reasonableness, any democratic political system has the obligation to be transparent, use societal relevant rationales in decision making, allow revisability of decisions in the light of new evidence and enforce the three previous conditions.

4.1 TRANSPARENCY CONDITION

Each system has its strengths and weaknesses when assessed using the accountability for reasonableness framework. Despite this, and taking into account differences in organisation of the decision procedures, we identified one main common area for improvement: transparency, especially in the appraisal process.

Although documentation of the decision is publicly available in all five countries, the decision making process is often not transparent. All five systems can improve upon disentangling assessment and appraisal. This might be achieved by the establishment of both an assessment and an appraisal committee, but can also be achieved by other means. Every country needs to decide which mean fits best within its own national and historical context. Most important is to more clearly separate the assessment and appraisal phase, increase transparency in the division of responsibilities for the assessment and appraisal and increase transparency in the applied criteria.

Furthermore, transparency of the decision process requires an explicit framework specifying the decisions to be made. We developed a framework for drug reimbursement decision making, allowing to increase transparency of the procedures as well as consistency in the criteria used at the various stages of the procedure. It enables the improvement of the legitimacy of decision making and hence the accountability of the system. Our framework connects the "transparency"-condition with the "relevance of the decision criteria"-condition for accountability for reasonableness.

The discussion on the relevance of the decision criteria provides opportunities for increasing transparency. The actual criteria to be used in drug reimbursement decision making is a societal choice. Societal choices need to be made and for transparency reasons they need to be made explicit. Therefore, the framework includes suggestions for possible criteria without making strong recommendations on their appropriateness or measurement.

4.2 RELEVANCE CONDITION

The decision framework consists of five central questions for a drug reimbursement process with for each question possibly relevant criteria. The five questions are:

1. Is there a medical, therapeutic and societal need for treatment/prevention of this condition?

   Relevant criteria might be severity of the condition (threat to live, severity of symptoms), prevalence, availability of effective alternative treatments, inequalities in health.

2. Are we, as a society, prepared to pay for a treatment that will improve this indication out of public resources?

   Relevant criteria might be personal responsibility or relationship with life style

3. Are we, as a society, prepared to pay for *this* particular treatment, given that we in general would be prepared to pay for *a* treatment for this indication?

   Relevant criteria might be the relative safety, efficacy and effectiveness of the treatment compared that of alternative treatment(s) and significance of health gains

4. Given that we, as a society, are prepared for this treatment out of public resources, are we prepared to pay *more* for this treatment than for the best alternative treatment available?

   Relevant criteria might be the added therapeutic value, induced savings, level of evidence, uncertainty, reward for added value, acceptability of cost sharing

5. *How much more* are we willing to pay out of public resources for this particular treatment?

   Relevant criteria might be budget impact, incremental costs, added therapeutic value, cost-effectiveness ratio, disease severity, induced savings, reward for added value, limits of cost sharing

Crucial in this process is the societal acceptability of the criteria for each decision. The criteria mentioned above are only examples of possible criteria, there is no scientifically right or wrong set of criteria. A discussion about their societal acceptability must take place.

We analysed for each country whether relevant decision criteria were used in the drug reimbursement process, how they were operationalised and whether we could obtain an impression of their relative weight in the decision process. We did not intend to give any value judgement on the performance of each country's reimbursement system.

All countries address the five questions of our framework in the reimbursement decision making process. Several questions are interrelated and might have to be reconsidered throughout the decision making process. However, we found that the degree to which the questions are answered explicitly and how the relevant criteria are operationalised and implemented varies across countries.

Added therapeutic value seems to be the most prominent criterion in decision making in all countries, and all have operationalised this criterion quite extensively. The importance of added therapeutic value addresses the system objective of high quality of care. Also disease severity and rarity seems to be important in decision making reflecting the system objective equity. The detail in which disease severity is operationalised varies across countries. Further refinement could enhance the relevance and transparency of this criterion. Cost-effectiveness, operationalised as the ICER, is a tool to find a balance between the policy objectives quality of care and financial sustainability. The ICER is a reimbursement criterion in all countries but France. However, none of the countries uses a fixed ICER threshold value, even ranges do not seem acceptable. Budget impact, which reflects the system objective sustainability, is considered in all countries either at the national decision level or at the regional decision level. Also cost sharing policies are implemented in all countries alongside social protection mechanisms to ensure equity in terms of affordability.

Although the relevance of decision criteria (relevance condition) seems important in all countries, the appraisal criteria and their relative importance are not always made explicit (transparency condition). This can result in differences between systems in their accountability for reasonableness.

4.3 REVISABILITY CONDITION

The third condition for accountability for reasonableness presumes revisability of decisions in the light of new evidence. Revisability is especially important in cases of much uncertainty regarding the evidence. Case-by-case revisions are embedded in most countries. However, systematic group-wise decisions are only implemented in some countries. Large across-group revisions could potentially increase prioritisation according to medical needs and ensure revisability.

4.4 ENFORCEMENT CONDITION

Finally, accountability for reasonableness requires enforcement of the three previous procedural requirements. All countries implemented formal appeal options against reimbursement decisions within the system. The critical evaluation of the reimbursement processes and the roles of the key actors within these processes is in all countries limited to external (parliamentary) audits. Outcomes assessment of drug reimbursement systems is mostly limited to systematically monitoring pharmaceutical expenditure. Evaluation on other health system objectives is limited to measures such as overall health and differences in overall health. These general indicators cannot, however, distinguish outcomes attributable to the drug reimbursement policy from outcomes not attributable to the drug reimbursement policy. More efforts should be made to evaluate performance on procedures, content and outcome systematically. Follow-up indicators may require further refinement or should be developed.

4.5 FUTURE RESEARCH

Future empirical research on the appraisal processes in different countries, based on the review of real reimbursement dossiers, would be worthwhile to examine to what extent the actual appraisal differs between countries. Moreover, it would be interesting to compare actual decisions with stated system objectives and stated preferences and subsequently derive country-specific social welfare functions.

Key messages

- **All five health systems have three main objectives: system sustainability, equity and quality of care. An acceptable balance has to be found between these objectives.**
- **In a democratic system, accountability for reasonableness of drug reimbursement decisions requires transparency of procedures, relevance of criteria, revisability of decisions, and enforcement of the three previous conditions.**
- **In deliberation-driven drug reimbursement models relevant stakeholders are part of the expert committee and in assessment-driven models, relevant stakeholder are consulted by expert committee members.**
- **Added therapeutic value seems the most important criterion. Cost-effectiveness is a criterion in all countries but France. However, none of the countries has a threshold value and thus the relative importance is not clear. Disease severity seems important in all countries, but the operationalisation is not always clear and varies per country.**
- **All countries seem to balance the added therapeutic value, disease severity and costs. This reflects the trade-off between the high quality of care, equity and system sustainability.**
- **Documentation of the reimbursement decision is publicly available, however, the decision-making processes is often not transparent.**
- **Case-by-case revisions are embedded in most systems. Systematic group-wise revisions are only implemented in France and Sweden.**
- **All systems monitor their performance in terms of pharmaceutical expenditures, which addresses system sustainability. Other performance indicators are non-drug policy specific. Ad hoc process evaluations are performed, either by parliament or by external parties.**

General recommendations

- **Assessment of a product and appraisal of its value should be disentangled and performed in different phases in the reimbursement process. The roles and responsibilities of different actors should be clearly defined.**
- **An assessment report should include a critical assessment of all the available evidence and uncertainty, assign a level of evidence and highlight where evidence is missing. Experts should obtain a declaration from companies that all relevant evidence is presented in their drug reimbursement request file, including information from ongoing studies.**
- **Neither the reimbursement request file of the company nor the assessment report should include a reimbursement proposal and/or conclusions about the added therapeutic value.**
- **The appraisal process should make use of an explicit framework specifying, for each advice, the social choices and decisions made during the process as well as the relevant criteria on which these choices and decisions are based. The following questions should be addressed explicitly:**
  - **Does the product target a medical, therapeutic and societal need?**
  - **Are we prepared to pay for a treatment that will improve this indication out of public resources?**
  - **Are we prepared to pay for this particular treatment out of public resources?**
  - **Are we prepared to pay more for this treatment than for the best alternative treatment?**
  - **How much more are we willing to pay out of public resources for this particular treatment?**
- **There should be a balanced representation or consultation of all stakeholders in the drug reimbursement appraisal process.**
- **The appraisal and decision-making process should become more transparent, revealing societal decision criteria and valuation of each of these criteria during the appraisal process, to increase coherence and justification of decisions.**
- **Decisions should be revisable, especially when uncertainty about relative effectiveness, cost-effectiveness and budget impact is high.**
- **Reasons for revisions should be: new treatment opportunities (including non-pharmaceutical) becoming available, excess of the predicted budget impact, and a changing economic and/or societal context.**
- **Revision should include the possibility of delisting of products, rather than just lead to a change in reimbursement modalities.**
- **Large across-group revisions should be performed to ensure prioritising the highest medical, therapeutic and societal needs.**
- **Performance of the system in terms of transparency, relevance of decision criteria and revisability of decisions should be systematically monitored.**
- **Follow-up indicators of drug reimbursement policy-related outcomes may need to be developed or refined through future research.**

5 LESSONS FOR BELGIUM

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Based on the international comparison of drug reimbursement systems and consultations of the different stakeholder groups represented in the expert committee, i.e. Drug Reimbursement Committee (CRM/CTG), we attempted to define opportunities for improving of the accountability for reasonableness of the Belgian drug reimbursement system. The Daniels & Sabin framework describes the requirements for accountability for reasonableness in an ideal world. Our suggestions for improvement focus on realistic modifications of the drug reimbursement procedure in the Belgian context.

We first briefly describe the roles of the different key actors in the Belgian drug reimbursement decision process, then identify the strengths of the Belgian drug reimbursement system and the key issues with respect to the Belgian process. Finally, we formulate some recommendations for the Belgian policy maker.

5.1 ROLES OF THE DIFFERENT ACTORS IN THE PROCESS

The roles of the different actors are defined in the law. In this paragraph, we briefly summarize the practical implementation of the legal rules (for a more extensive description, see appendix).

The pharmaceutical company, i.e. the applicant submits a drug reimbursement request file that includes the clinical evidence, price requested for the product, budget impact estimate and, for products for which the company claims a Class 1 (added therapeutic value), an estimate of the cost-effectiveness ratio. The applicant formulates a proposal regarding the reimbursement conditions in the reimbursement request file.

The internal RIZIV/INAMI experts prepare the assessment report ("day 60"-report), describing and critically assessing the evidence presented in the drug reimbursement request file. By law, the experts are required to assess the reimbursement request file, not the pharmaceutical product as such. They assess the added therapeutic benefit, the quality of the evidence presented and the level of uncertainty. In addition, they critically assess the drug reimbursement proposal, including the reimbursement modalities, suggested by the company. The assessment report is presented at the CRM/CTG meeting. What follows is a discussion on the assessment elements as well as on the relative importance of each of these elements and the reimbursement proposal of the company. Based on the assessment report and the discussions during the meeting, the technical department prepares a preliminary reimbursement proposal for the CRM/CTG ("day 120"-report). Companies can react on this preliminary proposal. Based on the reactions of the company on the "day 120"-proposal, the RIZIV/INAMI experts prepare a preliminary proposal (day 150), which is submitted to the CRM/CTG for voting. First, the CRM/CTG votes on "positive reimbursement advice, under the stated modalities". If no 2/3 majority is obtained, the CRM/CTG votes on "negative reimbursement advice". Depending on the outcome of the voting procedure, the internal experts prepare a final motivated proposal for the CRM/CTG on which the CRM/CTG votes again ("day 150"-report). The RIZIV/INAMI experts are hence responsible for preparing the assessment report and for formulating a preliminary and final reimbursement proposal based on the discussions held during the CRM/CTG meetings. All documents are prepared on behalf of the CRM/CTG.

The role of the CRM/CTG is to discuss the assessment file, to appraise the therapeutic value (i.e. deciding on whether the added therapeutic benefit has a social value) and to weigh, further in the process, the different drug reimbursement criteria in order to formulate a reimbursement proposal to the minister. If there is no 2/3 majority for the proposal formulated at day 150, the minister receives no proposal. In case of a 2/3rd voting majority, a preliminary proposal becomes a 'final' proposal (which not yet a decision). The CRM/CTG carries the full responsibility for the reports supporting the advice and/or proposal.

The minister of social affairs makes a reimbursement decision, after hearing the advice of the minister of budget. The minister can deviate from the final proposal of the CRM/CTG (a proposal is an advice supported by 2/3 of the voting members of the CRM/CTG), but he/she can only do so for "social or budgetary reasons". "Social reasons" are not further specified in the law.

5.2 STRENGTHS OF THE BELGIAN REIMBURSEMENT SYSTEM

In general, the establishment of a separate committee for the assessment and appraisal of drug reimbursement request files is considered positive by all actors in the process. The procedure is clear, has clear deadlines with sanctions if the deadlines are not kept. This has increased the transparency and enforcement of the procedure.

The establishment of the independent committee is considered important to deal with the main threat of the system: the ever increasing expenditure on drugs for marginal improvements in benefits. Most members of the CRM/CTG recognise the 3 main health system objectives of sustainability, equity and quality of care. Most members are aware that choices have to be made in order to meet these objectives and that trade-offs are sometimes necessary.

5.3 ISSUES RELATED TO THE DECISION PROCESS

This section presents our reflections on issues related to the drug reimbursement decision process. Our reflections and suggested solutions result from the integration of the issues identified during the consultation of all groups represented within the CRM/CTG in the framework of accountability for reasonableness.

5.3.1 Composition of the CRM/CTG

The CRM/CTG is composed of representatives of the physicians, pharmacists, universities, sickness funds, who have voting rights, and of representatives of the pharmaceutical industry, the ministers of social affairs, public health, economic affairs and budget and the RIZIV/INAMI, who have not voting rights. The voting members are appointed by the minister of health, following a proposal by the respective stakeholders' organisations. They should express the preferences of the different stakeholders (population groups affected by drug reimbursement decisions) and endorse the remit of the CRM/CTG, i.e. to advice on the reimbursement of drugs in a fair way, within a context of limited health care resources.

We identified the following issues with regard to the composition and the roles of the CRM/CTG members:

- Some members have predictable voting behaviour. This might have two reasons:
  - Current drug reimbursement procedures do not allow members to vote on separate elements of a reimbursement proposal but only on a complete proposal, including the reimbursement conditions. Members that do not agree with one element in the proposal will have to vote negatively on the entire proposal. Solving this problem requires a change in the procedure of formulating proposals.
  - Some members represent stakeholders that do not endorse the basic premise that choices have to be made within health care due to limited resources – and thus some drugs should not be reimbursed – and that this should happen in a fair way. According to the accountability for reasonableness framework this might be problematic, because one of the basic conditions for accountability for reasonableness is that all stakeholders are willing to discuss the fairness and reasonableness of a reimbursement, given the social context of limited resources and the consequent need to set priorities.
- CRM/CTG members tend to focus their contribution on specific different aspects of the drug reimbursement request. For example, some members contribute relatively more to the discussion about the most appropriate patient population or the conditions for use of the product than to the

discussion on the reimbursement basis. It is often a reflection of stakeholders' and by consequence their representatives' expertise or specific preferences. This is as such not a problem, as long as the representatives are prepared to vote on reasonable grounds.

- The sickness funds consider themselves as the representatives of the patients within the CRM/CTG. Unless the preferences of the patients are identical to the preferences of the sickness funds, patients themselves are not represented within the CRM/CTG. This is a social and political choice and related to the role given to sickness funds in the Belgian health care system.

5.3.2 Assessment by the RIZIV/INAMI experts

During the interviews, we identified the following issues with regard to the current assessment process:

- Ideally, the eventual decision should be based the value of the *product*, rather than on the appraisal of the proposal as submitted by the company applying for reimbursement. The CRM/CTG is legally held to assess the motivation of the drug reimbursement proposal. There is discussion whether assessing motivation includes searching for missing information. Companies do not have to declare that the evidence provided is complete.
- The basis of the discussions during the CRM/CTG meetings are the evaluation reports prepared by the internal experts only. The CRM/CTG members do not read the original reimbursement request file of the applicant.
- According to the opinion of some interviewees, some assessment reports are considered to be biased or incomplete. According to what we learned during the interviews, this perception of bias is related to a perceived unbalanced reporting (perceived by these interviewees to be sometimes intentional, sometimes unintentional) of the negative versus positive elements related to the evidence presented in a drug reimbursement request and not to potential conflicts of interest. Given that the assessment report is not accompanied by the original submission, this perception can only be based on prior knowledge about a specific product (e.g. through membership of a scientific committee at the European Medicines Agency (EMA) or through first-hand information from the applicant).
- Some CRM/CTG members criticise the fact that the RIZIV/INAMI experts re-assess the efficacy and safety of a product, an assessment that has been done already in the context of the registration of the product at the EMA. The RIZIV/INAMI experts note that the evidence requirements for obtaining marketing authorisation are insufficient for drug reimbursement decision makers, because decision makers need to compare the safety and efficacy of a product with an active comparator that can even be a non-pharmaceutical intervention. Safety and efficacy compared to placebo is therefore insufficient. The assessment of the EMA therefore needs to put into the perspective of the broader treatment opportunities available in Belgium.
- Before the establishment of the CRM/CTG in 2002, the evaluation reports were prepared by academic experts. With the establishment of the CRM/CTG, the academic experts became full CRM/CTG members with voting rights, but with no explicit role anymore in the scientific evaluation and critical assessment of the evidence presented by the applicant.

5.3.3 Appraisal by the Drug Reimbursement Committee (CRM/CTG)

During the appraisal process, the CRM/CTG has to weigh and consider the elements presented in the assessment report and other elements relevant to society but not included in the assessment report. The result of this weighing exercise is context-specific. It depends, for instance, on available budgets, needs and social preferences. Quantifying the relative weights of the appraisal criteria applied in a range of decisions and applying these to future decisions would not necessarily lead to better decision making, because such a purely quantitative approach to decision making makes abstraction of the changing societal context. Systematic transparency in how the different appraisal criteria are judged, however, would give the decision making system a kind of memory. This memory can serve as a basis to take coherent decisions and, if a seemingly incoherent decision is taken, a stronger basis for justifying the decision.

The following issues have been raised regarding the appraisal process:

- The drug reimbursement request file has to contain a reimbursement proposal from the applicant. This is considered important because the reimbursement modalities defined in the proposal determine the results of many of the analyses presented in the file (e.g. budget impact and cost-effectiveness analysis). The RIZIV/INAMI experts comment on this proposal and sometimes present an alternative proposal based on their critical assessment, with its consequences for the estimated budget impact. Even though the CRM/CTG carries the full responsibility for the proposal, starting from an suggestion for proposal is different than formulating a proposal based on the raw assessment elements, presented for varying reimbursement condition scenarios.
- Budget impact seems to have a very important weight in the final reimbursement proposals. Almost all members recognise that budget impact is an important element to consider during the appraisal process. However, there are differences in viewpoints on how to budget impact should be controlled or influenced: some members tend to focus more on the reimbursement basis during the discussions, while others tend to focus on the volume of use. This difference is legitimate. The issue is, however, that there seem to be differences in viewpoints on how the volume should be controlled. Different possibilities exist: chapter IV (reimbursement subject to prior approval by the supervising physician of the sickness fund), chapter II (ex post control of reimbursement) or limiting the patient population eligible for reimbursement. Different stakeholders clearly expressed different preferences with respect to this.
- The law defines the criteria the CRM/CTG needs to take into account when discussing the reimbursement of a drug: efficacy, effectiveness, side-effects & safety, user-friendliness, added therapeutic value, cost-effectiveness, budget impact, therapeutic and social needs. In practice, also other criteria are taken into account. One example is the prospect of further innovations, the underlying idea being that the reimbursement of a new product with a small or no added therapeutic value may however lead to the discovery of a product with a more significant added therapeutic value. This is not problematic if society believes the health care budget should also be used for stimulating further research on a promising new technology, besides for reimbursing currently effective health care. If it is a social choice to stimulate primary research through other means, such as research budgets, it is a problem to use it as a argument to reimburse a specific drug. Moreover, it is currently not a legitimate reason according to the law.

A number of issues were raised about the voting procedure, the documentation of the motivation behind the votes and the documentation of the outcome of the voting procedure:

- During the voting procedure –done by a showing of hands– all CRM/CTG members are present, including the non-voting members such as the representatives of the pharmaceutical industry and the representatives of the ministers.
- A secret voting can be requested by any voting DRC member according to the law but this rarely happens.
- The final proposition is sometimes hard to justify or to be supported by clear arguments if during the discussions the arguments in favour or against the preliminary proposal have not been clearly put forward. The results of the voting therefore not necessarily reflect the tenor of the discussions at the CRM/CTG. This may happen if, for instance, one group of representatives has a clear point of view regarding the proposal and expressed this viewpoint while others with a different view, have not actively participated in the discussions. As members do not have to justify their vote, the motivation behind the results of the voting might be unclear. This may lead to expert committee members finding their point of view not reflected in the appraisal report.
- Because CRM/CTG members vote on a complete proposal and different members put emphasis on different aspects of the proposal, the 2/3rd majority is not always obtained for drugs with a Class 1 claim and orphan drugs and hence no proposal is formulated to the minister for these products. Between 2004 and the first semester of 2009, this happened for 26.6% of Class 1 products and 22.0% for orphan drugs.65

5.3.4 Price and reimbursement basis

The maximum price of a drug is determined by the ministry of economic affairs. The pricing decision should in principle depend on the added therapeutic value of a drug and the, from a societal point of view, adequate return on investment.

Sometimes a company asking for reimbursement of a product with added therapeutic value decides not to claim a Class 1, because:

- the price of the comparator product is acceptable to the company;
- an economic evaluation is not required as part of the drug reimbursement request file, and
- the company expects an important market share once the product is reimbursed because it nevertheless offers an additional therapeutic benefit to the patient compared to the alternative products.

There are two important issues with respect to the price of products and the reimbursement decision.

- The maximum pricing decision is made before the added therapeutic value has been discussed at the CRM/CTG. As a consequence, the maximum price granted does not and cannot yet take the therapeutic value into account. The maximum price is therefore usually based on a preliminary assessment and a limited appraisal of the drug and on prices in other countries. This preliminary assessment is usually limited to addressing the therapeutic cluster of the product in the context of the internal reference pricing.

- The ministry does not dispose of an estimate of the return on investment. According to the companies, it is impossible to grant more transparency in the pricing. Therefore, the ministry uses prices in other European countries as a reference. A similar process is applied in other European countries. The fact that all countries are looking at each other's prices is not very helpful, as this practice will only lead to companies starting off with asking a high price in the first country they submit their reimbursement request to and to negotiate with the government to keep the high facial price. Direct negotiations are therefore rewarding, not only for one national market but for Europe in general. Moreover, as companies know that the only direction in which the price decision goes is downwards, they are actually given an incentive to ask a high price.

The CRM/CTG is entitled to propose a lower reimbursement basis than the maximum price to the company, but if the company does not accept the proposal, there is not much room for further discussion within the CRM/CTG. The CRM/CTG must then vote on a reimbursement proposal with a given reimbursement basis, equal to the reimbursement basis requested by the company. If the reimbursement basis is considered too high, given the added therapeutic value, the CRM/CTG will give a negative advice.

After a negative CRM/CTG advice or proposal, companies will try to negotiate on the price directly with the minister of budget and the minister of social affairs. This post-CRM/CTG process is not transparent. Moreover, as the CRM/CTG members do not vote on separate elements of the drug reimbursement proposal and as the votes do not have to be motivated, the minister cannot know for sure whether the price or budget impact was the main hurdle within the CRM/CTG for giving a negative advice on the reimbursement, although he/she will usually have some idea based on the reports of his/her representative at the CRM/CTG. Only when the reimbursement proposal was negative because the price or budget impact was considered too high, it would seems acceptable that a directly negotiated price reduction would turn a negative proposal into a positive decision. And still, even in this case it can be questioned why a company did not accept the lower reimbursement basis proposed by the CRM/CTG to increase its chances for a positive CRM/CTG proposal if it consequently agrees on a lower price in direct negotiations with the minister. The difference is, of course, that with the minister an agreement can be made to reduce the price of other products produced by the applicant, in return for keeping the facial price of the new product, which may be relatively more interesting for the company from a strategic point of view (cf. price referencing between countries). Since 2010 a company with a recognised Class I drug can express its wish to the minister to negotiate a contract with the RIZIV/INAMI in case of a negative CRM/CTG proposal. The opportunities and potential threats of these contracts will be studied in a future KCE report. Therefore, no recommendations related to these contracts will be formulated in this report.

5.3.5 Reimbursement category

The level of reimbursement, or reimbursement category, is rarely discussed within the CRM/CTG. A recent Belgian study of 71 drug reimbursement requests, has shown that drugs in Category A (100% reimbursement) have a 4 times higher chance of getting a positive reimbursement advice.[63] The reimbursement category mainly reflects the disease severity. However, as highlighted in the context of our suggested framework for accountability for reasonableness (chapter 3), it is crucial to consider the medical need *given the already available treatment options*. As of yet, the definition of reimbursement categories seem to be more indication-based than medical needs based.

An issue evoked by several CRM/CTG members is that the system of the drug reimbursement categories has become very complex and difficult to use. This is, amongst others, related to the accumulation of policy measures in an attempt to meet to the best possible extent all three health system objectives. Cost sharing mechanisms are used to avoid overconsumption. Exceptions to the general rules are, however, made for specific patient populations in order to meet the equity objective. Although this might be legitimate, their practical implications need to be considered.

An extensive analysis of cost- sharing mechanisms in outpatient care, including the system of drug reimbursement categories is planned at KCE in 2011. The current report will therefore not elaborate further on this topic.

5.3.6 Decision by the Minister

In practice, it has been noticed that the minister sometimes deviates from the advice of the CRM/CTG based on arguments that have been taken into account already at the level of the CRM/CTG advice (e.g. budget impact). It seems surprising that a democratically chosen minister, acting on behalf of society, can draw a different conclusion than a representative committee based on the same assessment and appraisal criteria. However, it is legitimate, according to the Royal Decree of 15 February 2007.[66] According to this article, the minister can deviate from the CRM/CTG proposal for social and budgetary reasons or a combination of both, *within the limits of the criteria defined for inclusion, modification or removal of a drug from the list of reimbursed drugs, being therapeutic value, price and reimbursement basis, importance of the drug in clinical practice in function of the therapeutic and social needs, budget impact and cost-effectiveness ratio.* This means that the minister is legally entitled to deviate from the proposal of the CRM/CTG based on health-care related elements only and not on non-health care sector related elements. It seems to be in conflict with the procedural concept and principle behind the establishment of the CRM/CTG.

In allocating public resources the benefits of using resources for one purpose should ideally be weighed against the benefits of using these resources for another purpose. This means that for drug reimbursement decisions as well, an assessment should be made of all socially relevant considerations related to a specific drug, including health and potentially non-health related considerations (e.g. local employment opportunities). All the relevant assessment elements should be weighted by a committee that is fully representative for the society and is capable of defining the relative social value of health care compared to other sectors. As in other countries, the CRM/CTG cannot be considered to be such a committee, because it assess and appraise only the health-related outcomes of a drug and assess the drug on its value for money within the health care sector, isolated from other sectors with a public interest. This is in line with the remit of the CRM/CTG, which is to formulate advices about the efficient and ethically acceptable allocation of *health care* resources. The minister of social affairs, who takes a decision, has the remit to take a broader social perspective. Ministers responsible for other sectors of public interest are not systematically consulted, with the exception of the minister of budget. The minister therefore has a rather large discretionary power in taking his/her decision.

The fact that the minister of social affairs can take a decision that differs from the reimbursement proposal of the CRM/CTG leads to frustration within almost all members of the CRM/CTG. The motivation of decisions deviating from a CRM/CTG proposal is often not clear. Moreover, it is felt unjust that a proposal based on a thorough assessment and appraisal process and having obtained a 2/3rd voting majority within the CRM/CTG can be overruled so easily. This lack of transparency may lead to:

- Expert committee members feeling disconnected to the drug reimbursement decision process;
- Stakeholders not involved in the process, including the general public, not understanding the reasoning behind the decision
- The public becoming suspicious of the political processes.

The minister of budget plays an important role in the decision making process in Belgium. A positive reimbursement proposal by the CRM/CTG can be turned into a negative decision if the minister of budget considers the reimbursement unaffordable. A negative reimbursement proposal can still result in a positive decision if the minister of social affairs considers reimbursement appropriate and the minister of budget agrees with the reimbursement. This means that the minister of budget has a large power in the drug reimbursement decision procedure. This is a rather remarkable situation, because the CRM/CTG considers the budget impact as an important appraisal criterion and takes it into consideration when formulating an advice.

A representative of the minister of budget is present at the meetings where the discussions take place and is allowed to intervene.

5.4 DISCUSSION

The following discussion on the observed characteristics of the Belgian system when compared to the ideal framework of 'accountability for reasonableness' takes a theoretical, non-political stance, in the sense that considerations on practical feasibility in terms of legislative complexity, acceptability, timeliness or possible ripple effects on other aspects of reimbursement regulations are not taken into account. Any judgement regarding the political opportunity, timing and feasibility of the identified potential improvements clearly lies beyond the scope of this study.

5.4.1 Transparency

According to the law, the RIZIV/INAMI experts should evaluate the drug reimbursement *file and proposal* of the company. This creates confusion about the use of evidence the company did not include in the file. Some argue that identifying which evidence, although available, is missing from the file is part of the assessment process, others would argue that this goes beyond the evaluation of the file as such and that searching for evidence missing from the file and fully exploring this evidence is not feasible within the timeframes imposed by the EU Transparency directive. The CRM/CTG currently does not require companies to sign a declaration that all evidence currently available is presented in the drug reimbursement request file, including information on ongoing studies.

An assessment report includes a critical assessment of all the evidence presented in the drug reimbursement request file, the associated level of evidence for each piece of evidence and the uncertainty associated with the evidence presented (i.e. "what do we know"). The level of evidence depends on the quality of the studies presented in the file. It is important to also state in the assessment file which evidence is missing (i.e. what do we not know).

Drug reimbursement request files submitted to the CRM/CTG contain a reimbursement proposal from the company, the rationale of this approach being that the reimbursement modalities determine the results of the clinical and economic analyses. However, any proposal implies a societal value judgement and making these judgments is essentially the task of the CRM/CTG as a committee representing society.. The disadvantage of having a proposal in the reimbursement request file is that the CRM/CTG does not have the opportunity within the given timeframe of 180 days to fully appraise the societal value of a drug under different reimbursement modalities. This might have important societal consequences, such as some patient groups not getting access to the treatment because the company did not include specific indications in its reimbursement proposal. Even if the CRM/CTG would like to consider the value of the drug for these indications, it would not have the opportunity to do so because (1) the time frame is too tight and (2) the company decides whether or not it wants to request reimbursement for this indication. The same applies to all cases where the CRM/CTG wants to deviate from the reimbursement modalities suggested by the company in its initial reimbursement request file.

The minister can deviate from a proposal of the CRM/CTG for social or budgetary reasons. There seems to be an inconsistency in the law with respect to this, as the law further stipulates that the minister can only deviate "*within the limits of the criteria defined for inclusion, modification or removal of a drug from the list of reimbursed drugs*", which are exactly the criteria the CRM/CTG has to take into account in its procedure.

Negotiations between the minister and the applicant for reimbursement (the company) may occur if there is no reimbursement proposal from the CRM/CTG or in case of a negative proposal. The negotiation process is not transparent. The "reasonableness" of the criteria considered during this negotiation process can therefore not be verified by the general public, which might treat the accountability for reasonableness of the outcome of the negotiation process and the final decision.

5.4.2 Relevance of the appraisal criteria

In relation to the decision tool presented in chapter 3, we notice that the identification of the medical, therapeutic and societal need in Belgium is currently missing in the early phases of the Belgian decision making process. Policy makers should first of all respond to the question: "are we really waiting for this product"? The medical need question is now often only raised during or after the discussions on the class of the product.

To define societal health care needs, one should start from the disease and the currently available treatments or preventive strategies for this disease and *not* from the characteristics (effectiveness, cost-effectiveness etc) of the new treatment or preventive product asking for reimbursement. An exception applies to generics or products with similar therapeutic value as existing treatments. In this case, the decision about the relative importance of the disease-treatment combination has already been made when a decision was taken about the appropriateness of reimbursing the original product.[r]

Defining needs is not easy. Relevant criteria for defining needs are: the severity of the disease, threat to life, availability of alternative treatments, duration of the disease, patient characteristics (age, socio-economic status), health inequalities. In chapter 3 three approaches for defining medical needs, as part of overall needs, have been presented. It is important to highlight that disease severity should always be considered 'given the treatment options available'. It is unclear whether disease severity is always interpreted in this way in Belgium for the purposes this criterion is used.

As for the price and reimbursement basis decision, it should be emphasised that the societal willingness to pay for a product must be higher than or equal to the price and the price must be higher than the cost for a product to be socially and economically acceptable. In the current drug reimbursement systems, companies are given incentives to start off asking relatively high prices because many countries use international reference pricing to determine a price and in practice companies always experience pressure on prices during the reimbursement decision process or in negotiations with the minister. Therefore, it is in their best interest to ask a comfortable margin, allowing them to reduce prices when the reimbursement decision risks to be negative.

In Belgium, products with added therapeutic value are almost always entitled to a higher price. However, it might be the case that a product has an added therapeutic value, but that this added therapeutic value is not worth paying for out of public resources. Added therapeutic value should be a necessary but insufficient condition for granting a higher reimbursement basis.

5.4.3 Revisions

Revisions are currently performed for all Class I pharmaceutical products and on an ad hoc basis for classes of drugs. Although modifications in the reimbursement modalities are common after revision, de-listing rarely occurs.

5.5 CONCLUSION

The Belgian drug reimbursement system is a deliberation-driven system in which balanced representation of societal preferences in the expert committee is of utmost importance. The accountability for reasonableness of the Belgian system could in theory be improved by applying the general recommendations for drug reimbursement systems formulated in chapter 3. The extend to which these recommendations should be translated into concrete actions and the ways to do so depend on political choices, which lie beyond the scope of this report.

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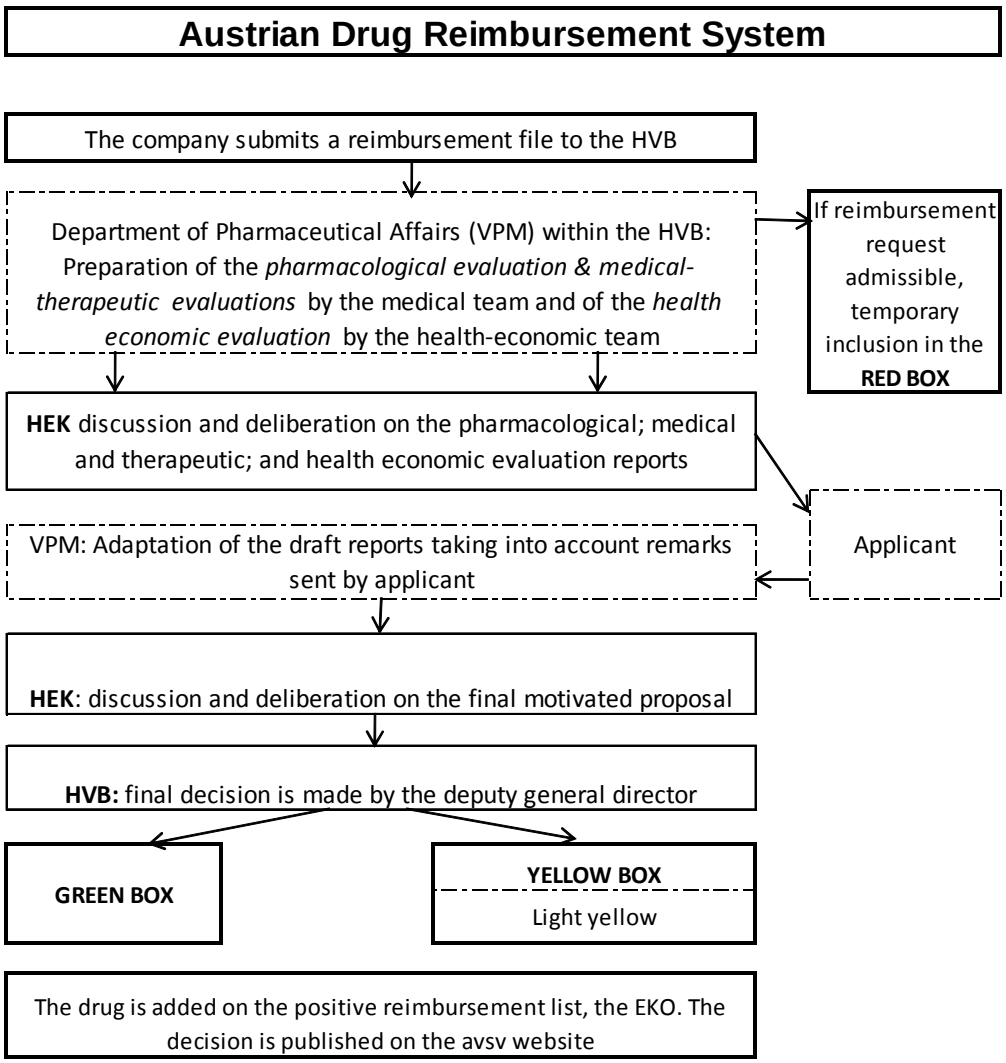
[r] Although the introduction of a new product on the market might increase the extent of the market, as described above. A relative reduction in the price may then be considered.

6 APPENDICES

DRUG REIMBURSEMENT SYSTEM IN AUSTRIA[s]



Abbreviations: VPM: Department of Pharmaceutical Affairs/ *Abteilung Vertragspartner Medikamente*; HVB: Main association of Austrian Social Security/ *Hauptverband der Östereichischen*; HEK: Pharmaceutical Evaluation Board/*Heilmittel-Evaluierungskommission*; EKO: Reimbursement Code/ *Erstattungskodex*; AVSV: Official Journal of Austrian Social Security/ *Amtliche Verlautbarung der österreichischen Sozialversicherung*

[s] We are grateful to Mrs Yvonne Schroeder from HVB for reviewing this chapter.

HEALTH CARE STRUCTURE

Characteristics of the Health Care system

Responsibilities for health care policy in Austria are shared between the Federal Government and the government of the nine Länder at the regional level. The Federal Ministry of Health (BMG, *Bundesministerium für Gesundheit*) is responsible for the regulation of almost all areas of the health care system. The most notable exception is the hospital sector, in which responsibility of the federal government is limited to enacting the legislative framework whilst the Länder are in charge of legislation on enforcement and ensuring implementation. The General Social Insurance Act (ASVG, Allgemeines Sozialversicherungsgesetz) is the legislative basis that guarantees the legal right for almost every Austrian to access a wide range of services. 67, 68

Affiliation to the compulsory social health insurance is by means of health insurance funds or institutions. The choice of the insurance institution is not free but organised by Länder, i.e. regional sickness funds (Gebietskrankenkasse) or through professional groups. The Main Association of Austrian Social Security Institutions (HVB, Hauptverband der Österreichischen Sozialversicherungsträger) is a self-governing body responsible for the policy implementation. The HVB brings under the same umbrella health insurance funds and other social insurance institutions (e.g. accidents and pensions).68

Outpatient care is delivered by physicians in private practice. The majority are contracted doctors (*Kassenarzt*), meaning they have a contract with a health insurance fund. Contracted physicians are remunerated through a mix scheme of flat-rate fees per capita (for basic services) and fee-for-service (for services beyond the scope of basic services). The contractual relationship is governed by general agreements, concluded between HVB and the Medical Chambers at the provincial level.[67, 69, 70] The patient also has the option of consulting a non-contracted physician of his or her choice. In such case, the health insurance fund will reimburse 80% of the amount which would have been paid by the insurance provider to a contracting doctor if he had been visited.[70]

Health Care Funding and pharmaceutical expenditure

In 2008, the total expenditure on health care accounted for 10.5% of GDP. Of this amount, 76.9% was through public and 23.1% through private funding.[71] The Austrian health insurance is financed mainly through social security contributions (accounting for about 50% of total public health revenues) and general taxation (about 20%).[69]

Since the nineties, public pharmaceutical expenditure has significantly increased. The proportion of total pharmaceutical expenditure as a share of total health care expenditure rose from 9.8% in 1991 to 13.3% in 2008.[71] As a result, in 2004, the government decided to target an annual growth for pharmaceutical expenditure of around 3 - 4% per annum. Although this was achieved in 2005, partly due to the reform of the reimbursement system in 2005, the growth in pharmaceutical expenditure rose again to 7.7% in 2007.[69]

Pharmaceutical policy tools

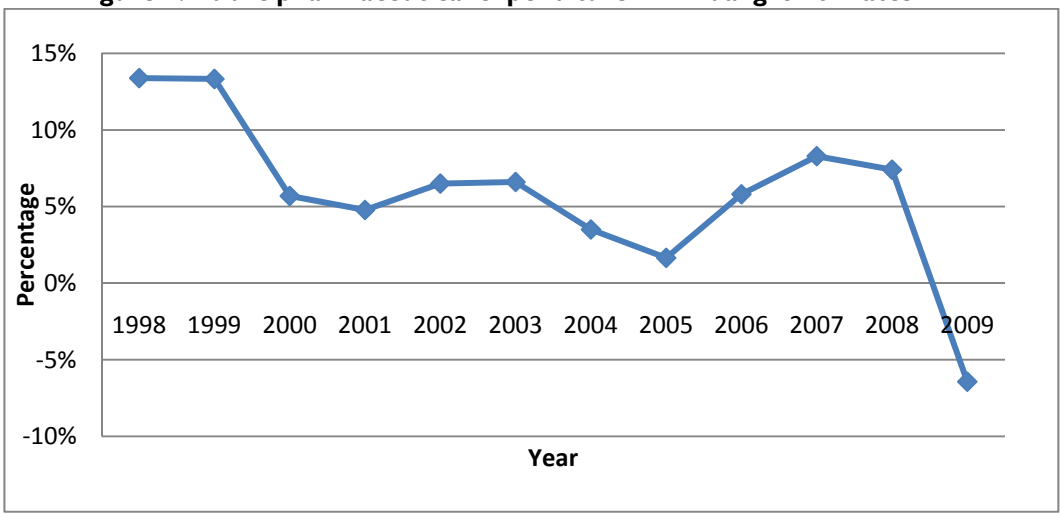
Several policies to contain pharmaceutical expenditure have been implemented over the last years. Measures targeted distributors (reduction of wholesale margins); pharmacies (recovery of excess turnovers), or patients (annual increases in the prescription fee). The pricing regulation was also deeply reformed, with prices of reimbursable pharmaceuticals today statutory controlled by the Ministry of Health, advised on this matter by the Pricing Committee (PK, *Preiskommission*). The upper limit for price negotiations is the average EU price. Unlike other countries, neither generic substitution nor prescribing by international nonproprietary names (INN) is permitted in Austria.[69, 72, 73]

Measures targeting physicians are mostly limited to the monitoring of prescription behaviour. Prescription patterns of contracted general practitioners and medical specialists have to comply with the HVB Guidelines on Economic Prescribing (RöV, *Richtlinien über die ökonomische Verschreibweise von Heilmitteln und Heilbehelfen*)[74]. These guidelines seek to safeguard the appropriate and economical use of pharmaceuticals. They encourage contracted medical doctors and specialists to prescribe cost-effective pharmaceuticals when several therapy options are available, meaning they should preferably prescribe pharmaceuticals from the "green box", and thereof the cheapest generic or parallel import if available (see Table 12 on reimbursement boxes arrangement).[73] Adherence to these guidelines is monitored by the sickness funds by routinely benchmarking the prescription cost or volume for a given doctor against colleagues in the same professional group and region. If the prescription cost or volume exceeds a certain limit above the average, the doctor is asked to explain and guidance is provided by the sickness funds. If the doctor cannot explain the unusually high prescription costs and persists in un-economic prescription habits, sanctions such as repayment may ensue as a final option.[69]

To promote a appropriate use of pharmaceutical products, both from a medical and health-economic perspectives the committee for rational use of medicines was established ("*Ausschuss Rationaler Einsatz von Arzneimitteln")* in 2009. Members of this committee are nominated by the Minister of Health and meet twice a year in non-public sessions.

Figure 9 presents the evolution of public pharmaceutical expenditure growth rates. While expenditure where growing at a very fast rate at the end of the nineties, containment of expenditure, observed in 2004 and 2005, reflects reforms and policy measures introduced in the pharmaceutical sector. The second steep reduction observed in 2009 is partly explained by the reduction of the VAT on pharmaceuticals from 20% to 10%. Without this measure, it is estimated that growth would have been positive for the year 2009 (around 1.70%).[75]

Figure 9: Public pharmaceutical expenditure – Annual growth rates



Source: Grillitsch, 2008 and 2010 (VAT incl.)[75, 76].

Cost sharing policies

Direct cost-sharing policies affects almost every service reimbursed by the Austrian health insurance. A large part of direct cost-sharing is related to the services of non-contracted physicians, followed by pharmaceutical prescription fees.[67]

Prescription rules in Austria are strict in comparison to other European countries. More or less 80% of the approved pharmaceuticals are subject to medical prescription compared to a European average of around 75%. Outpatient pharmaceuticals are either fully or not reimbursed at all. Fully reimbursed pharmaceuticals are dispensed at the pharmacy upon prescription presentation. The out-of-pocket expense is a fixed prescription fee per drug packaging dispensed (equal to of €5.00 in 2010). Pharmacies settle their account directly with the health insurance funds. The prescription fee is paid by the pharmacies to the social security institutions while in return pharmacies are paid the price as negotiated between the industry and the HVB by the health insurance funds.[69, 70]

Prescription fee exemptions exist for: (§136, Abs 4-6, of ASVG[56])

- People whose monthly net income is below a defined threshold
- Chronically ill people who can provide evidence of related over-average expenditure whose net income is below a defined threshold
- Socially disadvantaged people such as old-age pensioners with a low pension and patients with specific contractible, transmissible diseases/illnesses such as tuberculosis or HIV, civil servants and their dependents.

In addition, a ceiling cap was implemented in 2008, meaning that patient's annual expenditure for prescription fee is limited to 2% of the annual net income (§136, Abs 6, of ASVG[56]). In the beginning of the year 2010 it was estimated that about one-fourth of the population was exempt from paying the prescription fees for reimbursable medicines.[68]

Inpatient pharmaceuticals are not subject to this prescription fee or any other co-payment. Their costs are covered by the Austrian diagnosis-related remuneration system (*Leistungsorientierte Krankenanstaltenfinanzierung*) of hospitals meaning that expenditure for pharmaceuticals is part of the lump sum calculated. Patients participate in the cost of hospital care by means of fixed fees per admission day.[69, 77]

DESCRIPTION OF THE FOURTH HURDLE SYSTEM

Overview of the drug reimbursement system

To enter the Austrian market, the pharmaceutical must be granted the official notification for marketing authorization from the Federal Agency for Safety in Health Care (BASG, *Bundesamt für Sicherheit im Gesundheitswesen*) via decentralized and mutual recognition procedures or from the European Medicines Agency (EMA) through the centralized procedure, based on a positive efficacy, safety and quality assessment.

For outpatient drugs, the pharmaceutical company applies for the inclusion of the pharmaceutical into the positive list for outpatient reimbursable pharmaceuticals, the Reimbursement Code (EKO, *Erstattungskodex*).[69]

The HVB is responsible for determining the reimbursement, it is advised on these matters by the Pharmaceutical Evaluation Committee (HEK, *Heilmittel-Evaluierungskommission*).[69] As soon as the company introduces a valid and complete reimbursement request, the pharmaceutical is temporarily included in the so-called "red box" of the EKO (for a period a maximum 180 days). The "red box" entails full reimbursement provided that a 'head' physician of a health insurance fund approves the prescription *ex ante*. A positive reimbursement decision results in the inclusion of the reimbursable pharmaceuticals into one of the two remaining boxes: the "green box" and the "yellow box".

- The "green box" comprises pharmaceuticals considered medically and health-economically sound. These drugs are freely prescribed by contracted physicians.

- The "yellow box" includes pharmaceuticals with an important added therapeutic value and whose reimbursement is restricted to certain specified conditions (e.g. only for certain patient groups, for certain indications, prescribed by certain specialists, prior approval by a 'head' physician of the health insurance funds, ex-post volume control).

The reimbursement scheme applicable to pharmaceuticals used in the hospital care differs. Reimbursement fall under the responsibility of the pharmaceutical committee (*Arzneimittelkommission*) present in each hospital or joint pharmaceutical committees per owner organization. These committees decide about the appropriate use of pharmaceuticals and on the list of pharmaceuticals which are used in hospital care (hospital pharmaceutical formulary). They consist of the chief pharmacist, the chief doctor, the chief nurse, the administrative director as well as regional sickness funds representative.[77]

Austria has increased Health Technology Assessment (HTA) as a method to support decision-making. Since 2000, HTA is used on a regular basis for pharmaceuticals that are under access-control in the "red box" and as the basis for deciding on the hospital pharmaceutical formularies in hospitals' pharmaceuticals committees. In 2006, the Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA) was established in Vienna. This scientific independent body provides, on request of the Ministry of Health, scientific support for decision-making regarding health technologies. However until now there is no formal link with regard to reimbursement decisions as their recommendations of the LBI-HTA are not binding.[78]

Policy Implementation Level

Establishment

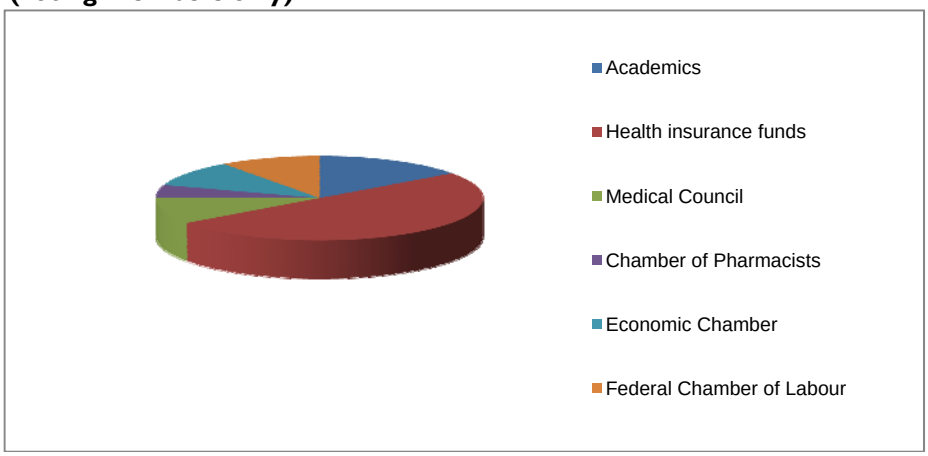
The Social Insurance Law (ASVG, Allgemeines Sozialversicherungsgesetz) constitutes the legal basis of the basic mandatory social insurance. The article § 351G of the AVSG establishes the basis for the reimbursement system for outpatient pharmaceuticals. The legal procedure for reimbursement is described in the Procedure Code for Reimbursement (VO-EKO, *Verfahrensordnung Erstattungskodex*) first published in June 2004. The main parties involved are the Ministry of Health (BMG), the Main Association of Austrian Social Security Institutions (HVB) including the Pharmaceutical Evaluation Board (HEK). The legal bases of the Austrian fourth hurdle process were deeply reformed with the establishment of the HEK in 2004 and the introduction of the EKO and the boxes system in January 2005.

The **BMG** does not take a significant role in the reimbursement and pricing process. It is mainly responsible for enacting the basic principles and law. Only for pricing, the collection analysis and calculation of average EU prices is done by the Pricing Committee (PK), a department within the BMG.

The **HVB** is the umbrella organization of the Austrian social insurance funds. It is responsible for safeguarding the general and economic interests of the social insurance system, providing central services for the social insurance funds, and the coordination of the administrative activities of individual insurance funds. It has the task of drawing up binding guidelines, policy proposals, reports and statements, and concludes general agreements with interest groups. The HVB plays an important role in the further development of social insurance law and of the Austrian public health care system in general. Regarding pharmaceuticals, it is responsible for deciding on the inclusion of pharmaceuticals in the EKO. It relies for this matter on the recommendations formulated by the HEK.[67] The reimbursement procedure is launched at the initiative of the company, which submits its reimbursement request to the HVB. The HVB itself is legally entitled with launching a reimbursement; however in practice this is very rare.[79]

The **HEK** is an has the legal responsibility to advice the HVB on the admission of drugs on the positive list for outpatient pharmaceuticals. It consists of 21 members nominated for a period of 5 years. [67, 69]. It is composed of ten representatives of the health insurance funds; three representatives from Austrian universities nominated by the Austrian Academy of Science (either with medical and/or pharmacological skills), two representatives from the Medical Chamber (ÖÄK, *Österreichische Ärztekammer*); two representatives of Economic Chamber (WKÖ, *Wirtschaftskammer*); two representatives from the Federal Chamber of Labour (BAK, *Bundesarbeiterkammer*); one representative from the Austrian Chamber of Pharmacists (ÖAK, *Österreichische Apothekerkammer*); and one representative from the federal state. With the exception of the federal state representative, all members have a voting right in the Committee. The HEK is alternately chaired by representatives of universities. Members are obliged to participate in the meetings that take place once a month.[80]

Figure 10: Composition of the Pharmaceutical Evaluation Board (HEK) (voting members only)



Source : Procedure Code for Reimbursement (VO-EKO)[80]

Within the HVB, the Department of Pharmaceutical Affairs (21-VPM, *Abteilung Vertragspartner Medikamente*) is responsible for the preparations of the HEK meetings. The department includes a medical and a health economic team. The health economic team incorporates 2 full time and 3 part-time employees whereas the medical team consists of 3 full-time and 2 part-time employees.

Table 11: Key actors involved in the reimbursement process

Institution/ Actor	Function(s)
Main Association of Austrian Social Security Institutions (HVB)	Is responsible for the drug reimbursement process from application to reimbursement decision; The Department of Pharmaceutical Affairs (21-VPM) communicates with applicant, prepares the assessment for the HEK The HVB deputy general director makes the final decision advised by the HEK
Pharmaceutical Evaluation Board (HEK)	Is responsible for the reimbursement advice
Ministry of Health (BMG)	Is responsible for pharmaceutical policy and regulations

System objectives

The main principles of the Austrian health care system are solidarity, affordability and universality.[68] The health care system seeks to ensure equitable access to high-quality medical services for all inhabitants irrespective of their age, sex, origin, social status or income. Equitable health care for all patients is also put forward by implementing exemptions from paying co-payment to defined vulnerable patients.[68] The Austrian Social Insurance Law (ASVG) states that patients must be granted all necessary forms of medicinal and medical treatment in a sufficient and appropriate way as long as adequacy of resources are guaranteed.[69]

The procedure code for pharmaceutical reimbursement (VO-EKO) states first that enlisting of pharmaceuticals in the EKO should be done transparently in the light of the best available scientific evidence. The procedure states that the reimbursement process should "taking equally account of the interests of insurances, patients and pharmaceutical companies". Finally, the system must guarantee access to high-quality pharmaceuticals for patients while maintaining the financial sustainability of the health insurance.[81]

Implementation

The HVB makes the final decision on the reimbursement for outpatient drugs, i.e. the inclusion in the reimbursement code (EKO). It then publishes it on the website of the Official Journal of the Austrian social security (AVSV, *Amtliche Verlautbarung der österreichischen Sozialversicherung*). Final reimbursement decisions are mandatory for the health insurance funds.

In the inpatient sector, the eligibility of a pharmaceutical to be reimbursed is defined by the hospital pharmaceutical formulary. Each hospital has a pharmaceutical committee entitled to make decisions on inclusion in the pharmaceutical formulary. As soon as the decision is made, information is disseminated by the executive of the pharmaceutical committee to the hospital employees. As a result variations may be found for inpatient drugs between hospitals. Formularies are electronically available in the different hospital information systems but are not publicly available.[77]

Accountability

The impact of the drug reimbursement system is most limited to the monitoring of expenditure. The Austrian Court of Audit (RH, *Der Rechnungshof*), legally responsible for the efficient allocation of public resources, regularly conducts analyses of the evolution of pharmaceutical expenditure.

At the moment, pharmaceutical policies are not regularly monitored.[69] However the Minister of Health is responsible for the overall public health care and social security policies. He or she sets health care goals and can influence the drug reimbursement system by initiating new policies. He or she is consequently accountable to the Parliament for all matters related to the drugs reimbursement.

As the reimbursement systems differ between inpatient and outpatient care, Länder and hospitals are responsible for monitoring of pharmaceutical expenditure in the hospital care whereas the HVB is responsible for monitoring expenditure for outpatient drugs.

Technology Decision Level

Assessment and appraisal

The HEK is responsible for the assessment of outpatient drugs and the final advice regarding their inclusion in the EKO. The assessment is mainly based on three successive evaluations: pharmacological; medical and therapeutic; and health-economic. The HVB employees within Department Pharmaceutical Affairs (VPM) assist the HEK members and prepare the assessment for the HEK meetings. For each reimbursement request, one member of the medical team and one member the health-economic team are appointed. The medical team is in charge of the pharmacological, medical and therapeutic evaluation while the health economic team assesses and evaluates the pharmacoeconomic studies provided by the company.

The Annex of the VO-EKO clearly details the information required for the pharmacological, medical and therapeutic and health-economic evaluations. The assessment must rely on published data from peer-review journals as well as assessments performed by independent authorities and institutions (e.g. LBI-HTA). Reports and unpublished studies, only in justified exceptional circumstances, might be taken into account.[82] Pharmacoeconomic studies submitted by the applicant should take into account the direct costs for compulsory social health insurance. Binding pharmacoeconomic guidelines are not available for Austria, but the *Guidelines on Health Economic Evaluation* is a guidance document of consensus.[83] If the evidence submitted by the company is not clearly understood by the HEK members, they can decide by one-third majority vote to invite the applicant to a hearing for clarifications.[81]

The **pharmacological evaluation** assesses the product from a pharmacological point of view in the context of available therapeutic alternatives (including non pharmacological treatments alternatives). It determines comparable pharmaceuticals with the same dosage (if appropriate, on ATC 4 level) already listed in the EKO. Last it assesses the degree of pharmacological innovation according to an established eight point scale:[72, 81, 82]

1. Same active ingredient, same strength and practically the same pharmaceutical form as one or more previously listed drugs
2. Same active ingredient and practically the same pharmaceutical form but a new strength
3. New combination of active ingredients already listed
4. New pharmacological form of an already listed ingredient(s)
5. New active ingredient belonging to an already listed therapeutic group with a uniformly defined active principle
6. New active ingredient with a new active principle for treating illness fo which treatments are already listed
7. New active ingredient providing first treatment with a drug for an illness previously treated otherwise
8. First treatment for a disease for which no treatment was previously available

The **medical and therapeutic evaluation** looks at potential patients groups that may be treated with the new medication, the expected duration of treatment and frequency of drug administration. Second it assesses the drugs' therapeutic benefit for patients compared with existing therapeutic alternatives. This assessment answers the questions: "*Is the benefit clinically relevant in comparison with its therapeutic alternatives? Is there a benefit for the patient in comparison with its therapeutic alternatives?*" Third, it reviews the validity of medical and therapeutic data and assumptions submitted in the economic evaluation studies. Prospective and double-blinded randomized controlled trials (RCT) in a large sample of the representative population are the gold standard, followed by systematic reviews. Opinions of experts receive the lowest score of validity.

This evaluation concludes with an assignment of the drug in to one of six therapeutic value scale classifications. The higher the classification, the higher the therapeutic benefit. [72, 81, 82]

1. No added benefit for patients (because it has the same active ingredient);
2. Analogous or similar therapeutic benefit for patients;
3. Added therapeutic benefit for a subgroup of patients;
4. Added therapeutic benefit for the majority of patients;
5. Substantial added therapeutic benefit for a subgroup of patients; and
6. Substantial added therapeutic benefit for the majority of patients.

The **health-economic evaluation** evaluates the cost-effectiveness of the drug in the context of available and comparable treatment alternatives. This evaluation takes into account the results of the medical and therapeutic evaluation. For drugs with similar and analogous therapeutic value, the drug is deemed cost-effective if its cost is sufficiently lower than the cost of the best therapeutic and reimbursable alternative. For drugs with an important added benefit the results of the pharmacoeconomic study submitted by the company are considered. There is no official threshold for the incremental cost effectiveness ratio (ICER) meaning there is no specific guideline for the interpretation and acceptability of the ICER value.

The "green box" eventually includes all drugs deemed cost-effective (i.e. generics meeting the pricing conditions[t]; off-patent original drugs for which the price decreased according to the legal rules; and other original on-patent drugs). Drugs with important added therapeutic benefit may be included in the "green box" if the applicant demonstrates that free prescribing (i.e. no prior authorization by the physician of the health insurance funds) is reasonable and justified from an health-economic perspective, in light of the cost-effectiveness ratio. The "yellow box" includes drugs with significant therapeutic added value. The applicant must demonstrate that the access to restricted reimbursement is health-economically reasonable and justified, in light of the cost-effectiveness ratio.

If there is a likelihood that the advice regarding the reimbursement may be negative, the applicant is informed and motivation for the negative appraisal is given. In such case, the applicant is given a chance to respond by sending written comments to the HEK. To make the final advice, at least 50% of HEK members should be present. Voting is done by a show of hands – except if minimum three members ask a secret voting and advice – are approved by majority of votes. The final recommendation is made within 90 days and includes the binary resolution on the inclusion into the EKO, the box and possible restrictions/conditions for reimbursement.[79]

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t Cost-effectiveness for generics is established if the price of the first generic is at least 48% below the price of the off-patent drug. Cost-effectiveness is assumed for the generic followers if they offer a sufficiently high price difference (15% decrease for the second follower compared to the first; 10% decrease for the third follower compared to the second).

Table 12: Reimbursement boxes arrangement

	Scope	Conditions	Ex factory price
RED BOX	All pharmaceuticals that have applied for reimbursement a awaiting the final reimbursement decision.	Ex-ante approval of the physician of the health insurance funds.	Price at the EU average price or price suggested by the company. Price increments are decided by the HVB within 90 days of receipt of the PK recommendation
YELLOW BOX	Pharmaceuticals with an important therapeutic added value	Ex-ante approval of the physician of the health insurance funds. Reimbursement is restricted to a specific disease, to a specific age group, if prescribed by a specialist or in limited quantities	Price may not exceed the EU average. Applications for price increments are decided by HVB within 90 days.
LIGHT YELLOW BOX		Ex-post volume control by physician of the health insurance funds possible (doctors have to keep a record of the reason for prescription)	
GREEN BOX	Pharmaceuticals with similar therapeutic value in comparison with existing alternatives (mainly generics and off-patent products) Pharmaceuticals with therapeutic added value *if* reasonable and justified from an health-economic perspective.	No conditions. Possibly restrictions based on age group or prescription by specialists.	Below the EU average (Special pricing rules for generics)

Source: Adapted from PPRI Pharma profile – Austria.[69]
Abbreviation: PK: pricing committee

Pharmaceuticals receiving a negative decision are not included in the EKO. There is a list of not reimbursed categories of pharmaceuticals (§ 351c, abs 2, of the ASVG). Under the ex-ante approval of a physician of the health insurance funds, the pharmaceutical is reimbursed for one patient if and only if the treatment is proved essential for therapeutic reasons and if no other medication for the treatment of the disease is available in the EKO.[79]

It is worth noting that price setting and reimbursement are closely linked in Austria. There are special pricing rules for drugs applying for inclusion in the EKO which are defined in function of the reimbursement box assigned. In addition, prices may be furthered negotiated with the HVB.[84]

For inpatient drugs, hospital committees are responsible for the assessment and the decision to include the product in the hospital drug formulary. As pharmaceutical companies can decide whether to provide their drugs in the outpatient or hospital care, they may opt to restrict prescribing to hospital care and consequently avoid close scrutiny by the reimbursement experts.[72]

Decision Process

The HVB is responsible for the final decision within the 180 day timeline, on the basis of the recommendation formulated by the HEK. In practice, the deputy general director of the HVB makes this decision. There is no set rule stipulating under what circumstances the recommendation from HEK can be overruled; the deputy general director is allowed to deviate although in practice, it rarely occurs.

As soon as the positive decision is made, the EKO is modified within a month. The EKO is monthly published via the internet (www.avsv.at). An hard copy is printed twice a year (January and July).[79] but only the EKO available online is legally binding.

Output and implementation

A consequence of the box arrangement is the so-called "traffic light-system" ("*das ampelsystem"*). As stated in the prescription guidelines (RöV), medical doctors are expected to prescribe first and foremost pharmaceuticals from the "green box". If none is available for the treatment, they prescribe reimbursed pharmaceuticals from the "yellow box". And lastly, pharmaceuticals from the "red box" should be used only in special circumstances.[69]

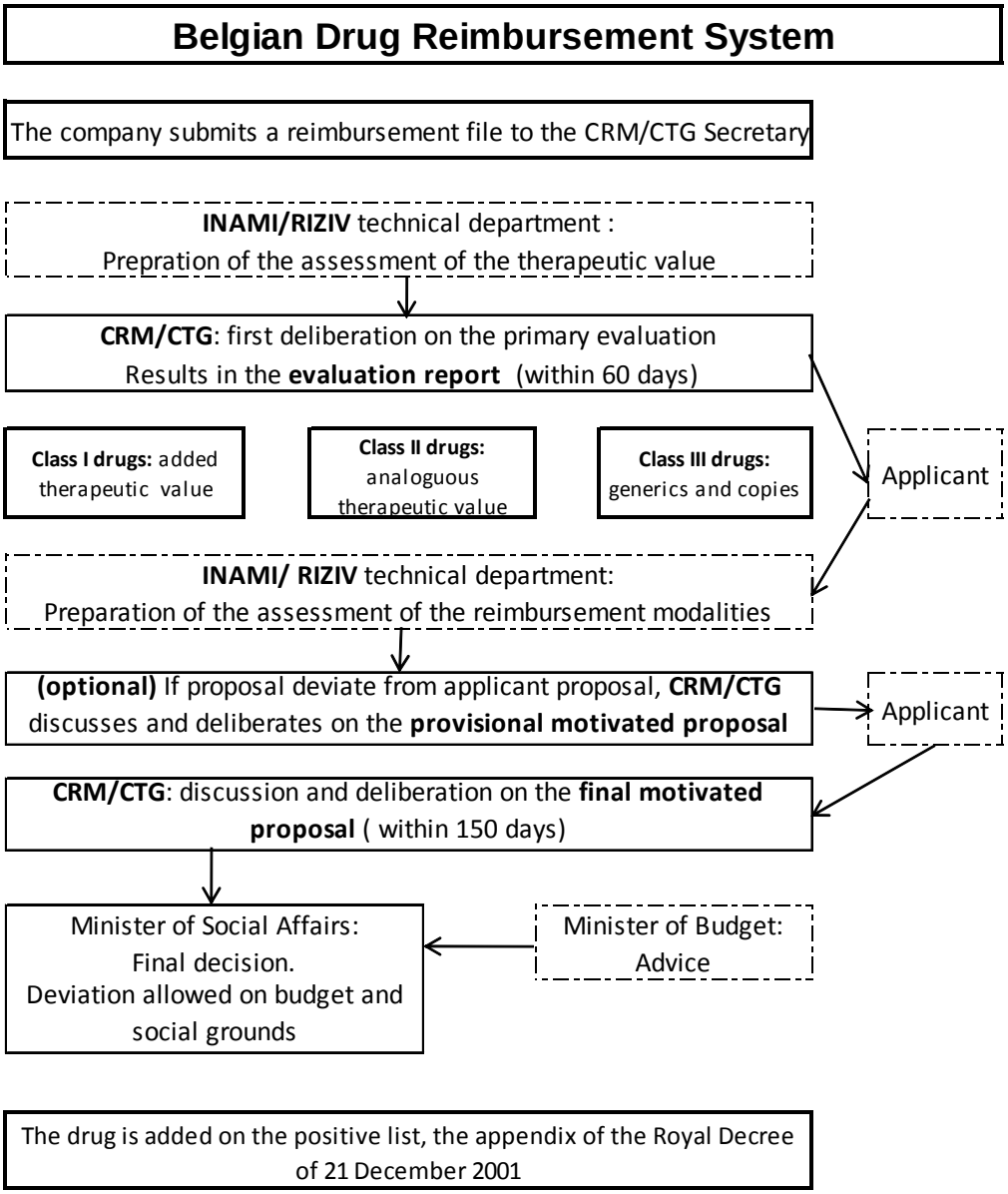
The country does not have a history of systematic reassessment of reimbursement decisions. In the wake of new pharmacological, medical-therapeutic or health-economic evidence; a reassessment may take place at the initiative of the HVB, advised by the HEK. This could result in either delisting or changing the reimbursement conditions. The pharmaceutical companies have the right to appeal against any such decision to the UHK.[69]

The Independent Pharmaceutical Commission (UHK, *Unabhängige Heilmittelkommission*) was established in 2002 and acts as an appeal court to whom pharmaceutical companies may turn in case of a negative decision for their reimbursement application. All UHK members ("*Beisitzer*") are independent experts nominated by several public bodies such as the Chamber of Commerce (WKÖ), the Chamber of Labour (BAK), the Medical Chamber (ÖÄK), Chamber of Pharmacists (ÖAK) and HVB etc.[69]

Key points Austria

- **HVB is a centralized social security association responsible for outpatient drug reimbursement**
- **Reimbursement request to be enlisted in the positive reimbursement list for outpatient drugs (EKO) is primarily submitted by the company.**
- **The HEK is the expert committee advising the HVB on the drug reimbursement decision.**
- **The HEK is composed of academics, physicians, pharmacists and representatives from sickness funds, employees, industry and the government. The government representative has no voting right.**
- **The drug evaluation consists in three successive phase: pharmacological evaluation; medical and therapeutic evaluation and health economic evaluation.**
- **Evaluation reports of the HEK are not publically available.**
- **Voting within the HEK is done by a show of hands. Approval requires a simple majority.**
- **The HEK formulates the recommendation within 90 days and HVB the final reimbursement decision within 180 days.**
- **There is no rule stipulating under which circumstances the HVB can deviate from the HEK advice. Anyway in practice, it rarely occurs.**
- **Drugs are enlisted in "reimbursement boxes". The box system aims to guarantee access to innovative drugs while trying to contain reimbursement expenditure.**
- **The company may, in case of a negative reimbursement decision, turn to the appeal court, i.e. the UHK. This Independent Pharmaceutical Commission consists of representatives from physicians, pharmacists, employees, industry and HVB.**

DRUG REIMBURSEMENT SYSTEM IN BELGIUM[u]



Abbreviations: CRM/CTG: Drug Reimbursement Committee/ *Commission de Remboursement de Médicaments/ Commissie Tegemoetkoming Geneesmiddelen*; INAMI/RIZIV: National Insitute for health and Disability Insurance/ *Institut National d'Assurance Maladie-Invalidité/ Rijksinstituut voor Ziekte- en Invaliditeitsverzekering*

[u] We are grateful to Mr Francis Arickx (RIZIV/INAMI) for reviewing this chapter

HEALTH CARE STRUCTURE

Characteristics of the Belgian health care system

Belgium has a Bismarck-type of compulsory national health insurance which covers almost the whole population and has a very broad benefits package.[85, 86] Responsibility for health care policy is shared between the federal government and the regional governments. The federal authority is exercised by the Federal Public Service (FPS) Public Health, Food Chain Safety and Environment; the FPS Social Affairs; and the National Institute for Health and Disability Insurance (INAMI, *Institut National d'Assurance Maladie-Invalidité* – RIZIV, *Rijksinstituut voor ziekte- en invaliditeitsverzekering*) and is responsible for the regulation and financing of the compulsory health insurance; the determination of hospital accreditation criteria; the financing of hospitals and heavy medical care units; the legislation covering different professional qualifications; and the registration of pharmaceuticals and their price control. The regional authorities are exercised by the Dutch-, French- and German-speaking Community Ministries of Health and are responsible for health promotion; maternity and child health services; different aspects of elderly care; the implementation of hospital accreditation standards; and the financing of hospital investment.[85, 86]

At a centralised level, the INAMI/RIZIV which falls under the responsibilities of the Minister of Social Affairs is responsible for the organisation and the reimbursement of health care expenses. This federal institution establishes the rules for the reimbursement and determines the tariffs of the health care services (the so-called "nomenclature") and pharmaceuticals. It organises, manages and supervises the implementation of the compulsory health insurance and inspects both the sickness funds and the health care providers to see whether they correctly apply the rules of the health care and health insurance system. The INAMI/RIZIV is directed by the General Council, composed of representatives from the trade unions, the employer's associations, the providers, the largest sickness funds and the government. It is responsible for taking decisions regarding global political health care objectives and approving the budget.[85, 87]

At a more decentralised level, reimbursement of the health care costs is left to the sickness funds (the so-called '*mutualities*'). Everybody is free to choose of among six private, non-profit and one public sickness funds. Private-for-profit health insurance companies accounts for only a relatively small part of the complementary health insurance market.[85, 87, 88]

Health care funding and pharmaceutical expenditure

In 2008, total health expenditure were 10.2% of GDP; and health expenditure per capita was estimated at US$3,677.[71]Of this amount, public funding represents approximately 72.6% while 29% comes from private source.[71, 86] Generally speaking, 67% of the social security funding comes from employee's and employer's contributions, 19% from the alternative financing (e.g. indirect taxes and excise duties) and approximately 10% from government subsidies.[88, 89] While the social contributions remain the main revenue source, its relative share has tended to decline over the last years while alternative financing has seen its share increased.

There is no closed budget for the compulsory health insurance. However insurers, providers and the government yearly negotiate health care budget target (about €25.869 billion for 2011), and partial budget targets (e.g. the pharmaceuticals budget target, €4.028 billion for 2011). On a quarterly basis, a special commission confronts each sub-sector with its expenditure and budget target. In case of a significant danger of overrunning the target, negotiations on corrective measures – such as an adjustment in the fee schedule or an increase in copayments – can be undertaken.[87, 88]

The pharmaceutical budget is negotiated in a separate procedure. The Minister of Social Affairs is first advised by the INAMI/RIZIV General Council, which determines budget taking into account expenditure and the predicted budget impact of forthcoming drug policies. Since 2001, discussions are also warranted with representatives of the pharmaceutical industry. At the suggestion of the Minister of Social Affairs, the budget proposal is then deliberated and approved in a government meeting.

Lastly, the decision is published in the Official Journal during the month of October (Art 69, §5 of the Coordinated Law of 14 July 1994[90]).As these predictions may underestimate (to a lesser extent, overestimates) real pharmaceutical expenditure a buffer system funded by the pharmaceutical industry ensures that the budget is maintained in balance in case of excessive pharmaceutical public expenditure. In 2008, public expenditure on inpatient and outpatient drugs amounted to €3,722 million, accounting for approximately 18% of public health care expenditure.[91] Outpatient pharmaceuticals accounted for approximately 70% of the expenditure.

Inpatient pharmaceuticals are integrated in the prospective budget (based on the hospital's case-mix and the national average cost per APR-DRG (all patient refined diagnosis related groups) and severity of illness) for approximately 75% of their value, the remaining 25% being reimbursed per product.[88, 92]

Drug policy tools

Several policy measures were initiated to contain drug price and use. Containing drug prices is primarily done through government direct control of it. Price freezes were also enforced from 1995 to 2005 and again in 2009 and 2010; and price cuts are frequently applied on the so-called '*old*' drugs (reimbursed for more than 12, 15, and/or 17 years). In 2001, a reference reimbursement scheme (*système de remboursement de référence - referentieterugbetalingssysteem*) was introduced. The cluster definition includes all drugs with the same active ingredient independently of the dosage and administration routes and the reference price is defined as a percentage reduction in the reimbursement basis of the original drug. In 2006, a tendering process was introduced for off-patent drugs with same active ingredient and similar indications. The manufacturer that bids the lowest price receives the best reimbursement whilst the other drugs are still reimbursed, but at a lower level. The first invitations to tender were issued at the end of 2006 for cholesterol and blood pressure lowering pharmaceuticals (i.e. simvastatine and amlodipine, respectively).[85] But due to some complexity in the legal procedure no other tender has been launch since then.

Policy measures affecting prescribers were also introduced: publication of prescription guidelines, information campaign targeted at physicians and prescribing quotas for low-cost drugs (i.e. generics or original drugs whose price decreased). Implemented in 2006, these quotas vary with the specialty (from 9% for the gynaecologists to 27% for general practitioners and 30% for dentists). All these measures have been complemented with physician's prescribing monitoring. Every physician received individual feedbacks on his prescribing patterns and those not complying with the guidelines and/or quotas receives additional support for low-cost prescribing.[93] Moreover, International Non-proprietary Name (INN) prescription allows pharmacists to deliver first low-priced drug. In contrast with many neighbouring countries, generic substitution by the pharmacist is not allowed (yet)[v].

Figure 1 presents the evolution of public drug expenditure. Over the years 2002-2008, total drug expenditure increased by an annual growth rate of approximately 6%. The steep rise in 2008 is partly explained by the integration of pharmaceutical reimbursement (included in the so-called 'low-risk' coverage) for self-employees as of January 2008.[91]

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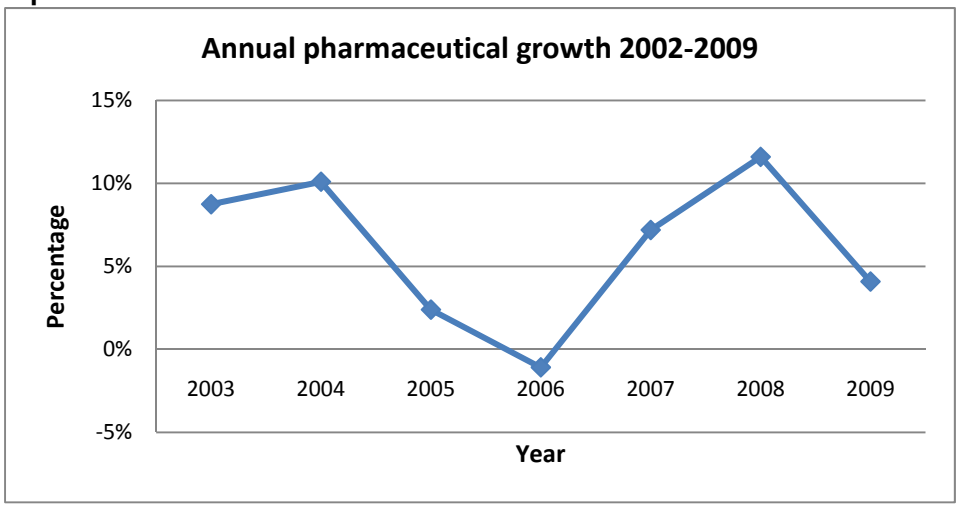
[v] Generic substitution is provided for by the law (Art. 34 of the Law of 6 August 1993 introducing art. 11 in the Royal Decree of 10 November 1967) but the Royal Decree required for its implementation is still lacking.

Figure 11: Evolution of the annual growth in public pharmaceutical expenditure



Source: Own calculations based on total pharmaceutical expenditure data from the statistical report on the health care sector. INAMI/RIZIV website : http://www.inami.fgov.be/information/fr/statistics/

Cost-sharing policies

Belgium applies two different systems of co-payments. The first is a *reimbursement system* that applies for ambulatory care in which the patient pays first the full cost of services and then obtains a refund for part of the expense from the sickness fund. The second is a *third-party payer scheme*, applying to inpatient care and pharmaceuticals, for which the sickness fund directly pays the provider while the patient only pays co-payment, supplement and non-reimbursed service.[85]

Cost-sharing policies differ with inpatient and outpatient drugs. Since 1983, hospitalised patients participate in hospital drug costs by means of a drug-specific deductible (€0.62) per admission day charged irrespective of actual consumption. For outpatient pharmaceuticals, patients participate in the cost by means of co-insurance that varies with the reimbursement category assigned to the pharmaceutical specialty[w]. There exists five different categories (*A*, *B*, *C*, *Cs*, *Cx*) according to disease severity. For example, category *A* contains medicines against life threatening diseases, such as insulin or medication for cancer treatment, that are fully reimbursed by the national health insurance whereas category *B* contains antibiotics. Moreover patient share per drug package is capped to avoid unaffordable co-payments. As such, in exchange for a prescription, the patient only pays the non-reimbursed share of the drug price. The patient's sickness fund pays the reimbursed amount directly to the pharmacies through the third-party payment system.[85]

In addition, cost-sharing for outpatient drugs differs with the status of the insured. Socially and economically vulnerable groups are entitled to a higher reimbursement.There are identified (art.37, §§1,19 of the Law of 14 July 1994[90]):

- On the basis of a granted social benefit: Beneficiaries of Preferential Intervention status (BIM, *Bénéficiaires de l'intervention majorée* – RVV, *Rechthebbende verhoogde verzekeringstegemoetkoming*). This category includes persons entitled to a social integration revenue from the Public social welfare centre; persons entitled to similar aid from the Public social welfare centre (CPAS, *Centre public d'action sociale* – OCMW, *Openbaar centrum voor maatschappelijk welzijn*); persons who perceive the income guarantee for the elderly; and persons entitled to one of the benefits for disabled persons.[94]

[w] The formulas vary with outpatient drugs supplied in community pharmacies or in hospitals. Generally speaking, the reimbursement basis equals the drug pharmacy retail price.

- On the basis of a status as far as the income does not exceed a certain limit: also BPI status. This category include orphans, invalids, pensioners and widows, disabled children with a physical or mental incapacity, and persons older than 50 years who have been unemployed for at least one year.[94]
- On the basis of the available income of the family (determined after control of this income by the insurance institution): Omnio status. This category includes families with modest incomes who submit an Omnio request file to get access to preferential intervention.[94]

As far as medical costs are not entirely reimbursed and that the patient share may be high in case of long-term or serious illness, the Maximum Billing scheme (MAF, *Maximum à facturer - Maximumfactuur*) gives the beneficiary and his family the guarantee that the personal shares do not exceed a fixed ceiling. As soon as the fixed ceiling is reached, the costs for further care are entirely reimbursement by the mutual insurance funds. The ceiling varies in function of the beneficiary's social category; his age or in function of the family income.[94]

DESCRIPTION OF THE FOURTH HURDLE SYSTEM

Overview of the fourth Hurdle System

The Federal Agency for Medicines and Health Products (AFMPS, *Agence Fédérale des Médicaments et des Produits de Santé* – FAGG, *Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten*) is responsible for the quality, safety and efficacy of drugs on the Belgian market. Market authorisation are granted either by the European Medicines Agency (EMA) via the centralised (or Community) authorisation procedure or by the AFMPS/FAGG via decentralised and mutual recognition procedures.

Pharmaceuticals do not automatically qualify for reimbursement. Only inpatient and outpatient drugs included on the positive list of reimbursement (i.e. appendix of Royal Decree of 21 December 2001) are covered by the compulsory health insurance. As soon as market authorisation is granted, the pharmaceutical company can submit its drug reimbursement request to the Drug Reimbursement Committee (CRM, *Commission de Remboursement des Médicaments* – CTG, *Commissie voor Tegemoetkoming Geneesmiddelen*).

The reimbursement pathway procedure slightly varies with the "Class" claim. **Class 1** is restricted to drugs with added therapeutic value, **Class 2** is for drugs with similar or analogous therapeutic value and **Class 3** includes generics and copies. If the applicant considers that its product offers added therapeutic value, he introduces a claim for Class 1. The experts and the CRM/CTG first evaluate the Class 1 claim (i.e. added therapeutic value) with regard to efficacy, effectiveness, safety, comfort and applicability as compared with the standard alternative therapy. If the claim is rejected the pharmaceutical is assigned a Class 2. Receiving a Class 1 is in principle not a pledge for positive reimbursement decision but it gives an significant label power and allows, if eventually reimbursed, the negotiation for a price premium.

The drug reimbursement proposals are appraised by the experts and CRM/CTG members and subsequently voted during CRM/CTG meetings. The motivated positive or negative reimbursement proposal is transferred to minister of social affairs within a limit of 150 days. Then the minister is responsible for the final decision, which is to be taken before 180 days. However, he or she is allowed to deviate from the CRM/CTG reimbursement proposal.

A final positive decision typically contains the reimbursement modalities that are necessary for its implementation:

- Reimbursement basis: In general, it equals the pharmacy retail price. This is the key variable for calculating the cost-sharing.
- Reimbursement conditions: Conditions restricting the access to reimbursement, e.g. age range, preliminary diagnostic examinations, maximum dosage, authorisation of the counselling physician of the patient's sickness fund. Some conditions are sorted into "Chapters".
- Category of reimbursement : The category that defines the cost-sharing mechanism to be applied (capped co-insurance). There are five categories (A, B, C, Cx and Cs) conferring some reimbursement by the national health insurance.

The reimbursement decision is valid for the whole country and is implemented after the drug is added on the appendix of Royal Decree of 21 December 2001, by means of a Ministerial Decree.

Policy Implementation Level

Establishment

The Belgian reimbursement procedure underwent notable changes in 2001 with both the publications of the Law of 10 August 2001[95] and the Royal Decree of 21 December 2001[96]. First, strict timelines were introduced in order to comply with the European Transparency Directive regulating the pricing and reimbursement of pharmaceuticals in the EU members states. Second, the CRM/CTG expert committee was established to appraise the reimbursement requests introduced by the pharmaceutical companies and formulate advice to the minister of social affairs, the final decision-maker. The overall reimbursement procedure was substantially detailed to enhance transparency and use of objective criteria.[97] Accordingly, since January 2002, four actors are involved, with varying extent, in the fourth hurdle system.

The **Drug Reimbursement Committee** (CRM/CTG) is a committee of experts in pharmaceutical reimbursement set up within INAMI/RIZIV. It is responsible for monitoring the assessment of the reimbursement files submitted and appraising the reimbursement proposals. The legal missions of the CRM/CTG are the following (article 29bis of the Coordinated Law of 14 July 1994[90]):

- formulating proposals to register pharmaceuticals on the list of reimbursable pharmaceuticals;
- advising, on request of the Minister, on political aspects related to pharmaceuticals reimbursement;
- formulating proposals for the Committee for Health Care Insurance of the INAMI/RIZIV of interpretation rules regarding the pharmaceuticals reimbursement.

The CRM/CTG is composed of one chairman and thirty members.[98].Twenty-three members are entitled to a voting right while the others have a consultative voice only. Among the voter members, seven are representatives from Belgian universities selected for their scientific skills, eight are representatives from the six main sickness funds, three are representatives from pharmacists and four are representatives from medical doctors. Aside from the voter members, two representatives from the pharmaceutical industry (Pharma.be), one representative from the generic pharmaceutical industry (Febelgen), four representatives from ministries (social affairs, public health, economic affairs and budget) and one representative from the INAMI/RIZIV Service for Evaluation and Medical Control[x] are entitled to participate in the discussions but have no voting rights.

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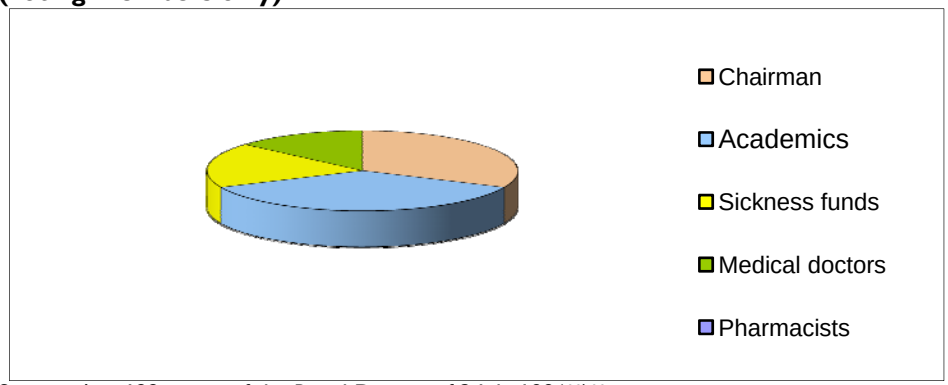
[x] The Service for Evaluation and Medical Control records breach of the law or any regulations in relation with the National Health Insurance.

Members, nominated by the organisation or professional association they represent, are appointed by the minister of social affairs for maximum six years, renewable after three years (article 122nonies, §2 of the Royal Decree of 3 July 1996[98]). Figure 12 summarises the composition of the CRM/CTG voting members.

Figure 12 : Composition of the Drug Reimbursement Committee (CRM/CTG)
(voting members only)



Source: Art. 122nonies of the Royal Decree of 3 July 1996[98])[98].

Legally, representatives of universities have medical, pharmacological and/or health economics skills and nominated by their universities although currently they are medical and pharmacological experts. Although representatives of ministries have a consultative voice, key respondents acknowledged that in practice they are foremost observers in the discussion mainly to obtain inside information on the discussion. For each effective member, there is one corresponding substitute. Those are entitled to attend the meeting and participate in the discussion but have no voting right when their effective member is present.

The CRM/CTG **secretary** is responsible for the administrative evaluation of the submissions. It consists of employees of the INAMI/RIZIV from the Management Unit for Pharmaceutical specialties. The secretary prepares the agenda of the meetings, report the decisions on proposals and ensure the respect of the strict time limits (art. 122decies of the Royal Decree of 3 July 1996[98]). The CRM/CTG **Board** is composed of four members appointed by the Minister: the chairman, two vice-chairman (selected among the academics) and one additional member (selected among the voter members). Missions of the Board include the organisation of the activities of the Committee; the appointment of internal of external experts in charge of the assessment of the reimbursement file and to observe relationships between experts and the Committee (art. 122nonies, §6 of the Royal Decree of 3 July 1996[98]).

In order to appraise the reimbursement request file, the CRM/CTG is entitled to appeal to **external and/or internal experts** (internal experts are employees at the INAMI/RIZIV) with sound scientific clinical and/or economic evaluation skills (art. 122terdecies of the Royal Decree of 3 July 1996[98]). Experts are responsible for the critical assessment of the request for added therapeutic value and to draft reimbursement proposals for the CRM/CTG. In practice internal experts are systematically involved in the preparation of the scientific assessment of the submission. Those are contracted medical doctors selected by the INAMI/RIZIV and state-employed pharmacists (approximately 6 medical doctors and 8 pharmacists in full time equivalents). Additional external experts might also be contracted when requested by the Board members or the internal experts.

Conflicts of interests are monitored by the Board. CRM/CTG members and experts are expected to transfer a written statement on any potential conflict of interest, mentioning direct and indirect relationships with the pharmaceutical industry. Their statement is renewed annually (art.122quinquies-decies of the Royal Decree of 3 July 1996[98]).

The **minister of social affairs** makes the final drug reimbursement decision. He or she is advised by the CRM/CTG although entitled to deviate for social and/or budgetary reasons. When no two-thirds majority is reached at the CRM/CTG on a reimbursement proposal within the limit of 150 days, he or she makes the reimbursement decision independently although informed about discussions held at CRM/CTG meetings by its representative.

The **minister of economic affairs** plays an indirect role to the reimbursement process by being responsible for fixing the maximum ex-factory price. The minister is advised by Committee of Pricing for Pharmaceutical Specialties (CPSP, *Commission des Prix des Spécialités Pharmaceutiques* – PFS, *Prijzencommissie voor de Farmaceutische Specialiteiten*). Maximum prices for Class 2 products are set in function of prices abroad and prices of comparator products. Maximum prices for Class 1 products can benefit from a price premium and be set above comparator prices. In accordance with the EU Transparency Directive, the maximum pricing decision must be communicated to the applicant within 90 days.[y] Noteworthy is that price can be further negotiated, although with a limited extent, between the CRM/CTG and the company.

Lastly, before adding a pharmaceutical on the positive reimbursement list, the **minister of budget** is entitled to advice the minister of social affairs on budgetary considerations.

> In early 2005, the minister of budget sent negative advice for every drugs drug reimbursement request claiming added therapeutic value (Class 1). Negative decisions were made by the minister of social affairs although some had received a positive reimbursement proposal from the CRM/CTG expert committee. The reason for those negative recommendation was mainly the pharmaceutical budget overshoot in 2004.

Table 13 summarises the main actors and their direct or indirect responsibilities in the drug reimbursement process.

Table 13: The key actors involved in the reimbursement process

Institution / Actor	Function(s)
National Institute for Health and Disability Insurance (INAMI/RIZIV)	The technical department for pharmaceuticals within INAMI/RIZIV receives the applicant's request, prepares the assessment, drafts advice reports and published the reports online
The Drug Reimbursement Committee (CRM/CTG)	Is responsible for supervising the assessment by the INAMI/RIZIV and external experts; appraising the relative therapeutic value of pharmaceuticals for drugs claiming a Class 1; and appraising reimbursement proposal, voting proposals and sending motivated reimbursement advice to the Minister of Social Affairs.
Minister of social affairs	Is responsible for the final reimbursement decisions.
Ministry of budget	Gives its consent to the final positive reimbursement decision.
Ministry of economic Affairs	Is responsible for the *maximum* ex-factory price.

y The pricing procedure is legally described in the MD of 29/12/89 about pricing of reimbursable pharmaceutical products. Members of the Pricing Committee include representatives from trade unions, pharmacists, sickness funds, pharmaceutical industry and Government.

System objectives

One stated mission of the key institution in organising health care, the INAMI/RIZIV, includes *guaranteeing the access to high quality health care at adequate prices for the largest population.*[99] In 2005, a Parliament report on Drug Policy stated as objectives of the drug policy: *the guarantee of accessibility, the rapid access for patient to high quality and innovative drugs, the financial sustainability of the social system*.[100] In 2009, the Minister of Public Health and Social Affairs in her Policy Brief stated as central objectives *the accessibility of pharmaceuticals and the financial sustainability of the reimbursement system*. A recent report jointly published by the INAMI/RIZIV and KCE on the performance of the Belgian health care system stated as main health care objectives accessibility, sustainability, quality of care, equity, and efficiency.[101]

Scope of the system

The Pharmaceutical Act, i.e. the Royal Decree of 21 December 2001[96], determines the scope of the reimbursement system. It states that only drugs listed onto its appendix are subject to reimbursement by the social health insurance. The system applies to inpatient as well as outpatient drugs.

Implementation

The minister of social affairs makes the positive reimbursement decision by means of a Ministerial Decree in the Official Journal (*Moniteur belge – Belgische Staatsblad*). In practice, the positive list is an appendix to the Royal Decree of 21 December 2001 and consists in three different parts: appendix 1 (N1) enumerates all reimbursed pharmaceutical products classified in *reimbursement chapters*; appendix 2 (N2) enumerates the different *reimbursement groups*; and the appendix 3 (N3) contains all the documents required to access certain conditional reimbursement.

The decision comes into force the first day of the month that follows a ten day period after the publication in the Official Journal. From that day onwards, in exchange for a medical prescription, the patient pays only for the co-payment, with the balance of the amount being covered by the third-party payer mechanism.

In principle, positive and negative decisions taken by the Minister are published on the INAMI/RIZIV website. Information on drug prices and reimbursement are compiled in the *Commented Drug Directory* (*Répertoire Commenté des Médicaments – Gecommentarieerd Geneesmiddelen Repertorium*) and the *Memento-Pharma*. The first register is published by the independent Belgian Center for Pharmacotherapeutic Information (CBIP, *Centre Belge d'information Pharmacothérapeutique* – BCFI, *Belgisch Centrum voor Farmacotherapeutische Informatie*) while the second is a booklet published by the INAMI/RIZIV in collaboration with the CBIP/BCFI. These are directed at prescribers and pharmacists to help them in their prescription choice. A copy-print version of *Memento –Pharma* is sent once a year the every prescribers and pharmacists. A monthly updated version is available via INAMI/RIZIV website.[102]

Accountability

The minister of social affairs is responsible for the overall public health care and social security policies and accountable for the drug reimbursement policy. He or she sets health care goals and can influence the drug reimbursement system by reforming the drug policy . Moreover, he or she takes the drug reimbursement decision. He or she is consequently accountable on these matters to the Belgian Parliament.

The impact of the fourth hurdle is currently limited to the monitoring of pharmaceutical public expenditure. Since 2008, the *Monitoring of Reimbursement Significant Expenses (M.O.R.S.E)* reports are published twice a year on the INAMI/RIZIV website. These reports are performed by INAMI/RIZIV experts and aim to give a detailed information on the evolution of public pharmaceutical expenditure.[91]

At the moment, impact of the reimbursement system on financial accessibility for patients or on improvement in health outcomes are not systematically evaluated. The Institute for Public Health (ISP, *Institut Scientifique de la Santé Publique* – WIV, *Wetenschappelijk Instituut Volksgezondheid*) monitors global health care outcomes. Occasionally, the Belgian Health Care Knowledge Centre (KCE) conducts, at Minister's or INAMI/RIZIV requests, studies related to the impact of the drug policy and the reimbursement system. As an example in 2010 it conducted studies on impact of the reference price system on drug affordability for patients and on the impact of changes in reimbursement criteria for statins on the cardiovascular outcomes in the Belgian population.[61, 93]

Technology Decision Level

Assessment

The assessment slightly varies with the Class claim introduced. As mentioned above, *Class 1* is restricted for pharmaceutical product for which the company claims an added therapeutic value, *Class 2* claim for drugs with similar or analogous therapeutic value, and *Class 3* for generics and copies.

Only for pharmaceuticals claiming a Class 1, the primary evaluation is limited to the scientific assessment of the **added therapeutic value**. If the claim is rejected, the drug is assigned a Class 2. This first evaluation is important for companies as its gives a "label" power for marketing and only Class 1 are entitled to negotiate price premium. The recognition of Class 1 is in principle not a pledge for a positive reimbursement decision, although a study conducted by Van Wilder and colleagues showed that pharmaceuticals granted Class 1 have a significant higher probability to receive a positive reimbursement decision.[103]

For the added therapeutic value assessment, the CRM/CTG board designates a group of INAMI/RIZIV experts. The CRM/CTG Board and the experts jointly assess the applicant's claim of an added therapeutic value and writes an first **assessment report** to be published within 60 days. The report is sent to the applicant allowed to send remarks and/or objections to the CRM/CTG secretary within 20 days or to request extra time to react to the report.

The therapeutic value assessment is the result of the aggregated evaluation of all relevant characteristics of a pharmaceutical specialty. The evaluation takes into account the five criteria presented inTable 14. Added therapeutic value is recognised if the drug use in a given treatment demonstrates an impact on mortality, morbidity and/or quality of life.

Table 14: Therapeutic value assessment criteria

-	Efficacy	A drug is effective if clinical trials demonstrates a better efficacy
-	Safety	The extent to which a drug is free from undesirable side-effects as defined by the Law of 3 July 1969.
-	Effectiveness	A drug is efficient if it is effective and if it achieves the desired results when provided under usual circumstances of health care practice
-	Applicability	The extent to which the drug characteristics, e.g. contraindications, limit the drug use for certain groups of patients and/or require special precautions
-	Comfort	The extent to which the use of the drug by the provider and/or the patient improves administration comfort and/or prevents errors related to drug use.

[1] Criteria are legally defined in art. 1st, 16°-20°, of the Royal Decree of 21 December 2001[96] and the therapeutic value in art. 1st, 21°, of the Royal Decree of 21 December 2001.[96]

For each of the five-above criteria, the pharmaceutical is compared with the relevant alternative treatment already reimbursable. There is no explicit hierarchy in the criteria although key respondents recognised efficacy, safety and effectiveness as being relatively more important. Efficacy and safety criteria are assessed with the International Conference on Harmonisation Good Clinical Practice (ICH GCP) procedures adopted by the European Medicines Evaluation Agency. The randomised controlled trial (RCT) remains the golden standard for assessing efficacy of pharmaceutical products. In practical terms, added therapeutic value is granted if and only if there is at least one positive superiority trial on primary end points against an active control or against a placebo control if there is no alternative treatment.[97, 104]

Second, the reimbursement request itself is evaluated. Again, the CRM/CTG board designates a group of INAMI/RIZIV and/or external experts. The group of experts assesses the reimbursement modalities submitted by the applicant and then drafts a motivated appraisal report sent to CRM/CTG members. During the plenary session the draft is presented by the experts and appraised by the CRM/CTG members. The CRM/CTG members can approve, modify or refuse the proposal. If the reimbursement modalities approved by the CTG/CRM differ from those requested by the company, a **provisional appraisal report** is sent to her. She is given the chance to react within 10 days or to demand extra time to send remarks and/or objections. For Class 1 drugs, the applicant is can ask for a hearing at the CRM/CTG meeting.

Criteria for the assessing the reimbursement request vary with the Class claim introduced as presented in Table 15. Again there is no hierarchy in the criteria although some key informants recognised therapeutic value weighing relatively more followed by budget impact and cost-effectiveness. For cost-effectiveness analyses, applicants are advised to use the guidelines for pharmacoeconomic evaluations in Belgium written by Cleemput and colleagues(2008)[105]. Health technology assessment (HTA) reports conducted by the Belgian Health Care Knowledge Centre (KCE) can also be used to inform experts.

Table 15: Reimbursement criteria according to the Class claim

	Class 1	Class 2	Class 3
- Therapeutic value	√	√	
- Drug price and equivalent reimbursement basis proposed by the applicant	√	√	√
- Clinical effectiveness and likely impact of the product, taking into account therapeutic and social needs	√	√	√
- Budget impact for INAMI/RIZIV	√	√	√
- Cost-effectiveness of the product from the perspective of the INAMI/RIZIV	√		

Criteria are mentioned in the Law of 14 July 1994, art. 35bis, §2 and in the Royal Decree of 21 December 2001, art 4.

There are two important remarks related to the assessment. First, the CRM/CTG is legally entitled to evaluate "the drug reimbursement request and its *justification*" (art. 15 of the Royal Decree of 21 December 2001[96]). This implies that experts who assess the reimbursement request are strictly speaking not expected to search for evidence beyond the evidence presented in the request file. Second, the pharmaceutical price and the reimbursement basis are considered assessment criteria as well as elements of the reimbursement modalities. In practical terms, the CRM/CTG is given a chance to narrowly negotiate the price with the applicant (always below the maximum price decided by the Minister of Economy) by once suggesting a price diminution to the company. In such case, the applicant is free to accept or bid a new price and reimbursement basis while the CRM/CTG takes into account this new price in its final recommendation.

Before the establishment of the CRM/CTG in 2002, the academics representatives within the Technical Council for Pharmaceuticals (*Conseil technique des spécialités pharmaceutiques/ Technische raad voor farmaceutische specialiteiten*) prepared the scientific assessment reports on behalf on this Council. With recent reforms in 2001, INAMI/RIZIV (and external) experts became responsible for preparing the assessment reports on behalf of the CRM/CTG members. Since then, the role of the academic representatives is restricted to discussing the assessment report and the appraisal of the product within the CRM/CTG meetings (except for those also members of the CRM/CTG Board). Some key informants expressed discomfort with this situation as they perceived their expertise to be particularly relevant for the scientific assessment of the pharmaceuticals.

Appraisal process

During the appraisal process, if the reimbursement modalities discussed by the CRM/CTG differ from those requested by the applicant, the CRM/CTG votes on a **provisional appraisal report** within 120 day time limit. Voting requires at least twelve voter members to be present and is done by a show of hands (except if at least three voter members request a secret voting) in the presence of the all members (consultative members as well). Approval *and* rejection of proposals requires a two-thirds majority.[106]

This provisional proposal is then sent to the applicant which is given the chance to send remarks. Within 150 days the CRM/CTG votes on the **final appraisal report**. Rejection of a proposal (also to be approved by a two-third majority) implies that a negative advice is sent to the minister. The two-third majority voting rule on approval and rejection may result in no proposal at all. Between 2002 and the first semester of 2009, this occurred in 26.6% and 22.0% of Class 1 and orphan drugs, respectively.[65]

Although being rationalized by clear criteria and substantiated with clinical and economic data, the appraisal phase remains a deliberation process between people. Moreover experts also represent stakeholders. As a result, they are likely to have their own value judgment in which formal as well as informal criteria are used.[62]

Some key informants expressed concern about the presence of consultative members during the voting phase by a show of hands. Especially the fact that representatives of the pharmaceutical industry have a watchful eye on voting behaviour of members is considered inappropriate by some members.

Reimbursement modalities, elements contained in the advice

The final appraisal report summarises the results of the appraisal process: approval or rejection of the Class 1 claim, the reimbursement modalities and time frame and the elements required for the individual reimbursement revision. The **reimbursement modalities** are defined according to the following four following elements[z]:

- the reimbursement conditions;
- the price and reimbursement basis,
- the group of reimbursementaa
- the category of reimbursement.

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z The reimbursement modalities are legally described in Art 3, §1st, al.3, of the Royal Decree of 21 December 2001[96]). Elements are individually defined in art.1st, 12°-15° of the Royal Decree of 21 December 2001[96]).

aa There are 23 groups of reimbursement which correspond to a therapeutic chemical classification. For more details about the classification, please visit the INAMI/RIZIV website: http://www.inami.fgov.be/inami_prd/ssp/rem2/pages/RefundingGroupList.asp

Reimbursement conditions

Among the existing reimbursement conditions, some are sorted out in *Chapters*. There are 7 chapters (Art. 1st, 11° of the Coordinated Law of 14 July 1994[90]) with the most important being *Chapter I*, *Chapter II* and *Chapter IV*:

- Drugs in *Chapter I* are no subject to reimbursement restrictions but the drug indications officially registered.
- Drugs in *Chapter II* are subject to an *ex post* control by Service for Evaluation and Medical Control of the INAMI/RIZIV or by the medical officer of the sickness funds.
- Drugs in *Chapter IV* are subject to particular reimbursement conditions and to *ex ante* control, i.e. the prior authorisation by the medical officer of the sickness fund. Restrictions for reimbursement are fixed for health safety reasons (e.g. anti-tuberculosis drugs restricted to tuberculosis patients to prevent resistance) and/or budgetary concern.

Reimbursement basis

In general, the reimbursement basis is equal to the pharmacy retail price (art. 35bis, §2bis of the Coordinated Law of 14 July 1994[90]). The reimbursement basis varies with the Class attributed to the product. For Class 1 drugs, the reimbursement basis should take into account the added therapeutic value. In other words, the reimbursement basis can benefit from a premium that sets the reimbursement basis above those of the comparators. For Class 2 drugs, the reimbursement basis cannot exceed the reimbursement basis of the comparator with same or analogous therapeutic value. If there is no reference drug suggested by the applicant, the CRM/CTG fixes one. For Class 3 drugs, the reimbursement basis at time of admission is at least 30% lower than the reimbursement basis of the reference drug (Art. 8 of the Royal Decree of 21 December 2001[96])

Reimbursement Category

There are five **category of reimbursement** (*A*, *B*, *C*, *Cx*, and *Cs*) that define the level of cost-sharing for the patients. The actual categorisation is a function of the severity of the diseases with drugs in category *A* for life-threatening diseases and drugs in category *C* for symptomatic treatments.

In 2010, formulas defining the level of cost-sharing for outpatients drugs supplied in community pharmacies were adapted following the reform of pharmacists remuneration (April 2010). The reform sought to improve pharmacists remuneration while keeping the cost-sharing level of patients constant. Table 16 presents the cost-sharing levels for the five reimbursement category for outpatient drugs supplied in community pharmacies and hospitals. The two formulas lead to approximately the same level of cost-sharing for patients as the reform should explicitly not affect patients. Noteworthy is the protecting mechanism aimed at vulnerable patients[bb] (the so-called 'preferred' beneficiaries) for whom cost-sharing is slightly lower. Category *B* is by far the largest category of reimbursable pharmaceutical specialties. In 2007, it accounted for 78.6% of the global pharmaceutical expenditures in the ambulatory sector.[107] Noteworthy is that drugs with no reimbursement and thus fully paid by patients are sometimes referred as category *D* drugs.

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bb Vulnerable beneficiaries have access to an increased public reimbursement. Those beneficiaries are identified with the help of the article 37, §§1,19 of the Law of 14/07/1994.

Key informants acknowledged little discussion on the drug category product by product. In fact, a detailed drug classification exists to determine the reimbursement category, but is inherited from the 1980s. This historic classification was motivated by offering financial protection in function of the needs and the severity of the diseases. However, most interviewees shared dissatisfaction with the current classification as it is perceived outdated or inadequate to meet the primary cost-sharing objectives. A KCE project on cost-sharing policies and drug reimbursement categories is currently ongoing and will be published by the end of 2011.

Table 16 : Cost-sharing mechanisms for outpatient drugs supplied in community pharmacies and hospitals

Category	Therapeutic importance	Cost Sharing in community pharmacies defined as a percentage of the $RB_{ex\text{-}fact}$	Cost-sharing in hospital pharmacies defined as a percentage of the RB
A	Vital drugs (e.g. insulin, cancer drugs)	0%	0%
B	Therapeutically significant drugs for non-life threatening diseases (e.g. antibiotics, antiasthmatics, antihypertensives).	Ordinary patients: 44.20% if $RB_{ex\text{-}fact}$< €14.38 €2.5 + 27% if $RB_{ex\text{-}fact}$ > €14.38 Capped co-insurance: - €10.80 (€16.10)[2] - €13.50 (€or 24.20)[2] for large packaging[1] Preferred patients: 26.52% if $RB_{ex\text{-}fact}$< €14.38 €1.5 + 16% if $RB_{ex\text{-}fact}$ > €14.38 Capped co-insurance: - €7.20 (or €10.80)[2] - €8.90 (or €16.10)[2] for large packaging[1]	Ordinary patients: 25% Capped co-insurance: - €10.80 (€16.10)[2] - €13.50 (or €24.20)[2] for large packaging[1] Preferred patients: 15% : Capped co-insurance: - €7.20 (or €10.80)[2] - €8.90 (or €16.10)[2] for large packaging[1]
C	Therapeutically less significant drugs for systematic treatment (e.g. antiemetics, spasmolytics)	88.39% if $RB_{ex\text{-}fact}$< €14.38 €5 + 54% if $RB_{ex\text{-}fact}$ > €14.38 Capped co-insurance: Ordinary patients: €13.50 (or €24.10)[2] Preferred patients: €8.90 (or €16.10)[2]	50% Capped co-insurance: Ordinary patients: €13.50 (or €24.10)[2] Preferred patients: €8.90 (or €16.10)[2]
Cs	Drugs used in certain chronic illnesses (e.g. antihistamines and vaccines)	106.07% if $RB_{ex\text{-}fact}$< €14.38 €6 + 65% if $RB_{ex\text{-}fact}$ > €14.38	60%
Cx	Contraceptives and antispasmodics.	141.43% if $RB_{ex\text{-}fact}$< €14.38 €8 + 86% if $RB_{ex\text{-}fact}$ > €14.38	80%

RB = reimbursement basis (it usually equals the pharmacy retail price). $RB_{ex\text{-}fact}$ = Reimbursement basis ex-factory (it usually equals the ex-factory price)

[1] Large packaging contain more than 60 units.

[2] This applies for drugs for which a generic/copy exists from ATC 4 level.

Transparency in the assessment and appraisal processes

Since 2007, the appraisal process has gained in transparency toward the general public. For positive reimbursement decision, the following documents are available on the INAMI/RIZIV website (art. 3, §1, al. 2 Royal Decree of 21 December 2001[96]):[cc].

- the **evaluation report** of the reimbursement request file**,** as approved by the CRM/CTG expert members,
- the written **remarks and/or objections** of the applicant, and
- the **CRM/CTG reply** to the applicant's remarks and/or objections.

The applicant can ask to conceal confidential information. Noteworthy is that neither the key issues discussed in the plenary sessions, nor the result of the voting, nor the final drug reimbursement proposal sent to the minister are currently publicly available.

Decision Process

The minister of social affairs makes the final decision, advised by the proposal of the CRM/CTG, within the strict 180 day timeline. If there is no recommendation from the CRM/CTG, the minister takes a motivated reimbursement decision independently. He or she is allowed to deviate from the proposal for budgetary and/or social reasons although within the room of the reimbursement criteria. A negative decision for budgetary reason may be recommended by the minister of budget allowed to advise on that matter. Positive reimbursement decisions are published by means of ministerial decrees, although the decision process and rationale is not documented. Negative decisions are currently not publicly available.

> Key informants acknowledged that the decision process at the ministerial level is far from transparent. In case of a CRM/CTG reimbursement advice, the rationale for deviation is not always clearly communicated or clearly understood by the CRM/CTG members.

The positive reimbursement decision typically includes the drug Class and the reimbursement modalities. For some drugs, it also contains the time frame and elements required for the individual revision. In particular, the decision contains possible restrictions for reimbursement e.g. age range of patients, preliminary diagnostic examinations, prior authorisation by the medical officer of the sickness fund. In 2009, 324 unique dossiers for reimbursement were submitted to the CRM/CTG. Out of the 324 unique dossiers submitted in 2009, the Minister took a decision within the same year for 262 files. A positive reimbursement decision was taken in 94.66% of the decisions cases.

Financial risk-sharing arrangements

Since 2010, the Minister may allow the negotiation of a reimbursement contract[dd] for Class I drugs for which there was a negative or no proposal from the CRM/CTG. The contract negotiation is motivated by an excessive reimbursement basis claimed by the applicant or by uncertainties related to the drug budget impact. Some CRM/CTG members and the applicant negotiate the terms for the drug reimbursement that is limited to minimum one year and maximum 3 years but contracts should not be voted within CRM/CTG plenary meetings. Contracts aim to guarantee some reimbursement and thus patients access to the drug until sufficient evidence is available to justify the requested reimbursement basis.

[cc] The URL to access the reports is the following: http://www.inami.fgov.be/drug/fr/drugs/decisions_report/report_crm_cgt/report.htm

[dd] For more details, see art. 81-85 of the Royal Decree of 21/12/01[108].

Outcomes and implementation

As soon as the minister's decision is published in the Official Journal, reimbursement applies on the first day of the month that follows the 10 days after the publication. As public health and social affairs are federal matters reimbursement decisions are implemented on a national level and cannot be modified by regional authorities.

The applicant is entitled to appeal the minister's decision to the Administrative Court (*Conseil d'Etat – Raad van State*) but only on procedural grounds. Other stakeholders are, in principle, entitled to appeal the decision although in practice, it rarely occurs.

The reimbursement decision can be subject to a reappraisal procedure. Reappraisals revise or confirm the drug reimbursement modalities. Reappraisals are either *individual* or *collective*; triggered by budget impact or uncertainty concerns.

- Individual reappraisal is primarily conducted for reasons of uncertainty with the aim to reassess the decisional criteria with new available evidence. It affects: (1) all drugs from Class 1; (2) drugs from Class 2 or 3 for which an individual revision was specifically requested by the Minister; (3) drugs whose reimbursement modalities have been modified and for which an individual revision was specifically requested. Class 1 drugs are systematically reappraised as the assessment of the added therapeutic value is often based on factors with surrounding uncertainty. Individual reappraisal usually takes place between 18 and 36 months after the positive decision. The applicant submits a reassessment report with up-to-date evidence regarding e.g. clinical efficacy and effectiveness; real-life cost-effectiveness; size of the target group; turnover and sales volume; reimbursement modalities in other EU member states; and any other elements asked for the individual revision[ee]. For Class 1 drugs, the CRM/CTG specifies a list of uncertain factors it had to take into account and for which the company is expected to deliver additional data. If the new data confirm the hypotheses taken into account for the initial reappraisal, the reimbursement conditions continue to apply. If not, the CRM/CTG decides on the modified reimbursement modalities, such as limiting the target patient groups for which the drug is reimbursed or restricting the group of prescribers for the medicine. At worst, the drug is withdrawn from the reimbursement list.
- On the CRM/CTG's or the Minister's initiative, the CRM/CTG can also conduct a group reappraisal, i.e. pharmaceuticals with identical or analogous indications. Group reappraisals are from two types: the general group reappraisal[ff] and reappraisal for budgetary concerns (the tendering procedure described in the paragraph on pharmaceutical tools)[gg]. General group reappraisals are conducted by members of the CRM/CTG and submitted to the voting procedure. In practice however, currently very few group reappraisals are conducted .

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ee For more details about the individual reappraisal of the reimbursement decision, please refer to the articles 62-71 of the RD of 21/12/01.

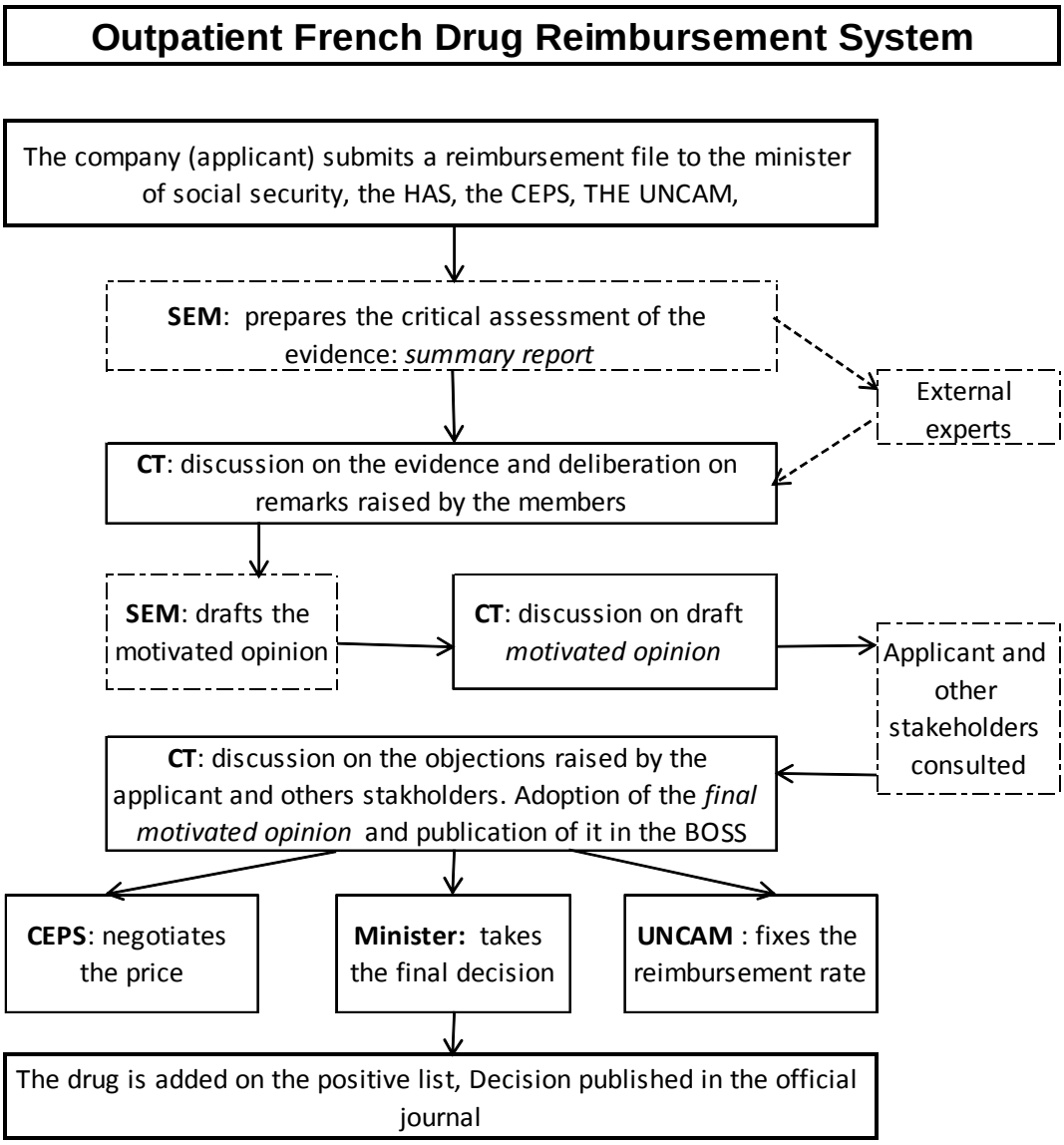
ff For more details about the general collective reappraisal, please refer to the articles 72-77 of the RD of 21/12/01.

gg For more details about the tendering procedure, please refer to the articles 72; 78-79 of the RD of 21/12/01.

Key points Belgium

- **Reimbursed inpatient and outpatient drugs are included in a positive reimbursement list.**
- **Reimbursement request is submitted by the company.**
- **The Drug Reimbursement Committee (CRM/CTG) is the expert committee advising the minister of social affairs, i.e. the final drug reimbursement decision-maker.**
- **Stakeholders involved in the CRM/CTG include representatives from academics, physicians, pharmacists and sickness funds (voting members) and representatives from the ministries, pharmaceutical industry, INAMI/RIZIV (consultative members).**
- **The CRM/CTG is assisted in its assessment work by INAMI/RIZIV and external experts.**
- **Appraisal reimbursement criteria are added therapeutic value; drug price and reimbursement basis, clinical effectiveness and likely impact of the product given the therapeutic and social needs, budget impact and cost-effectiveness.**
- **Voting at the CRM/CTG is done by a show of hands in the presence of consultative members. A two-third majority is required to approve or reject a proposal. This procedure sometimes leads to no proposal at all.**
- **In case of a proposal, the minister may deviate for budgetary and social reasons.**
- **Primary evaluation report and the reactions from the applicant are openly available on the INAMI/RIZIV website. However it is not always clear to the public which elements lead to the advice/decision as the main discussion points are not reported**
- **Reimbursement decision is made within 180 days. Otherwise, the applicant reimbursement request is enforced.**
- **The company may appeal the reimbursement decision to the Administrative Court only on procedural grounds.**

DRUG REIMBURSEMENT SYSTEM IN FRANCE[hh]



Abbreviations: HAS: National Authority for Health/ *haute autorité de santé*; CEPS: Economic Committee for Health Products/ *Comité économique des produits de santé*; UNCAM: National Union of Health Insurance Funds / *Union nationale des caisses d'assurance maladie*; SEM: Pharmaceutical Assessment Department/ *Service d'évaluation des médicaments* ; CT : Transparency Committee/ *Commission de la transparence*

[hh] We are grateful to Mrs Annne d'Andon from HAS for reviewing this chapter.

HEALTH CARE STRUCTURE

Characteristics of the Health Care system

The French population is almost universally covered by statutory health insurance. Affiliation to health insurance is by means of three different schemes: the General Scheme (*Régime général*), covers employees and accounts for about 89% of the population (CNAMTS, *Caisse nationale de l'assurance maladie des travailleurs salaries*; Portail de la Sécurité Sociale, 2009 #45}; the agricultural scheme for farmers and agricultural employees (MSA, *Mutualité sociale agricole*); and the scheme for self-employed (RSI, *Régime social des indépendants*). The National Union of Health Insurance Funds (UNCAM, *Union nationale des caisses d'assurance maladie*) puts together the three different schemes under the same umbrella. [109-111]

In addition to the statutory health insurance, the population can voluntarily subscribe to supplementary sickness funds (so-called '*mutuelles*') or purchase private insurance. Those are complement to the statutory insurance (*Complémentaires santé*) and totally or partly cover the charges that the mandatory coverage does not reimburse (i.e. the co-payments).[112] Since 1999, the Universal Health Coverage Act (CMU, *Couverture maladie universelle*) offers basic coverage to inhabitant of the country that meets some specific criteria, e.g. unemployed or low income.[109] It is a state-owned free complementary health insurance (CMUC, *Couverture maladie universelle complémentaire*). As a result approximately 93% of the population is covered by complementary health insurance.[109]. This two-level system of health insurance (mandatory and complementary insurances) is quite unique to France.[5]

Physicians are predominantly self-employed and get paid on a fee-for-service basis. Patients pay the provider directly and are later reimbursed, subject to a cost-sharing scheme. Patients are free to choose and consult any doctor. However, since 2005 general practitioners are given a role of gatekeeper to access the health care system. Patients not complying with this rule are financially penalised with co-payments increased by 50%.[112, 113]

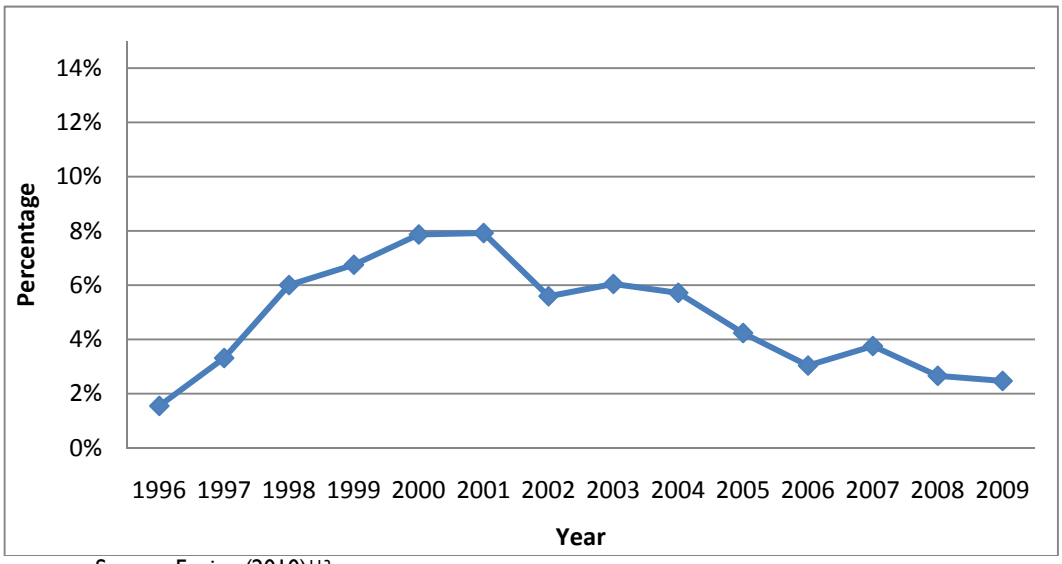
Health care funding and pharmaceutical expenditure

In 2008, total health expenditure accounted for 11.2% of the GDP, of which 77.8% came from public resources. Health expenditure per capita was US$2,404 (adjusted for purchasing power parity).[71] The financing of the health care insurance depends on two main sources: social contributions as a proportion of wages and salaries (approximately 46%); and taxes (approximately 45%). Other smaller sources of finding include state contributions.[109, 112]

Since 1996 the French Parliament annually votes on the Law on Financing Social Security (LFSS, *Loi de financement de la sécurité sociale*), stating the national target for health insurance expenditure (ONDAM, *Objectif national des dépenses d'assurance maladie*). The ONDAM depends mainly on macroeconomic variables such as the predicted GDP growth rate. However since its implementation, public health expenses have not yet been contained within the fixed limitation, with the highest deficit in 2004 running at 11.6% of the intended budget.[5, 114] For the year 2010, the growth in health care expenditure was fixed at 3% and 2.9% for 2011. The ONDAM is divided into six main sub-objectives and aims to monitor the evolution of sub-categories of health care.[115] There is no separate budget target for pharmaceutical expenditure but a ceiling rate for ambulatory drug sales (known as the *K* growth rate) annually fixed under the LFSS. The K-rate target was 1.4% for 2009 and 1 % for 2010.

In 2009, total pharmaceutical expenditure amounted to €35.383 billion. Of this amount, approximately 65% was covered by the statutory health insurance, 16.7% by complementary insurances and 17% by the patients. Pharmaceutical expenditure grew on average at 5.50 % between 1996 and 2005.[113] Since 2006, average growth rate declined to 2.98% as a result of new pharmaceutical policies. This was mainly achieved by moderation in drug prices and consumption of low-priced drug rather than drug use (volume increased by 5.8% on average over the same period). Figure 13 presents the evolution of total pharmaceutical expenditure.

Figure 13: Annual growth rates of total pharmaceutical expenditure



Source: Fenina (2010)[113]

Pharmaceutical policy tools

Facing one of the highest a pharmaceutical per capita expenditure in Europe (it ranked in fifth place for the level of per capita drug expenditure among OECD countries in 2008[71]) the government launched new pharmaceutical policies to contain drug use and costs over the last ten years.

Prices of outpatient pharmaceuticals have historically been regulated in France, but approaches to controlling prices have evolved. Today, drug prices are negotiated between the Drug Pricing Committee (CEPS, *Comité économique des produits de santé*) and the pharmaceutical company, taking into account three major criteria: the price of other available drugs with same therapeutic indications (i.e. internal reference pricing); the improvement in the medical services rendered (ASMR) and the predicted sales volume. For innovative drugs (ASMR I, II, III) companies propose their price to the CEPS (*procédure de dépôt de prix*) who accepts it as long as judged reasonable and consistent with prices in four EU neighbouring countries (Germany, Italy, Spain and United Kingdom). The CEPS is moreover entitled to implement pricing-related cost containment measures such as compulsory price cuts. Inpatient drugs prices are controlled by hospitals except innovative and costly drugs excluded from the per case based hospital's financing and drugs also sold for ambulatory patients for which companies propose their price the CEPS also in line with prices in neighbouring countries.[109, 116]

In 2003, a reference pricing scheme, the Flat Rate Liability (TFR, *Tarif forfaitaire de responsabilité*) was introduced for groups of drugs for which the level of generic market penetration is deemed insufficient (penetration rates lower than 50-60%). This scheme reimburses both generics and original equivalents based on the median price of the generics.

Measures aimed at encouraging the greater use of generics were also progressively introduced. Since 1999, pharmacists are allowed to substitute generics for original drugs, provided that the generic is cheaper, that the physician does not prohibit it, and that the patient approves it. Generic substitution is encouraged through financial incentives to pharmacists (higher remuneration margin)[109]. More recently, the system "Third-party payer for generics" *(Tiers payant contre génériques*) is now applied in almost every of French departments. Experimented in 2006, it aims to suppress the third-payer mechanism (but not reimbursement) when the patient refuses generic substitution. Beside the promotion of INN (International Non-proprietary Name) prescription, physicians are visited by health insurance representatives (DAM, *délégués d'assurance maladie*) who inform and encourage efficient prescribing behaviors.[109].

In France, most companies make agreements with the national pricing authority (CEPS) that define the annual rebates to be made to the national insurance if the growth rate objective is exceeded. The few companies that do not enter the framework agreement are subject to another regulatory mechanism known as the safeguard clause. This clause consists of a contribution to be paid by pharmaceutical companies when their pre-tax volume of French drug sales of reimbursable drugs exceeds the growth rate objective (*K*-growth rate). The amount of rebates each company pays back is not publically known.

Cost sharing policies

Private share on health expenditure in France is among the lowest in the EU. In 2008, it accounted for 7.4% of total health expenditure.[71, 113] This is partly explained by the two-level system of health care insurance. Health expenses are first reimbursed by the compulsory health insurance whilst the balance of the amount is mostly paid by complementary health insurance funds. Given the two-level system in health insurance, most cost-sharing strategies seeking to curb drug consumption have traditionally had a limited impact in France.[5] Only non-refundable deductibles have partly raise price sensitivity of patients. Since 2005, a deductible of €1 is applied for visits to physicians and raised to €4 for patients not complying with the gatekeeper rule.[109, 112, 113, 117]

Cost-sharing mechanisms vary with the nature of the service provided and the type of patients' needs.[112]. Pharmaceuticals cost-sharing mechanisms are based on co-insurance.The national health insurance reimburse a fixed percentage of the drug price or the reference price for drugs that included in the reference pricing scheme (TFR). Percentages vary with the level of medical service rendered (SMR, *Service médical rendu*). Drugs with insufficient SMR are not reimbursed by the compulsory health insurance whilst drugs with important SMR are usually reimbursed at 65%. Other products with moderate or mild level of SMR are reimbursed at 35% or 15%, respectively. For certain irreplaceable and costly treatments (e.g. cancer or AIDS drugs) or for patients with one of the thirty serious and chronic diseases listed (ALD, *Affections de longue durée*) such as diabetes or psychiatric illnesses, drug are fully reimbursed.[112, 118] Also costly drug treatments against diseases that constitute a progressive or disabling disorder, with a previous treatment period of over six months (the so-called "31st disease") and multiple diseases of over six months (the so-called "32nd disease") are fully reimbursed.[109] In 2008, 8.3 million of the population (more or less 14%) benefited from preferential reimbursement status.[119] Complementary health insurances mostly cover the balance of the amount. Facing the highest drug consumption per capita in Europe, a deductible of €0.50 per drug package was introduced in 2008 with an annual ceiling up to €50 per person in an attempt to moderate drug use growth.

DESCRIPTION OF THE FOURTH HURDLE SYSTEM

Overview of the drug reimbursement system

France applies two positive reimbursement lists which grants drug reimbursement for a therapeutic indication by the mandatory health insurance: one list for reimbursable drugs supplied in community pharmacies (*Liste des spécialités remboursables aux assurés sociaux*) and one list for the hospital sector (*Liste des spécialités agréées aux collectivités publiques*). A pharmaceutical product can be included on one or both lists. Inclusion on one or both positive list is motivated either by the level of medical service rendered (SMR) of the drug or the cost saved by means of the new product.

As soon as marketing authorisation is granted (AMM, *Autorisation de mise sur le marché*) either by the European Medicines Agency (EMA) for the centralised procedure or by the French Agency for the Safety of Health Products (AFSSAPS, *Agence française de sécurité sanitaire des produits de santé*) for the decentralised or mutual recognition procedures, the pharmaceutical company can apply for reimbursement by the compulsory health care insurance. The company submits simultaneously its pricing and reimbursement request files to the Transparency Committee (CT, *Commission de la transparence*) of the French National Health Authority (HAS, *Haute Autorité de Santé*) for technical advice; to the Drug Pricing Committee (CEPS, *Comité économique des produits de santé*) for pricing; and to the National Union of Health Insurance Funds (UNCAM, *Union nationale des caisses d'assurance maladie*) for the reimbursement rate. These are the three key institutions in the French reimbursement process.

The CT plays a key role in the assessment phase. It is mandated to conduct in-depth analysis of available clinical evidence and to provide accurate information on the appropriateness of a (possible) reimbursement. Two concepts are central to the pricing and reimbursement evaluation: the level of medical service rendered (SMR, *Service médical rendu*) and the improvement in the medical service rendered (ASMR, *Amélioration du service médical rendu*). The SMR rating evaluates the drug therapeutic benefit and varies from one to four (important, moderate, mild or insufficient) whilst the ASMR is assessed against comparable products available on the market in the same therapeutic area and ranks the pharmaceutical on a scale from I to V (I = major improvement, V = no improvement). The SMR is then used by the UNCAM to fix the reimbursement rate whilst the ASMR rating serves the CEPS to determine the ex-factory price with the company. As a rule, if the ASMR is of I to III, price is settled in line with to European prices. An ASMR V product can be listed only if the cost is under the comparator (impact on the price or on the economic impact of the drug) whereas an ASMR IV product can negotiate a price higher than the comparators.

The final decision – listing, with precision on the reimbursement rate and price – is taken by the Minister of Health advised in his or her decision by the Transparency Committee opinions. Lastly, the UNCAM fixes the rate of reimbursement by the compulsory health insurance. There are four different reimbursement levels: 100%; 65%; 35% and 15%. The reimbursement rate is fixed taking into account the SMR evaluation and the severity of diseases.[112] Reimbursement for pharmaceuticals supplied in hospitals differs as they are included in the per case based hospital's financing (T2A, *tarification à l'activité*). Except for costly pharmaceuticals that are enlisted in a specific list (*liste de médicaments facturables en sus des prestations d'hospitalisation*) which are financed on top of the payment per case system and for new innovative drugs benefiting from a provisional approval scheme (ATU, *Autorisation temporaire d'utilisation*).

Economic evaluation was long not central to the French reimbursement process. Growing criticism on the failure of the advisory body to perform health-economic evaluations led to reform on that matter. Since 2008, the HAS is entitled with a new mission of conducting health economic assessments. The Economic and Public Health specialised Committee (CEESP, *Commission évaluation économique et de santé publique*) was established in July 2008 for this purpose. The stated objective is to give opinions about the cost-effectiveness of treatments or treatment strategies although recommendations are not binding at the moment.[120]

Policy Implementation Level

Establishment

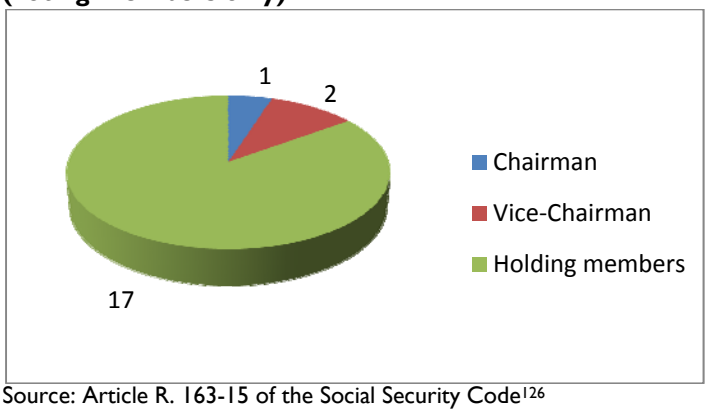
The Social Security Act (CSS, *Code de sécurité sociale*; art R163) and the Public Health Act (CSP, *Code de santé publique;* L162-17) establish the legal bases of the pharmaceuticals reimbursement. The main parties legally involved are French National Authority for Health (HAS), and more specifically the Transparency Committee (CT) within it; the Economic Committee for Health Products (CEPS); the National Union of Health Insurance Funds (UNCAM); and the Minister of Health and Social Security.

The **French National Authority for Health** (HAS) was legally set up in 2004 by the health insurance reform act with the aim to bring together under a single umbrella organisation a number of activities designed to improve the quality of patient care and to guarantee equity within the healthcare system.[121] HAS is not a governmental body but an independent public scientific institution with financial autonomy. The Board consists of one chairman and seven members appointed by government officials. Every Board member but the Chairman heads one of the seven Specialist Committees and is responsible for a specific mission or specific aspects of a mission. [122, 123] Of the seven specialist committees, one is involved in the fourth hurdle process for pharmaceuticals: the **Transparency Committee** (CT). The CT is legally mandated to [124]:

- Issue opinions on the pharmaceutical reimbursement requests;
- Regularly reassess the pharmaceuticals SMR;
- Issue information documents on drug indications, especially for reimbursed and costly pharmaceuticals.
- Issue opinions on any other subject (related to the SMR), on the request of the Ministry of Health, the Ministry of Social Security, or the HAS' Board.

The CT is composed of twenty voting, six deputies and eight consultative members who meet once every two weeks.[125] Voter members consists of one chairman, two vice-chairmen, and seventeen holding members, appointed by the HAS Board for their scientific skills for a three year mandate renewable twice. The nature of the scientific skills is not specified on a regulatory point of view; however current voter members were appointed for their pharmacological and medical skills. Consultative members consist of four representatives of the public institutions (Social Security Department, the Health Department, the Hospital and Health Care Organisation, and the AFSSAPS); three representatives of the main health insurance funds and one representative of the pharmaceutical industry. In addition, six surrogate member are appointed according to the same rules as the holding members, to replace them when absent.

Figure 14: Composition of the Transparency Committee (CT) (voting members only)



Source: Article R. 163-15 of the Social Security Code[126]

In addition, the CT chairman can appeal to one or more external experts (so-called '*rapporteurs*') for their particular skills with regard to the evaluation. Those *rapporteurs* are expected to transfer a written report to the CT and if, if necessary, to be present to the CT meeting session to answer questions raised by the members of the CT.[124]

Members of the CT as well as experts working for it are bound by professional confidentiality. A breach of this rule can lead to the suspension of the person's function. Members of the CT and experts are expected to publicly declare any direct or indirect link with the pharmaceutical sector. Conflicts of interest are monitored by the HAS Board and publicly available on the HAS website.[124]

In its assessment function, the Tranparency Committee is assisted by **internal assessors**, i.e. HAS' employees in the Service for Pharmaceutical Evaluation (SEM, *Service évaluation des médicaments*) from the Department of Medical, Economic and Public Health Evaluation(DEMESP, *Direction de l'Evaluation Médicale, Economique et de Santé Publique*).[127] Those are responsible for the support of the scientific evaluation of reimbursement file submitted by the pharmaceutical company as well as for searching additional scientific literature. The internal assessor is responsible of compiling a synthesis for the CT members.[124]

The **Economic Committee for Health Products** (CEPS) is mainly responsible for negotiating drug prices and monitoring the pharmaceutical budget (L162-17-3 of CSS). It consists of twelve members, ten with voting rights and two with consultative voice. The voting members are: the chairman and two vice-chairmen selected for the health economic skills; four representatives of Ministries (Health, Social Security, Industry and Finance); two representatives of the CNAMTS, one of the MSA or the RSI and one for complementary insurance funds. The two consultative members are the representative of the Directorate of Hospitals (from Ministry of Social Affairs) and the representative of the Ministry of Research.

Since 2004, the **National Union of Health Insurance Funds** (UNCAM) brings together the three major health insurance schemes (the CNAMTS, the MSA and the RSI). The UNCAM is responsible to[109]:

- Run the conventional policy (i.e. agreements between the health insurance funds and health care providers)
- Define the scope of services eligible for reimbursement
- Set up the health care reimbursement tariffs

In 2009, 657 opinions were provided by the Transparency Committee; 42% of these for first listing, 6% for indications extensions, 25% for renewals and 26% for other requests.

Table 17 gives an overview of the four main actors and their responsibilities in the reimbursement process.

Table 17: Key actors involved in the reimbursement process

Institution/organisation	Function(s)
National Authority for Health (HAS)	The technical department is responsible for receiving the reimbursement request, preparing the assessment, drafting the advice reports, and publishing the reports online
Transparency Committee (CT)	Is responsible for assessing (appraising) the drug medical service rendered (SMR) and the improvement in medical service rendered (ASMR)
Minister of Health	Is responsible for making the final reimbursement decision
Economic Committee for Health Products (CEPS)	Is responsible for the price of reimbursable pharmaceuticals on the the rate of reimbursement is calculated.
National Union of Health Insurance Funds (UNCAM)	Is responsible for the reimbursement rates for reimbursable pharmaceuticals

Objectives

In its mission, the HAS is responsible *to contribute to the sustainability of an high quality and equitable health care system*. The Minister of Health, during the presentation of the health care budget for the year 2011, also stressed the importance *to focus on efficient and appropriate health care services in establishing an health care policies*.

The Social Security Act states that all drugs with favourable benefit/risk ratio, as assessed by the CT should be accessible to patients through reimbursement, independent of their price although drugs that would potentially induce unjustified expenditure for the health insurance, either because there public interest is low (efficacy is not well proven), or because they bring a minor contribution in existing therapeutic strategies, or because of the absence of severity of diseases they address should not be reimbursed. (art. R163-1 of the CSS).[128]

Scope of the system

The Social Security Act defines the scope of the pharmaceutical reimbursement system. Drugs supplied by community pharmacies are fully or partly reimbursed if and only if enlisted in the specific list (*Liste des spécialités remboursables aux assurés sociaux*). Drugs supplied within hospitals are enlisted separately (*Liste des spécialités agréées aux collectivités publiques)*. Those lists are modified by Ministerial Decrees after the successful completion of the legal procedure for admittance onto the lists.

Implementation

The CT publishes it advice containing the SMR and ASMR evaluation online on the HAS website. The final reimbursement decision is taken by the Minister by means of a Ministerial Decree and published in the Official Journal. These decrees are available online through the Official Journal website. Final decision implies the mandatory reimbursement by compulsory health insurances. There is no local variation in the implementation. The pharmaceutical level of cost-sharing is identifiable by means of a label (*vignette*). The white crossed label is for expensive and life-saving drugs that are fully reimbursed, the white label is for drugs reimbursed at 65%; the blue label for drugs reimbursed at 35%. An extra orange label was added at the time of temporarily cuts in the reimbursement rate at 15%.

Accountability

The impact of the pharmaceutical reimbursement system is primarily assessed in terms of drug expenditure. Although there is no pharmaceutical budget limitation, the CEPS is responsible for monitoring pharmaceutical expenses in relation to the annual budget targets and to report three times a year. Besides that, the alert committee (C*omité d'alerte*) monitors the global evolution of public health care expenditure and warns the government, the parliament and health insurance institutions in case of high risks of overspending.

Health care system, including pharmaceutical policy is monitored by the High Council for the Future of Sickness Insurance (*Haut conseil pour l'avenir de l'assurance maladie*). This institution created in 2003 is responsible for diagnosing issues related to the health care system. The last annual report included a study on the pharmaceutical (reimbursement) policy. The impact of drug consumption on health effects is not systematically assessed. Although the Directorate for Research, Studies, Assessment, and Statistics (*Direction de la recherche, des études, de l'évaluation et des statistiques*) collects, processes and disseminates statistics in the area of health, the drug-related health impacts are not systematically evaluated.

The CT works under HAS' supervision and at least four times a year, the CT reports its activities to the HAS Board. Moreover minutes of CT's discussion meetings are made publicly available on the HAS website.[124, 125]. The HAS is itself accountable to the parliament and the government. The institution presents its annual report on the activities and performance of the committees once a year. Annual reports are freely accessible on the HAS' website.

The reimbursement procedure is subject to public scrutiny, as it is monitors by administrative and political stakeholders. The Audit Department for Social Affairs (IGAS, *Inspection générale des affaires sociales*) is entitled to conduct evaluation of the health care organisation and monitors the health-related state agencies. The parliament released in 2008 a comprehensive report on the drug policy.[9] Government members are also entitled to comment the drug policy. As an example, in his presentation of *Social Security Funding Act for 2009*, the Minister of Budget pointed the lack of health-economic evaluations within the HAS and called for new measures towards such considerations.

Technology Decision Level

Assessment

The CT is the key advisory body in the French drug reimbursement system. It is entitled to assess pharmaceuticals and to formulate opinions towards pricing and reimbursement decision bodies (CEPS, Minister of Health and UNCAM). In its legal mission, the CT is assisted by the Has, and more particularly by the Service of Pharmaceutical Evaluation. In the early phase of the assessment, an internal expert (employee of the HAS) is designated to monitor the critical assessment of data and evidence submitted by the applicant. Relevant additional scientific literature is also considered The review of the scientific evidence takes into account the internal validity of data (e.g. are the data reliable and not biased), the external coherence (are the findings consistent with other scientific literature available on the same subject) and the clinical effectiveness. A summary document is compiled and send to the CT members at the latest five days before the CT meeting. In case of revision only is the SEM entitled to write an opinion draft.[124]

At the opening of the CT meeting, the internal expert is invited to present the summary document. At the end of this presentation, the reimbursement request is discussed by the CT members. Members can also interview the external experts who were consulted if those are attending the meeting. At the end of the discussion, the CT chairman proposes to vote on a reimbursement opinion. Then, the internal expert drafts the CT opinion, according to the results of the vote. This draft is validated by the CT chairman and send to the members. The next meeting, the opinion draft is adopted by a majority of the votes and send to the applicant.

The latter is entitled to appeal the draft opinion by sending written comments or requesting a hearing to the CT within 8 days. If the applicant does not react, the opinion becomes the final opinion. Otherwise, further discussion about the objections raised by the applicant may lead the members to vote on an revised opinion. This revised opinion is the final opinion.[124] Final opinion should be made within 90 days, although in 2009 the average time was 73 days[129]

The final opinion formulated by the CT typically contains the following elements (art.R163-18 of the CSS):

- The level of medical service rendered (SMR)
- The improvement in medical service rendered (ASMR)
- The assessment of drug use modalities, especially treatment duration and dosage.
- The expected number of patients affected by the therapeutic indications
- The recommendation of the level of co-payment
- Recommendation of the status of medication of exception (to be considered as 'irreplaceable' and highly expensive)
- The assessment of the appropriate packaging with regard to the therapeutic indications.

To key difference between the SMR and ASMR is better understood by means of the questions they seek to answer. The SMR evaluates whether the drug is sufficiently clinically relevant to be reimbursed by the compulsory health insurance while the ASMR assesses whether the new drug improves the clinical state of the patient compared to the alternative treatments.

The **level of medical service rendered** (SMR) is a composite index that evaluates the intrinsic value of the drug for a specific therapeutic indication. Its evaluation is based on the five following criteria (Art. R163-3 of the CSS):

- The level of efficacy relative to adverse effects;
- The place of the drug in the therapeutic strategy, in particular with regard to the available alternatives;
- The severity of the disease treated;
- The properties of treatment: preventive, curative or symptomatic
- The public health benefit

Each criterion is more or less well defined.[125] *Efficacy relative to side effects* is assessed by means of the clinical information submitted by the company. *Place of the drug in the therapeutic strategy* is evaluated taking into account current national or international guidelines written by scientific medical associations. Views of rapporteurs (i.e. external specialist expert in the pathology) are often very important, provided they have no conflict of interest. This becomes especially difficult when it comes to orphan drugs for the treatment of rare diseases. When the new product belongs to a well-known therapeutic category, its efficacy is compared with similar drugs from the same category. For a product in a new therapeutic group, its efficacy is compared with products with the same therapeutic aim. The *severity of disease* criterion is gauged by means of the following questions: is the illness life-threatening? Does it produce a severe deterioration of quality of life? Does it cause serious physical impairments? According to Le Jeunne (2008)[125], this is a more an implicit appraisal, but without much debate around. By means of those first three criteria, the CT assesses the importance of the new drug by evaluating to which extent the new drug does respond to unmet health needs. The relevance of the fourth criterion, *treatment properties*, is less clear as it is not distinguishing in itself. There are multiple examples in which a product can be classified as both preventive and symptomatic. As a result, this criterion rarely determines the final decision.[125] *Public health benefit* was first defined as the direct or indirect improvement on the population's health.

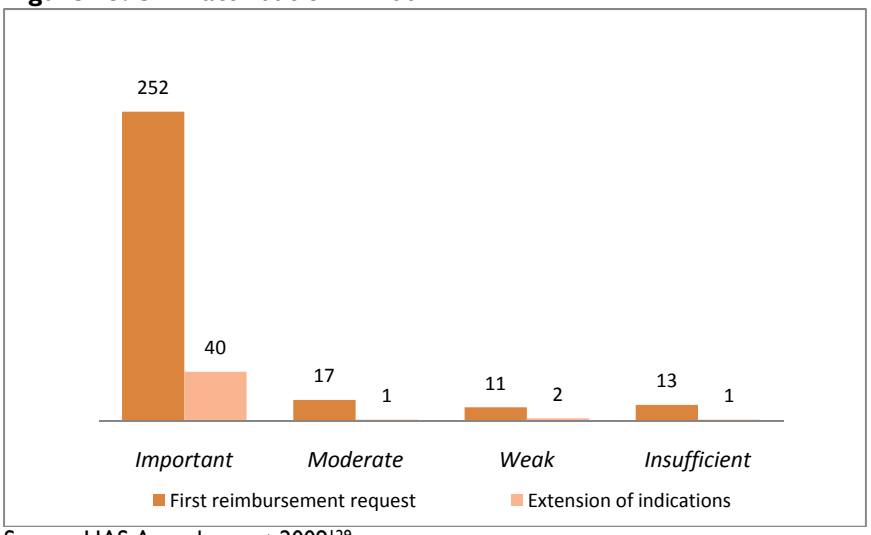
Since 2004, an ad-hoc working group Public Health Benefit (ISPEP, *Intérêt pour la santé publique et Etudes Post-Inscription*) is responsible to assess the pharmaceutical by means of the following dimensions: burden of the disease (incidence and severity of the disease), expected impact on the overall population's health in terms of mortality, morbidity and/or quality of life; expected impact to respond to public health needs; and expected impact on health care organisation, access to other related treatments and extrapolation and external validity of the results.

- The relative contribution of each criterion taken into account in the SMR appraisal is not explicitly known. According to Le Pen (2003), two criteria are key determinants in practice for the SMR rating for new inpatient drugs: efficacy relative to side effects and severity of the disease.[5].
- In 2008, a report commissioned by the French Parliament described clinical efficacy as the primary assessment factor while it pointed the lower impact of the public health impact criterion in the assessment of the SMR. According to the authors, this results in lack of selectivity

The SMR of the product is eventually recognised as *Important*; *Moderate*; *Mild*; or *Insufficient* Table 2 presents the different levels for the SMR. Only drugs with an *Insufficient* SMR are recommended not to be registered on the reimbursement list.[125] The SMR can change over time, varying with any modifications in the data and evidence that support it. The initial assessment often leads to the *expected* medical service rather than *actual* medical service rendered. As a result, the SMR is reassessed every 5 years.

Figure 15 presents the SMR evaluation and attribution for the year 2009 for firstly assessed drugs (first request for inscription for new drugs). One drug can be granted of several SMR levels according to MA *indication*. As only *Insufficient*- judged SMR implies the sending of a negative advice to the Minister of Health, 95% of products requesting reimbursement were deemed suitable to be included onto the positive list. According to the report commissioned for the French Parliament this is large rate of enlisting is partly explained by the current rigorous evaluation for drug market entry.[9] Institutions responsible for market authorisation, the EMA and the AFSSAPS request strong evidence on clinical efficacy relative to side effects from pharmaceutical companies while this criterion is also one of the primary decision factor in the SMR evaluation.

Figure 15: SRM attribution in 2009



Source: HAS Annual report 2009[129]

The **improvement of medical service rendered** (ASMR) complements the SMR and reflects the therapeutic progress.[116, 117]. The ASMR is thus a relative measure that compares the new product with similar available medicines already reimbursed (i.e. similar indications and same therapeutic category).[117]. If the product is first in the therapeutic category, the comparison is done with products similar therapeutic aim (Art.163-18 of the CSS). The relative medical value is assessed by means of direct comparison (the two products are compared in the same clinical trial, i.e. head-to-head comparison) or indirect comparison.[125] Despites well-known limitations, indirect or mixed treatment comparisons are often inevitable due to the fact that reimbursement requests submitted by drug companies usually contain clinical trials versus placebo, rather than an active comparator.[116, 130] As a result, the ASMR appraisal is not straightforward at present.[116] In order to tackle the problem, adjusted indirect comparisons, meta-regressions, mixed models, Bayesian network analyses are some of the tools frequently used to pool results of randomised controlled trials to enable a quantitative synthesis. More recently, the Transparency Committee developed the REAL procedure, a mixture of mixed treatment comparisons and effect model based on expert opinions. It aims to translate the efficacy observed in the trials into effectiveness expected in day-to-day clinical practice.[131]

The ASMR levels attributed by the CT ranges from I to V (Table 18). Drugs attributed an ASMR V can be reimbursed if and only if they allow cost savings for the mandatory health insurance.

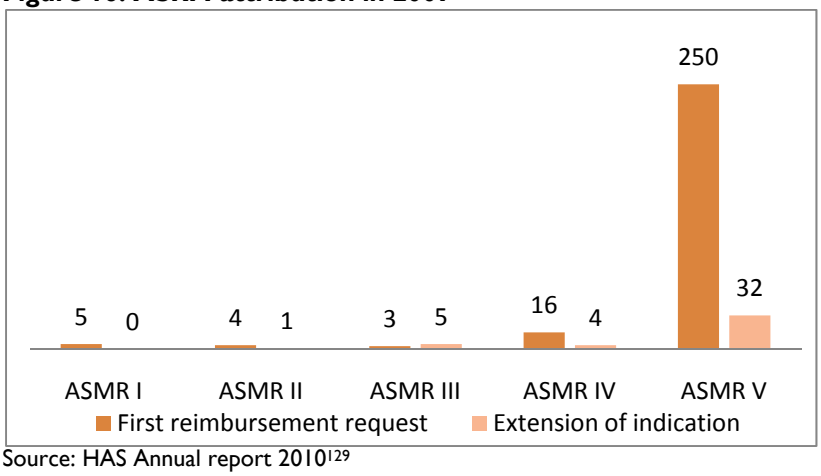
Table 18: the ASMR scale

ASMR I	Major therapeutic improvement
ASMR II	Significant improvement in efficacy and/or reduction in adverse effects
ASMR III	Moderate improvement in efficacy and/or reduction in adverse effects
ASMR IV	Minor improvement in efficacy and/or reduction in adverse effects
ASMR V	No improvement

Source: CT administrative rule[124]

According to Bouvenot (2006), the therapeutic added value reflects the recognition of quantitative improvement (the efficacy of A is twice the efficacy of B), qualitative improvement (A treats patients not responding to B), tolerability improvement, compliance improvement, or improvement in the therapeutic maintenance level.[130] The author states that the ASMR incorporates the expected or noticed therapeutic improvement, and is not simply an innovation premium independent of expected beneficial outcomes. In practice, attribution of ASMR I is rare and mainly restricted to orphan drugs or products that significantly reduce mortality. Noteworthy is the importance of the ASMR assessment for pharmaceutical companies, as it impact on drug-pricing.[125] Figure 16 presents the ASMR score attributed in 2009.

Figure 16: ASRM attribution in 2009



Source: HAS Annual report 2010[129]

According to the pharmaceutical companies association (LEEM, *Les Entreprises du Médicament*), the assessment process is clear and transparent. However they pointed requirements for demonstrating the improvement in medical service rendered (ASMR) that are more and more hard to please[6] resulting in a tendency of low reward for innovation with many products granted ASMR IV and ASMR V. According to the LEEM, systematic downgrading of the ASMR is overcautious as some products are seen truly promising; it results in relatively low drug prices in France and undermines pharmaceutical innovation.

The final CT opinion is the result of a deliberation process among the voter members. The deliberation requires at least twelve voter members to be present. Opinions are adopted with the majority of votes and voting is done by a show of hands, except if one member request secret ballots.[124] The final opinion is sent to the minister, the CEPS, the UNCAM, the CT members and the external experts who took part in the assessment. It is then published on the HAS website and in the official journal of the ministry of health.[124] Noteworthy is that the CT is responsible for advising all at once pricing and reimbursement decision-makers. Consequently, the reimbursement assessment process for a new product does not include a formal health economic evaluation as the price is still not determined by the CEPS. However, the Economic and Public Health specialised Committee (CEESP) is responsible since 2008 to conduct health technology assessment (single or multiple technology assessment) and to give opinions about the cost-effectiveness of treatments or treatment strategies.[120] Those health-economic assessments are often conducted at the time of reimbursement revisions.

Decision Process

The minister of health is responsible for final listing decision advised on that matter by the CT. Only pharmaceuticals with *Insufficient*-judged SMR are not recommended. The CT opinions are not legally binding therefore the minister is entitled to deviate from them. However, the vast majority of the decisions reflects the opinions delivered by the CT. There is one notable exception which is the minister decision regarding large group reassessment and consequent delisting recommendations. Between 1999 and 2001 4490 drugs were reassessed, and the CT concluded that 835 of them showed *Insufficient* SMR. These conclusions drew criticism from the industry and a number of patients and providers so that the minister decided to deviate from the opinions formulated by the CT.[120]

The UNCAM fixes the rate of reimbursement since 2004. The decision has to be taken 15 days after receiving the CT advice. The reimbursement rate must be set in relation to the level of medical service rendered judged by the CT (Table 19). Room for manoeuvre is limited as the UNCAM is entitled to deviate by 5 percentage points up or down.

Table 19: Reimbursement rates according to medical service rendered (SMR)

Medical service rendered (SMR)	Reimbursement rate [margin]
Important	65% [60-70%]
Moderate	35% [30-40%]
Mild	15% [20-30%]

Source: And Art R.322-1 of the CSS

The public health insurance fully reimburses the product in two cases: costly pharmaceuticals considered as irreplaceable (e.g. against AIDS and cancer) and drugs for patients with chronic diseases (the so-called ALD, *Affections Longue Durée*). Some diseases which are not in the list are also free-of-charge when they are costly and constitute a progressive or disabling disorder, with a previous treatment period of longer than six months (the so-called 31st disease), along with multiple diseases of over six month's duration (the so called 32nd disease).[109]

As the reimbursement is defined as a percentage of the price, the price fixing procedure impact on the eventual amount of reimbursement. The CEPS is responsible for the sale price negotiation with the pharmaceutical company (described in art.162-18 of CSS). The price is discussed taking into account the drug ASMR. For products with ASMR from I to III the price is settled taking into account international prices (UK, Germany, Spain and Italy). For products with ASMR IV, the reference is mostly existing reimbursable drugs with similar therapeutic indications although the price might be negotiated with a premium. For products with ASMR V, the drug can be listed only if the cost is under the comparator (impact on the price or on the economic impact of the drug). Other criteria used in the negotiation are the actual or forecasted drug sales; and actual or forecasted market size.[109, 116]

6.1.1.1 Output and implementation

After the Minister decision is published by means of a Ministerial Decree in the Official Journal the reimbursement decision comes in application. At this stage of the procedure, after the final decision has been taken, the pharmaceutical company may only appeal to the supreme administrative court (*Conseil d'Etat*).

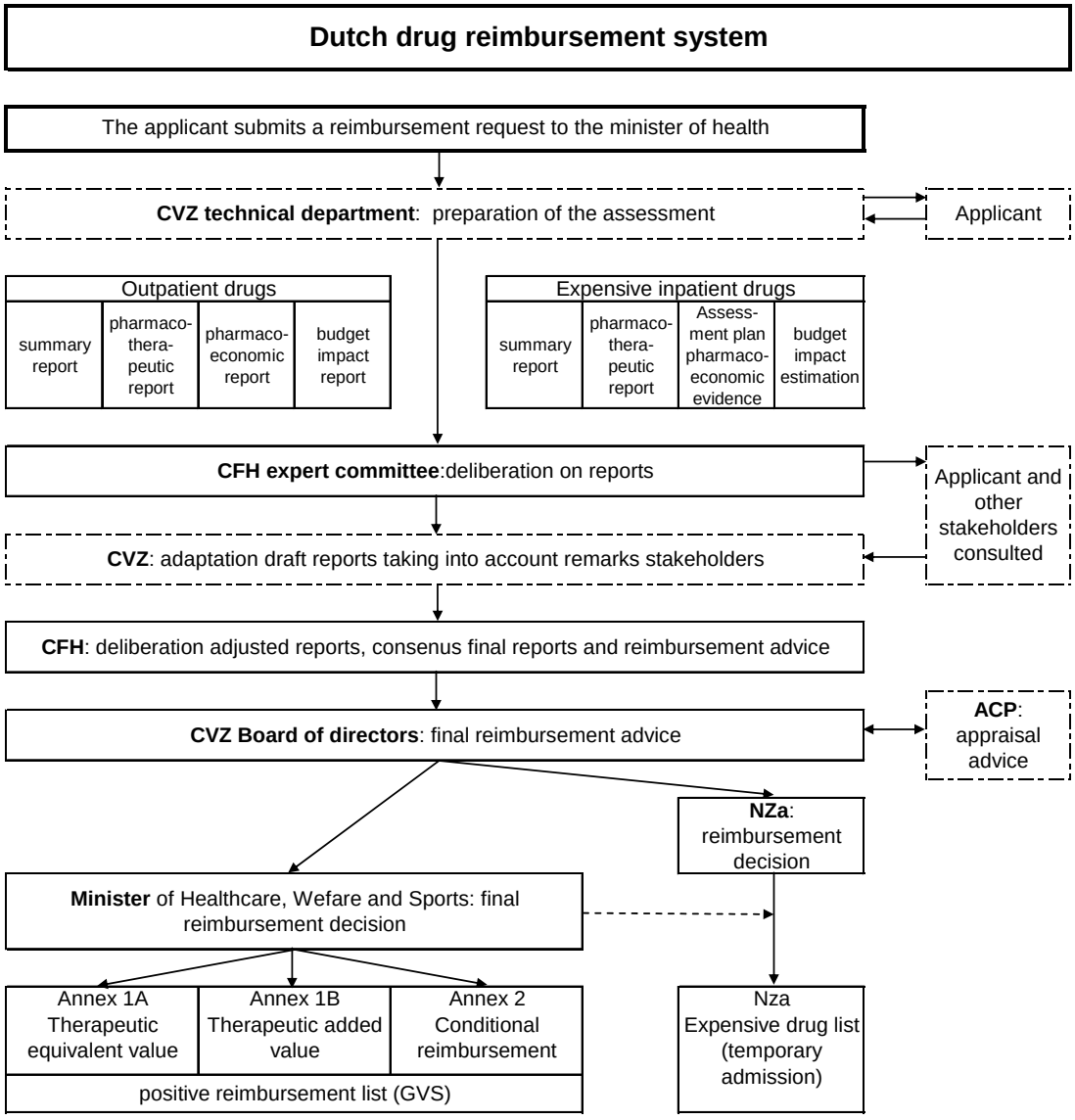
Since 1999, drugs are enlisted for a limited period of five years. The SMR is then systematically reassessed to keep up with up-to-date scientific evidence available. Consequently companies are expected to reintroduce a reimbursement request 180 days before the expiration of the 5 years period. Companies can be requested to conduct post-marketing studies to observe how the drug is used in practice and provide useful data to the CT for the reassessment. The CT analyzes then the *actual* medical service rendered (SMR) with the help of up-to-date scientific evidence and the real conditions of use.

At the same time of the reassessment provision, a vast group revision was launched fro drugs enlisted for decades. From 1999 to 2001, 4490 pharmaceuticals were reassessed. The CT concluded that 835 products had an *Insufficient* SMR, theoretically warranting no reimbursement whilst 840 products were rated with *Moderate* or *Mild* SMR. These re-appraisals were heavily contested by the industry as well as by some patients and physicians. As a consequence, the minister did not precisely follow the CT advice and instead preferred a re-evaluation in three different waves. In 2003, 72 products were removed from the positive list. In 2005, 364 out of 403 drugs were delisted whilst other products saw their reimbursement rate temporarily cut from 35% to 15% until delisting scheduled by 2008. Lastly, in 2006, 89 out of 238 were delisted and remaining products saw their reimbursement rates temporarily cut to 15% until 2008. Since then, group of drugs revision have been regularly reviewed and updated at the request of the Ministry of Health, the National Union of Health Insurance Funds, the HAS Board members or at the CT's own initiative.

Key points France

- **Only drugs included in the positive lists are reimbursed by the compulsory health insurance**
- **Reimbursement request submitted by the company.**
- **Minister of health responsible for the final enlisting drug decision whereas the UNCAM is responsible for level of coverage and the CEPS for the price.**
- **The Transparency Committee (CT) is the expert committee advising the final decision-makers by means of two evaluations: the medical service rendered (SMR) and the improvement in the medical service rendered (AMSR)**
- **SMR evaluation serves the enlisting and coverage decisions. It is gauged by means of: level of efficacy relative to adverse effects; place of the drug in the therapeutic strategy; severity of the disease; properties of treatment and public health benefit**
- **ASMR evaluation serves the enlisting and pricing decisions. It evaluates the therapeutic added value of the drug and use a five category scale.**
- **The CT mainly consists of academics and practitioners with notable pharmacological and medical skills. Representatives of the ministries, pharmaceutical industry and sickness funds have a consultative voice only.**
- **Voting is done by a show of hands. A simple majority is required to approve or reject a proposal.**
- **Minister of health is allowed to deviate from the CT advice but in practice it rarely occurs. CEPS and UNCAM may narrowly deviate from the CT advice.**
- **The final CT advice on SMR and ASMR are publicly available of the HAS website.**
- **The company may appeal the reimbursement decision although on procedural grounds only.**

DRUG REIMBURSEMENT SYSTEM IN THE NETHERLANDS



DUTCH HEALTH CARE STRUCTURE

Characteristics of the Dutch health care system

The Dutch government is responsible for the accessibility, efficiency and quality of health care, the implementation of health care arrangements mainly relies on actors outside the government.[132] This results in strong interdependencies in health policy between government, health insurers, providers and patient organisations.

Like many other countries, the Dutch system passed various waves of health care reforms as described by Cutler.[133] After the first wave of arranging universal coverage and equal access, the system advanced in the early 1980s to the second wave of cost containment and central control. From the late 1990s the health care reforms evolved to the third wave and focussed on the introduction of the market principle in health care. In 2006, the new Health Insurance Act (ZVW) came into effect and the health care system progressed to a regulated market with managed competition between insurers and providers.

Health care funding and pharmaceutical expenditure

In 2008, total expenditure for health care was 9.9%[ii] of GDP, which is slightly higher than the OECD average of 8.9%; health expenditure per capita was US$ 4063[ii].[71] The Dutch health system has a social health insurance system, funded from public and private sources. The long term care sector is primarily financed from income taxes. Private funding for the acute care sector is based on a social health insurance. Since 2006, all residents are obliged to take out universal basic health insurance under the new Health Insurance Act (ZVW) and competing health insurers are obliged to accept all applicants for the basic benefit package (Article 2.1 and 2.2 ZVW). Adults pay a flat rate premium, a subsidy scheme (*"Zorgtoeslag"*) relieves financial burden for lower incomes. In addition, supplementary private health insurance is offered on a voluntary basis.

Pharmaceutical expenditure increased around 5% per year during 1995-2007.[134] The rise in expenditure over the last decennium is foremost related to a rise in utilisation (volume) and only partly to higher prices.

In 2008, pharmaceutical expenditure per capita was €335, of which €52 is related to expensive inpatient drugs.[135] The expenditure per capita is 17% lower compared to the average of €403 in other western European countries (ibid.). From 2004 to 2008, expenditure for expensive inpatient drugs increased substantially from 130 million to 186, 266, 318 and 380 million respectively.[136]

Pharmaceutical policy tools

Several policies are applied to manage and control pharmaceutical expenditure. The government can enforce price reductions and impose maximum prices on the legal basis of the Act on Pharmaceutical Prices (WGP). The maximum price is based on a price reference system using prices from four countries, namely Germany, Belgium, France and the United Kingdom. The WGP prices are biannually revised. Another governmental tool to manage prices is the GVS (Drug Reimbursement System). Pharmaceuticals are only reimbursed if they are admitted on the positive reimbursement list in the GVS. The maximum GVS reimbursement limits were for the last time evaluated in 1999, therefore, the reimbursement limit is often higher compared to the maximum drug WGP price. In addition, a number of "claw-back" agreements have been made between the government and pharmacy retail in order to skim procurement rebates and bonuses. Several major health insurers have managed collectively to lower the reimbursed price of frequently used generic drugs (so called preferential policy) for cholesterol lowering and ulcer management in 2008.

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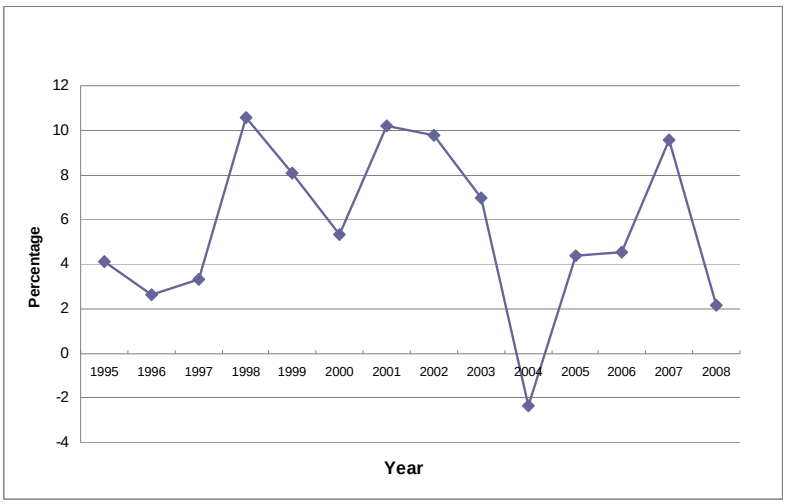
ii OECD estimate

jj OECD estimate

Figure 17 shows the effects of cost containment policies. Most evident are the introduction of the positive reimbursement list (1995), WGP (1996), (extended) claw-back agreements (1998, 1999, 2000 and 2004-2007), evaluation GVS reimbursement limits (1999) and insurers preferential policies (2008 and 2009). It is estimated that the combination of the claw-back agreements, WGP reference pricing and preferential policies saved €1,510 million in 2008.[134]

Figure 17: Annual pharmaceutical growth rates 1995 – 2008



Source: [134]

Cost sharing policies

The Netherlands has limited co-payments policies for consuming health care. The OECD estimates that out-of-pocket expenditure is accountable for about 5.7%[kk] of the total expenditure on health services.[71] The new Health Insurance Act introduced in 2006 a no-claim refund for all insured persons from 18 years and older. In January 2008 the no-claim was replaced by a compulsory deductible (€155 in 2009). Maternity care, General Practitioner care and care for persons under the age of 18 year are exempted from this cost sharing policy. Persons with a chronic illness or impediment, based on pharmaceutical cost groups, receive a financial compensation for this compulsory deductible (€50 in 2009). In addition, insured may choose for a voluntary deductible up to a maximum of €500 in exchange for a premium rebate.

Cost sharing for pharmaceuticals only applies to outpatient drugs. Drugs are reimbursed after admission on the positive reimbursement list. Therapeutic equivalent drugs are reimbursed until the average product price within a therapeutic group. Consumers have to pay costs beyond this reimbursement limit. In 2008 total national co-payments for these drugs were €37 million, only 0.7% of total pharmaceutical expenditure.[134] Drugs with a therapeutic added value are fully reimbursed. OTC drugs are not refunded; in 2008 consumers spent €725 million on non-prescription drugs, accounting for 12.1% of the total pharmaceutical market.[137]

kk OECD estimate for 2008

DESCRIPTION OF THE DRUG REIMBURSEMENT SYSTEM

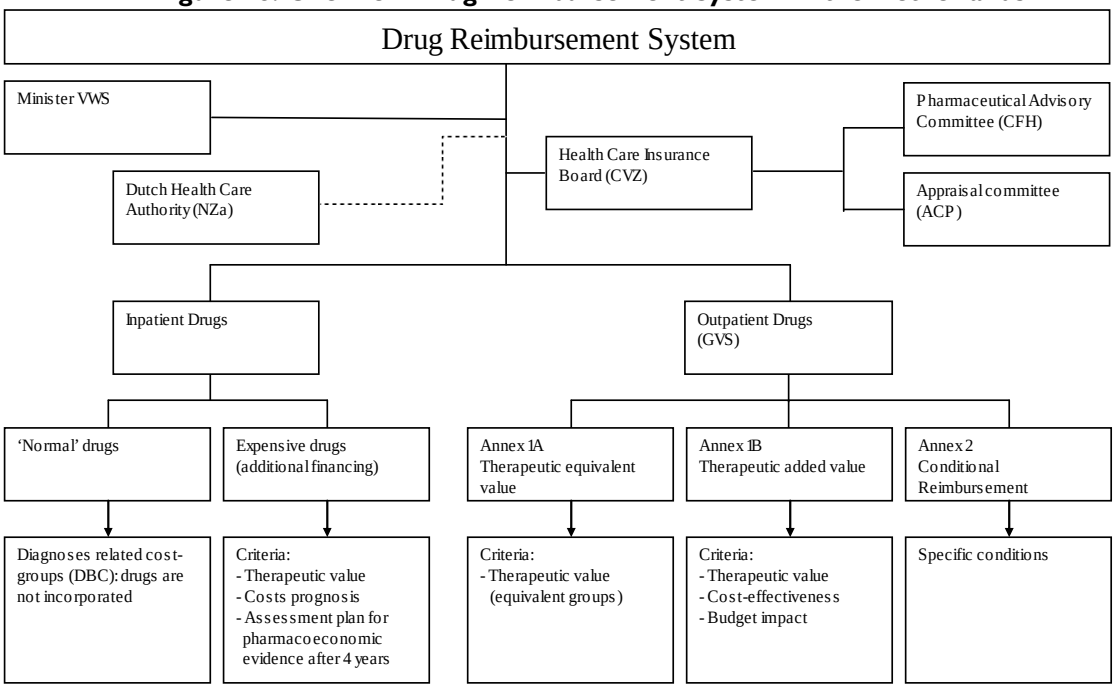
Overview drug reimbursement system

In accordance with the Act on Provisions of Pharmaceuticals (WOG), pharmaceuticals can enter the Dutch market after a positive assessment by the Dutch Medicines Evaluation Board (CBG) on quality, safety and effectiveness (the first three "hurdles"). A European trading licence can be obtained from the European Medicines Agency (EMA). After market approval, medicines do not automatically qualify for reimbursement. The drug reimbursement system (GVS), introduced in 1991, determines whether or not the product will be included in the basic benefit package (the so called "fourth hurdle").

Reimbursement schemes for inpatient and outpatient drugs differ. Outpatient drugs fall under the drug reimbursement system (GVS). The GVS determines the reimbursement level and whether medicines are prescription-only or self-medication drugs (OTC). Drugs on the positive reimbursement list can be placed on Annex 1A or 1B. In Annex 1A, therapeutic equivalent drugs are grouped into clusters of interchangeable drugs. The reimbursement level is limited to a historically determined average product price of the cluster. Pharmaceuticals that are not interchangeable and have an added therapeutic value are placed on Annex 1B. All drugs on Annex 1B are fully reimbursed. Manufacturers have to submit evidence of the therapeutic value in order to obtain a reimbursement decision. In addition, for Annex 1B, manufacturers have to provide evidence on cost-effectiveness and an assessment of the national budget impact. Drugs on Annex 1A and 1B can also be placed on the conditional reimbursement list (Annex 2) if specific conditions apply (e.g. prior permission or specific indications).

Inpatient drugs dispensed by hospitals are financed through hospital budgets based on diagnosis related cost groups. However, "normal" drugs are not separately specified within these groups. The Dutch government introduced in 2002 policy regulations (*"Beleidsregel dure geneesmiddelen"*) to relieve the financial burden of hospitals for expensive inpatient drugs. Since 2006, a "coverage with evidence development" scheme was introduced, in such that drugs are initially only temporarily admitted on the expensive drug or expensive orphan drug list of the Dutch Healthcare Insurance Board (NZa). Hospitals receive additional funding of 80% of the costs of these drugs (100% for orphan drugs). As condition, applicants are required to conduct outcomes research and thus have to provide evidence on appropriate drug use (*"doeltreffende toepassing"*) and real-world cost-effectiveness (*"doelmatigheid"*). After four years, a reassessment ought to be conducted in order to decide whether or not to continue the financial compensation for hospitals. Figure 18 provides an overview of the Dutch reimbursement system.

Figure 18: Overview Drug Reimbursement System in the Netherlands



Since the early 1980s HTA became a policy tool for priority setting in the Dutch health care.[132] It was mainly targeted at benefit package decisions for arising expensive health technology innovations. The Dutch Committee on Choices in Health Care explicated HTA as a tool for structured assessment of the entitlements in the basic benefit package package.[138] The suggested funnel of Dunning has four criteria to facilitate decision-making in determining a basic benefit package: the technology should be necessary, effective and affordable (e.g. individuals cannot bear the responsibility for the actual costs). Ever since, the Dutch government continued to expand the role of HTA in health care decision making, especially regarding drugs. Since 2002 the Dutch Health Care Insurance Board (CVZ) encouraged pharmaceutical companies to submit a pharmacoeconomic evaluation report alongside a therapeutic effectiveness report for new innovative pharmaceuticals. The submission of pharmacoeconomic evidence became mandatory in January 2005 for all drug reimbursement applications that claim to have a surplus therapeutic value and opt for admission on Annex 1B. The following section analyses the Dutch "fourth hurdle" system for entitlements for drug reimbursement in detail and describes the application of HTA within this system according to the Hutton framework.[40]

Policy Implementation Level

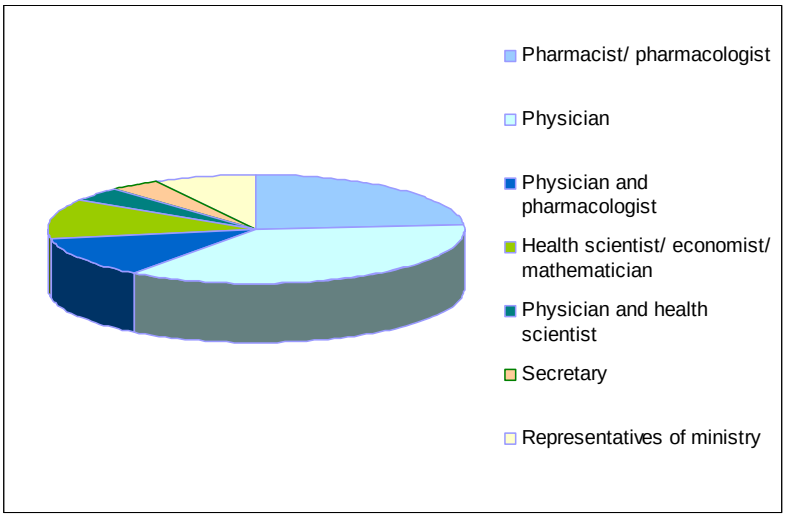
Establishment

The Health Insurance Act (Zorgverzekeringswet; Art. 63-66), Health Insurance Ordinance (Besluit Zorgverzekering; Art. 2.8) and the Health Insurance Decree (Regeling Zorgverzekering) establish the legal basis of the reimbursement system for pharmaceuticals. The main parties involved are the Minister of Healthcare, Welfare and Sports (VWS), Healthcare Insurance Board (CVZ) (including the Expert Pharmaceutical Advisory Committee (CFH) and the Appraisal Committee (ACP)) and the Healthcare Authority (NZa). Briefly, the reimbursement pathway is as follows. Manufacturers have to submit an application for a new drug for admittance on the positive list of the reimbursement system (GVS) to the Minister of Health. The CVZ performs the actual assessment and appraisal of the product and advises the minister who makes the final reimbursement decision. A different pathway exists for expensive inpatient medicines.

In this pathway, according to the Health Care Tariffs Act (WTG) the legal parties allowed to submit an application for additional funding of expensive drugs are the Dutch Federation of University Hospitals (NFU), the Dutch Hospitals Association (NVZ), Medical Specialists Association (OMS) and Dutch Health Insurance Organisation (ZN). The CVZ advises the NZa whether or not the drug should be provisionally admitted on the list for expensive inpatient drugs. In both pathways, the minister makes the final decision and can reject CVZ's advice and overrule NZa's decision.

The CVZ has the legal responsibility to manage and advise the minister on the entitlements of the basic benefit package provided by the Health Insurance Act (ZVW) and the Exceptional Medical Expenses Act (AWBZ). CVZ is an independent agency funded by the government with three executive board members appointed by the minister and approximately 400 employees. Within the CVZ, the technical department "benefit package management" has 12 employees with expertise in pharmacotherapeutics and pharmacoeconomics who prepare the assessment of the pharmaceutical reimbursement dossiers. The expert committee CFH has maximal 24 members with expertise in various medical disciplines, pharmacology, health science and economics (see Figure 19). Additionally, two or three representatives of the ministry are attending CFH meetings as observers. The committee meets once a month to assess pharmaceutical reimbursement dossiers. Annually, CVZ advises the minister on average on 30 to 40 reimbursement requests (including expensive inpatient drugs).

Figure 19: Composition of the CFH committee*



*Composition in June 2010

Furthermore, the ACP, committee advising CVZ's Board of Directors on the entitlements of the total basic benefit package (also non drugs), has, besides three CVZ board of director's members, six members with expert knowledge in social security, healthcare and health insurance from a scientific, daily practice and patient perspective. This committee meets every other month.

The NZa has two economists, who are responsible for the policy for expensive inpatient drugs and the judgement of the pharmaceutical reimbursement dossiers received from CVZ.

Finally, within the department GMT (Drugs Technology) of the ministry of Health, two senior policy employees consider CVZ's advice in the reimbursement dossiers and prepare the final decision which is taken by the minister of Health.

Table 20 provides an overview of the main actors and their responsibilities in the reimbursement process.

Table 20: Key actors involved in the reimbursement process

Institution/ Actor	Function(s)
Healthcare Insurance Board (CVZ)	Is responsible for the drug reimbursement process from application to reimbursement advice; the technical department communicates with manufacturer, prepares the assessment, drafts advice reports, sends the advice reports to the minister and publishes these reports online.
Expert Pharmaceutical Advisory Committee (CFH)	Is responsible for the assessment of the reimbursement advice.
Appraisal Committee (ACP)	Is responsible for the appraisal of the basic benefit package (including drug reimbursement advices).
Board of Directors of CVZ	Is responsible for the final reimbursement advice.
HealthCare Authority (NZa)	Is responsible for the expensive inpatient drug list.
Minister of Healthcare, Welfare and Sports	Is responsible for making the final reimbursement decision.

System objectives

The Dutch drug reimbursement system (GVS) has the objective to control the financing and the entitlements to outpatient pharmaceuticals.[139] The NZa policy for expensive inpatient medicines has the objective to ensure accessibility to expensive drugs by releasing the financial burden of hospitals. The minister states that pharmaceutical care aims to guarantee safe and efficient care according to individual patient's need and should be in concurrence with daily practice and scientific standards.[140] The CVZ has the legal responsibility to advise the minister on the basic benefit package. Their mission is to *"safeguard and develop the public preconditions for the health care insurance system, so that Dutch citizens can obtain their right to health care"*.[141] The main considerations for entitlements of the basic benefit package are: quality, accessibility and affordability.[142]

Scope of the system

The scope of the drug reimbursement system is determined as part of the legal basis in the Health Insurance Act and the Health Insurance Decree. To obtain a reimbursement decision, all new pharmaceuticals have to comply with the legal procedure to submit an application for admittance on the positive reimbursement list. The pathway for an application for Annex 1A is shorter compared to Annex 1B since the latter one also requires a pharmacoeconomic assessment. Drugs on the positive list are assessed at launch only and are not systematically reviewed, whereas drugs on the expensive inpatient drug list ought to be reviewed after four years. The first reviews are expected to be conducted at the end of 2010.

Implementation

The CVZ publishes its advice to the ministry online on its website. The final reimbursement decision is made by the minister of health and sent to Farmatec. This agency is responsible for setting the reimbursement limit and the maximum price. Both are biannually reported in the State Journal *("Staatscourant")*. The ministry puts the drug on the positive list in the "Health Insurance Decree", as published in the State Journal. Positive decisions on expensive inpatient medicines are online published by the NZa. Additionally, all new drugs are included in the *"Farmacotherapeutisch Kompas"*, an extensive national drug formulary issued by the CFH and CVZ with guidelines for physicians on the application of pharmaceuticals.

Final decisions are mandatory and health insurers are obliged to reimburse these drugs. In case of special conditions for reimbursement (Annex 2), health insurers should monitor the reimbursement.

Some local variation in prescribing may occur since physicians can interpret guidelines differently, hospitals may feel the burden of expensive pharmaceuticals despite the financial compensation (only 80%). In addition, health insurers can implement various "preferential" policies which may result in different applications of generics.

Accountability

The impact of the reimbursement system is assessed by monitoring pharmaceutical expenditure. Since 1988, the Drug Information System (GIP) of CVZ monitors utilisation and expenditure of outpatient prescription drugs, based on a sample of 75% of the Dutch population obtained from eighteen health insurers.[134] The Foundation for Pharmaceutical Figures (SFK) monitors expenditure for expensive and orphan inpatient drugs.

It should be noted that there are no national drug budget limitations, outpatient pharmaceutical expenditure is an open-ended part of the total health care budget. As mentioned before, expenditures are limited by setting maximum reimbursement limits, and utilisation is monitored by health insurers. The remaining costs (20%) for expensive inpatient drugs come under hospital budgets.

The impact of drug utilisation on health effects is not specifically evaluated at a national level. The National Institute for Public Health and the Environment (RIVM) monitors the health of the Dutch population at an aggregate level but does not observe drug related health effects.

The minister of health is responsible for healthcare policy and healthcare expenditure and is accountable to the Dutch parliament. The NZa and the CVZ, including CFH and ACP, are accountable to the minister. There is no system of recurring performance assessments on the impact of the reimbursement system; however, ad hoc evaluations occur when issues arise. For example, "Dutch guidelines for pharmacoeconomic research" were in 2005 evaluated and updated by an expert committee. In 2006, policy regulations for expensive inpatient drugs were evaluated after media attention regarding "postal code" describing of the drug Herceptin. As consequence, the previously varying reimbursement levels were set at a fixed percentage of 80%.

In 2008/ 2009, CFH started a project to improve transparency and consistency of decision making and CVZ commenced a similar project for pharmacoeconomic assessments. The work processes of CVZ are ISO certified and CVZ has signed the Dutch Charter Group Public Accountability. Consequently, CVZ is audited by independent external parties. CVZ also initiated ad hoc evaluations performed by external parties on parts of the drug reimbursement system (e.g. evaluation of the conditional reimbursement instrument Annex 2).

Most interviewees, representing different stakeholders, acknowledged that accountability of the drug reimbursement system is mainly established by relying on a system of "check-and-balances". If an issue arises in any part of the system, the system will put forward the message and actions will be taken accordingly.

Technology Decision Level

Assessment process

The assessment starts when a formal application is submitted and should be finalised within 60 days (expensive inpatient drugs) or 90 days (outpatient drugs). This deadline is not always met. CVZ often needs another four to six weeks before the final advice is sent to the minister, this delay is mainly ascribed to lack of staff capacity and increasing complexity of reimbursement dossiers. After the final advice, it takes another three to four weeks before the minister has made a final decision. Two CVZ reports describe in detail the assessment procedure for outpatient and expensive inpatient pharmaceuticals.[143, 144] Additionally, the CVZ published a report on managing the basic benefit package and a report with detailed guidelines on how to provide pharmacoeconomic evidence for a reimbursement application.[142, 145, 146]

At an early stage, CVZ offers applicants the opportunity to obtain scientific advice regarding the required pharmacoeconomic evidence. Manufacturers are encouraged to make use of this opportunity, which frequently occurs, especially regarding Annex 1B applications. CVZ assigns the reimbursement dossier to two persons from the technical department (i.e., secretariat or department "basic benefit package"), one person with pharmacoeconomic expertise and one person with medical or pharmacotherapeutic expertise. Additionally, CVZ offers manufacturers a consultation about the draft application before submission. CVZ promotes this pre-consultation and most applicants use it. CVZ attempts to assign a core team to a reimbursement dossier for the entire process from scientific advice until final decision on the reimbursement advice.

A formal application can be submitted as soon as a drug is registered and market approval has been obtained. Exception exists for early assessments of drugs for diseases where no other drugs are available or drugs that received an accelerated approval.[144] A formal application for Annex 1A should include pharmacotherapeutic evidence; an application for Annex 1B should also include cost-effectiveness evidence and a budget impact assessment. Generic products and parallel imported products applying for Annex 1A may follow a shorter pathway and are not evaluated on therapeutic value and cost-effectiveness by CVZ, these applications are sent directly to the ministry of health. Applications regarding expensive inpatient drugs require evidence on the therapeutic value, a cost prognosis and a detailed study plan for obtaining pharmacoeconomic evidence in daily practice.

The technical department prepares four draft reports for the CFH meeting: a summary report, pharmacotherapeutic report, pharmacoeconomic report and a budget impact report. All submitted evidence is assessed and a literature review is performed to search for additional evidence. In this preparation time, there is contact between the applicant and CVZ staff, applicants may be asked to present additional information. If deemed necessary by CVZ staff, experts and stakeholders are consulted. All evidence is accumulated in draft reports. One and a half week before the CFH meeting, the complete file, including all accumulated evidence, draft reports and economic models for pharmacoeconomic specialists, is sent to CFH members. The file contains a letter with a concise explanation and issues to be discussed.

In the next phase, the application is evaluated by the CFH. The technical department has a preliminary discussion before and a debriefing after every CFH meeting. Reimbursement dossiers appear at least twice at a CFH meeting. In every meeting, expert committee members have to express any conflict of interests, in which case they are excluded from taking part of the discussion or they might have to leave the room. CFH meetings are confidential and not open to the public. Two or three representatives of the ministry attend CFH meetings in order to obtain inside information on the process. They are only allowed to observe, they do not take part of the discussion nor have rights regarding the final reimbursement advice. The technical department first present the case to the CFH expert committee, after which the case and the draft reports are discussed. Reimbursement dossiers are not assigned to specific CFH expert committee members.

The first task is to establish the pharmacotherapeutic value of a drug and to evaluate if the drug can be clustered with other therapeutic equivalent drugs (Annex 1A) and determine the position of the drug within the national formulary (*"Farmacotherapueutisch Kompas")*. Drugs opting for Annex 1B additionally require a pharmacoeconomic assessment. All evidence and draft reports are discussed when a reimbursement dossier appears for the first time on the CFH agenda. In this phase, both CVZ and CFH can suggest to consult other experts in order to obtain more specific information. After the CFH meeting, the technical department discusses the required actions and sets deadlines for adjusting the reports. The technical department team members continue to work on the case. The CFH secretary sends the adjusted reports to the applicant and other relevant stakeholders. CVZ appoints these relevant stakeholders, the CFH can be involved in identifying stakeholders. Stakeholders are amongst others physicians, physician associations, patient associations, health care insurers, hospital associations. All stakeholders have one or two weeks to put forward their comments. In this phase, the applicant can ask for a "clock-stop" if assumed that more time is needed for acquiring additional data. All new evidence, adjusted reports and written replies from stakeholders will then reappear at the next CFH meeting. The last time a dossier is assessed in the CFH, comments for the final reports are evaluated.

> Although applicants have to submit a report on the expected budget impact and the budget impact is estimated in reimbursement dossiers, it is not a formal assessment criterion for the CFH expert committee. Nevertheless, budget impact might play an additional role in the appraisal and final decision-making phase. Several research papers have been published describing that budget impact influences decision making.[1-3]

The assessment phase of the CFH is followed by an administrative route within CVZ. This route has two different options, namely a shorter route in which the Board of Directors' chairman completes the dossier (e.g. Annex 1A applications) and a longer route in which case the dossier is discussed at the meeting of the Board of Directors. In the latter option, applicants and other relevant stakeholders receive the draft letter of advice to the ministry and have the opportunity to put forward their response. This route involves for example procedural issues, Annex 2 conditions and if the Annex assignment differs from the application. Additionally, the CVZ chairman can invite stakeholders to clarify their comments in a hearing. During the administrative route and in the case of potential societal implications, it is possible that the ACP discusses the reimbursement dossier. In principle, the ACP does not evaluate each individual reimbursement dossier. However, both the Board of Directors or ACP committee members can put individual reimbursement dossiers on the agenda. The meetings of the Board of Directors are every fortnight and are not public, whereas ACP meetings are public. This administrative route is the last phase in the reimbursement process within CVZ.

Assessment criteria

As mentioned before, main considerations regarding entitlements of the basic benefit package are: quality, accessibility and affordability.[142] For the actual assessment, CVZ uses four main principles, namely necessity, effectiveness, cost-effectiveness and feasibility, as inspired by the abovementioned "Dunning" report criteria.[145] CVZ maintains no hierarchy in these criteria.

The actual assessment of pharmaceutical reimbursement dossiers is conducted by CFH. Firstly, the pharmacotherapeutic value of the drug is evaluated, and the position of the drug in the professional *"Farmacotherapeutisch Kompas"* guidelines is determined. The CFH applies several criteria to assess the therapeutic value, namely effectiveness, efficacy, side effects, experience, applicability and user-friendliness. There is no formal hierarchy in these criteria; they are balanced per disease category and compared with usual care. Randomised clinical trials are seen as the golden standard for determining effectiveness and efficacy.[144]

Besides that, it is important that the drug is according to current medical standards or, in absence of such standards, considered as responsible and adequate care (Art 2.1 Health Insurance Ordinance). Uncertainty in effectiveness evidence may force applicants to submit enhanced evidence or lead to a lower estimate of the therapeutic value or to restricted reimbursement (Annex 2). Possible assessment outcomes are less value, similar value or added therapeutic value. Drugs with similar value are clustered together (Annex 1A) and are then placed within the national formulary guidelines *("Farmacotherapeutisch Kompas")*. It is important to realise that there is no rating of the amount or degree of added value.

Although there is no formal hierarchy in assessment criteria, most interviewees stated that effectiveness, efficacy and side effects were often the most important criteria determining the therapeutic value. Interviewees also acknowledged that the majority of time in a CFH meeting is devoted to determining the therapeutic value, less time is spent on assessing cost-effectiveness evidence.

Only drugs with an added therapeutic value can opt for Annex 1B. This requires an additional assessment of pharmacoeconomic evidence. Generally, pharmacists and medical experts focus on the therapeutic evidence and health scientists and economists deliberate on the pharmacoeconomic evidence. CVZ's report on pharmacoeconomic research guidelines describes the requirements for pharmacoeconomic studies.[146] These guidelines are used as a framework for the assessment of pharmacoeconomic evidence. The CFH expert members determine how solid and robust this evidence is, uncertainty around the estimated (incremental) cost-effectiveness will lead to less robust evidence. The outcome of these assessments is either sufficiently founded or insufficiently founded pharmacoeconomic evidence; no degree of robustness is applied. Thus far, the CFH states no formal opinion on the cost-effectiveness ratio of the drug.

The assessment of expensive inpatient drugs is mainly focused at establishing the therapeutic value of the drug, for which the same criteria are used as described above. At the first assessment, uncertainty regarding real-world (cost)-effectiveness is the rule. However, if the drug has proven to be effective in a trial, has an added therapeutic value and the expected cost are high (costs are >0.5% (5%) of the total annual hospital pharmaceutical budget for this expensive inpatient (orphan) drug), the drug is most likely admitted on the expensive drug list. After four years, a reassessment based on the actual costs, therapeutic value in clinical practice, appropriate use and real-world cost-effectiveness should be conducted. At the end of 2010, the first reassessments are expected.

The Guidance for Outcomes Research *("Leidraad voor uitkomstenonderzoek")* for expensive inpatient drugs recommends basing the decision which additional data needs to be collected on a Value of Information Analysis.[4] However, so far all study plans for outcomes research for expensive medicines opt for broad data collection. Interviewees acknowledged that the outcomes research study plan is almost certainly satisfactory if the plan describes that much data will be collected in the following years.

Appraisal criteria

CVZ's Board of Directors decides on the final reimbursement advice to the minister considering the final CFH reports and additionally taking into account other relevant policy criteria such as public interests, public support and ensuring the public preconditions of the health care system.[143, 144] As previously mentioned, if decided by the Board of Directors or ACP members, the ACP can evaluate an individual drug reimbursement dossier. The ACP has the task to appraise the technologies and balance the different criteria from a societal, scientific and patient perspective. The ACP was set up in 2008 and has formulated CVZ principles in more detail. For example, the ACP operationalised disease severity using the proportional shortfall approach.[142] The ACP makes a broad societal evaluation of pharmaceuticals, not only including disease severity, effectiveness, cost-effectiveness and feasibility, but also other societal aspects such as the necessity to insure a health care service, budget impact, rarity of diseases, the amount of informal care required and public health risks.[142] However, since the ACP only recently operationalised the appraisal criteria in more detail, it is at the moment still unclear to what extent ACP's appraisal criteria will influence CVZ's reimbursement advice.

The minister may consider additional appraisal criteria such as societal aspects and political developments. For example, interviewees stated that accessibility (e.g. drugs for orphan diseases) is extremely important and that different criteria should be balanced all together.

Finally, it is important to realise that the CFH and CVZ advice the minister on the robustness of the cost-effectiveness evidence and up till now do not appraise the actual cost-effectiveness ratio, whereas the minister makes the final decision. The minister does not state to use a threshold (range) for the cost-effectiveness criterion. At the moment, it is still unclear if the newly installed ACP committee will take the lead on advising on value for money in the near future. In 2006, the Dutch Council for Public Health and Healthcare suggested an upper threshold range of 80,000 euro per QALY gained for severe illnesses, which attracted much public debate.[147] In 2009, the CVZ published for the first time a threshold range from 10,000 euro per QALY for a less severe illness up to 80,000 euro per QALY for a severe illness in their report on managing the basic benefit package.[142] However, CVZ stated that this range is purely an indication and not a prediction for their final advice since the latter also takes other criteria into consideration. Moreover, the minister has neither confirmed nor taken over this threshold range.

Decision Process

The decision process can be separated into the decision processes at CVZ and the process at the ministry. As mentioned before, a reimbursement dossier appears at least twice at a CFH meeting. In the last meeting, the CFH usually reaches consensus on the final reports (CFH and pharmacotherapeutic report, and if applicable pharmacoeconomic and budget impact report) and the reimbursement advice, otherwise majority voting will determine the final advice. After consulting the ACP if applicable, the Board of Directors puts the final advice down in a letter to the minister. The advice modes are: no reimbursement, admission on Annex 1A or Annex 1B (GVS) or temporary admission on the NZa expensive drug list. Additionally, drugs may receive an Annex 2 restriction, such as restrictions for specific indications or user groups and access restrictions (e.g. specialist only prescriptions, consent requirement from health insurer). After the Board of Director's decision phase, the CFH reports and advice letter are sent to the minister, the applicant and all stakeholders. These final reports are also published online on CVZ's public website.

The GMT department of the ministry formulates a management summary for the minister based on CVZ's advisory reports and on the elapsed procedure. This management summary is not publicly available. The final reimbursement decision is made by the minister; CVZ's advice is seldom overruled.

Outputs and implementation

During the administrative route within CVZ, applicants and other relevant stakeholders can put forward procedural issues according to the "Participation Procedure" *("Inspraakprocedure")*. As mentioned before, they receive the draft letter of advice to the minister and are invited to express their response. The chairman of the Board of Directors can invite stakeholders to clarify their comments in a hearing in order to improve the process of careful decision making.[143, 144] Applicants can ask for a reassessment if circumstances have changed or new knowledge has become available.

According to Health Insurance Act (Art. 116), any involved party can appeal to a decision of CVZ or the minister at the Administrative Court. If applicable, the manufacturer is the party who appeals to the court. In the case of Plavix® the cardiologists association appealed. So far, most court cases were in favour of CVZ. Recently, it has become more common to start an "Expert Review" *("deskundigenbericht")*, which entails a reassessment of the reimbursement application by other external experts focused on the content of the application. Expert reviews often precede a court case in order to determine the opportunity to bring the case to court with the Expert Review as additional evidence. In contrast with the Expert Review, general court cases are based on procedural grounds. Interviewees, both from CVZ and the ministry, stated that the amount of Expert Reviews and court cases have increased the last years. At the moment around 7 new cases per year use these formal appeal options.

Implementation follows after the final reimbursement decision. Final decisions are mandatory and health insurers are obliged to reimburse these drugs. To facilitate the implementation of a new drug, all drugs are included in the national drug formulary. Diffusion of the drug might depend on professional guidelines, discussions in Pharmaco Therapeutic Consultation groups, regional formularies and insurers' policies related to generics. These instruments can either speed up or limit the dissemination of newly reimbursed drugs.

Once drugs are admitted on the positive reimbursement list (GVS), they remain on this list and are not systematically reassessed. The impact of the implementation of the reimbursement decision is only measured by monitoring pharmaceutical expenditure and not by evaluating direct health effects from drug utilisation. Manufacturers may submit new applications for the same drug for an extension of the indication or when new evidence has become available. In addition, both the minister and CVZ can initiate a review; this is however based on ad-hoc occurrences and no explicit criteria are described.

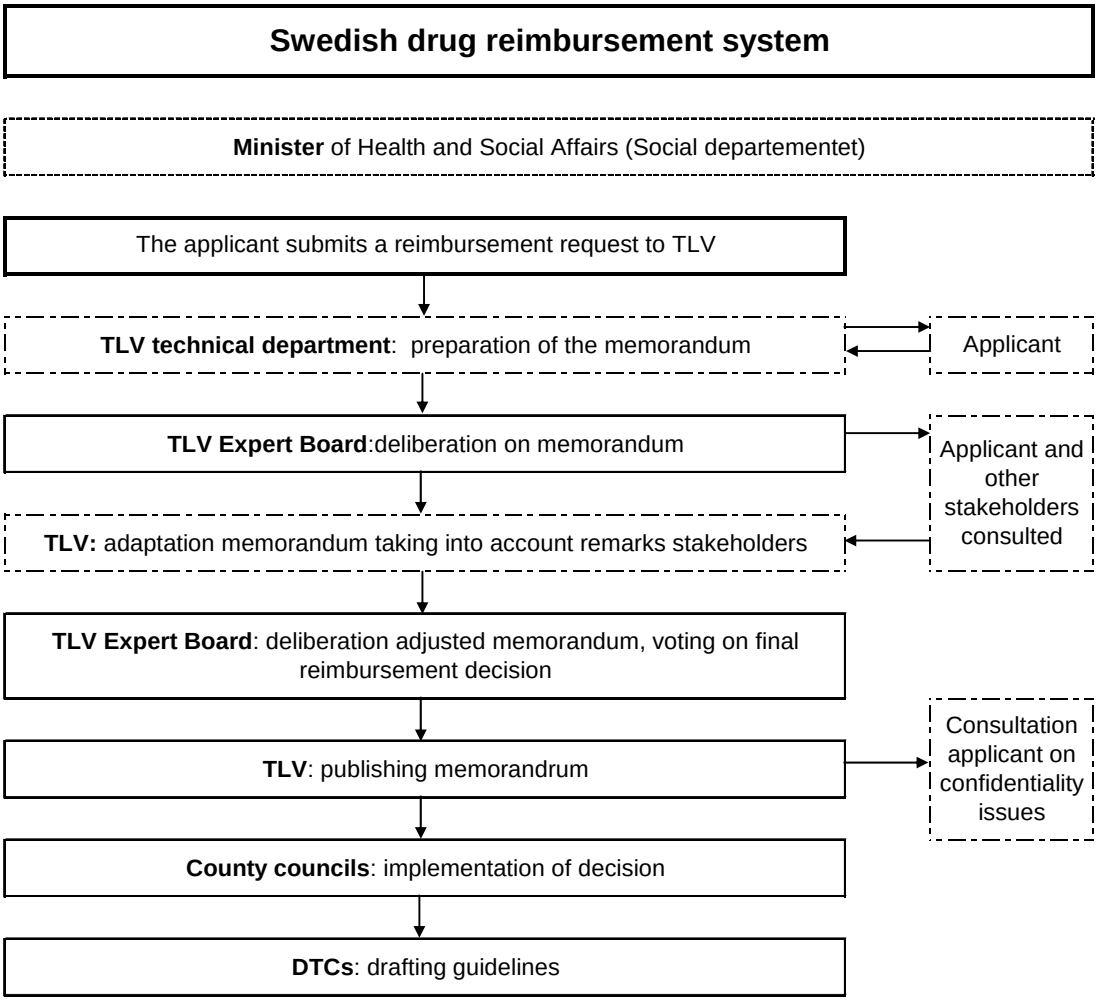
In contrast, drugs on the expensive inpatient drug list ought to be re-assessed on actual expenditure, therapeutic value, appropriate use and cost-effectiveness in daily practice four years after the initial positive reimbursement decision. However, so far none of the expensive inpatient drugs were reassessed; the first reassessments are expected at the end of 2010. Therefore, the consequences of these reviews (e.g. whether drugs will be delisted), will become clear in the near future.

The minister recently announced that expensive innovative outpatient drugs also might be reviewed similar to expensive inpatient drugs. The minister suggested starting with one therapeutic group (i.e., TNF alpha blockers) from 2011 onwards. However, this has been postponed until further notice.

Key points Netherlands

- **The Health Care Insurance Board (CVZ) is the national reimbursement agency.**
- **The minister of health makes the final reimbursement decision based on CVZ's reimbursement advice.**
- **This advice is based on the assessment and appraisal of CVZ's expert committee (CFH) and appraisal committee (ACP).**
- **The CFH mainly consists of experts with medical, pharmacological and (health-)economic expertise. CVZ appoints CFH expert members. CFH's meetings are not open to the public.**
- **The ACP was established in 2008 and consists of three CVZ board members and has six other expert members. CVZ appoints ACP members. ACP's meetings are open to the public.**
- **Stakeholder involvement is formally implemented.**
- **Therapeutic value is the most prominent reimbursement criterion.**
- **Cost-effectiveness is also a formal reimbursement criteria. The CFH formally only evaluates the robustness of the cost-effectiveness evidence.**
- **The ACP has made appraisal criteria more transparent.**
- **There is no formal hierarchy in assessment and appraisal criteria.**
- **There is no formal cost-effectiveness threshold (range).**
- **Documentation of CVZ's advice is publicly available. The decision-making process is often not documented.**
- **Outpatient drugs are not systematically reassessed.**
- **Delisting rarely occurs.**
- **CVZ has not yet re-evaluated any of the expensive inpatient drugs, the first reappraisals are scheduled at the end of 2010.**
- **Any involved stakeholder can appeal to a decision at an administrative court based on procedural grounds.**

DRUG REIMBURSEMENT SYSTEM IN SWEDEN



SWEDISH HEALTH CARE STRUCTURE

Characteristics of the Swedish health care system

Sweden is a parliamentary democracy with a national health service characterised by a compulsory and predominantly tax-based health care system covering the entire resident population. The system is organised at three levels: national, regional and local. On the national level, the central government is responsible for legislation, supervision and evaluation of the system. Sweden has a long tradition of decentralisation of responsibilities to regional and local government levels. Health care provision is decentralised to 21 county councils (county councils and local authorities, further referred to as county councils) and 290 municipalities. At the regional level, the county councils are primarily responsible for providing and financing health care services, whereas municipalities are responsible at local level for delivering and financing social welfare services including child care, care of the elderly and the disabled and long-term psychiatric patients.[148]

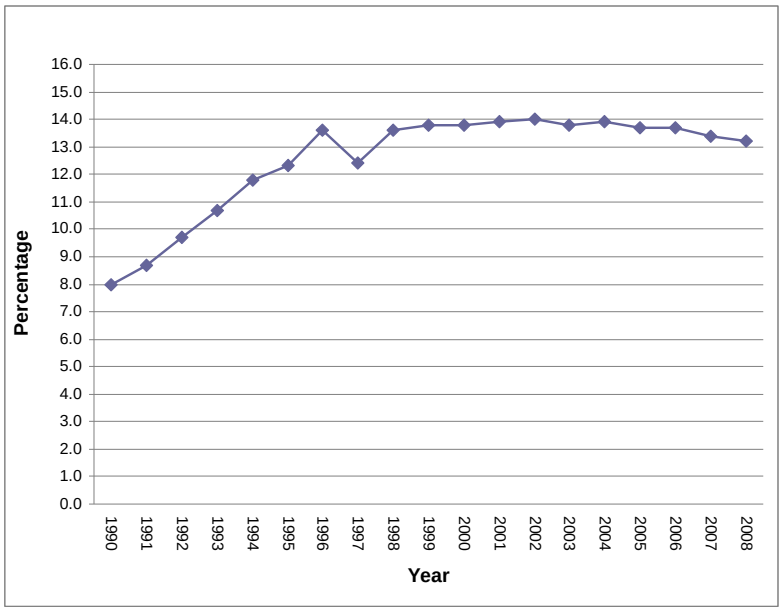
Health care funding and pharmaceutical expenditure

In 2008, total health care expenditure was 9.4% of GDP, of which 81.9% was public expenditure, and health expenditure per capita was 3,470 USD (adjusted for purchasing power parity).[71] The Swedish health care system is mainly financed through taxation. Both county councils and municipalities levy proportional income taxes on their residents and decide on the level of these taxes. On average, health services are accountable for around 91% of county councils' and 34% of municipalities' expenditure.[149] The revenues of the county councils and municipalities mainly emanate from local taxes (73 and 68%) and are amongst others supplemented by governmental grants (19 and 16%) and user charges (3 and 7%) (ibid.). Private health care insurance is very limited, only 2.3% of the population has a voluntary health insurance covering less than one percent of health care costs.[148]

Pharmaceutical expenditures are financed by three sources. First, inpatient drugs are publicly financed for which county councils carry the full responsibility. Second, outpatient drugs included in the Pharmaceutical Benefit Scheme are publicly financed through a governmental subsidy to county councils; on average nine percent of county councils' expenditure is related to these pharmaceutical costs. Third, patients have to pay user charges for outpatient drugs. County councils can further decentralise drug budgets to primary care centres or hospital clinics, an extensive variation exists in the degree of decentralisation of these budget.[10]

In the 1990s, pharmaceutical expenditure increased approximately 10% annually.[33, 150] From 2000, pharmaceutical expenditure as percentage of total health care expenditure reasonably stabilised and was on average 13.7% (see Figure 20). Since the introduction of the Pharmaceutical Benefit Board (LFN) in 2002, the average annual rise in pharmaceutical expenditure is limited to 1 to 3%.[12] In 2008, total pharmaceutical expenditure was 34.2 billion SEK (≈ €3.455 billion) of which 18.8 billion, 6.4 billion, 6.3 billion, 2.7 billion SEK was attributable to reimbursement of outpatient drugs, patient user fees for outpatients drugs, inpatient drugs and OTC drugs respectively.[151]

Figure 20: Pharmaceutical Expenditure as percentage of total health care expenditure



Source: [71]

Pharmaceutical policy tools

The pharmaceutical system is based on two main acts, namely the Medicinal Product Acts (Läkemedelslagen) based on the EU directives and the Act on Pharmaceutical Benefits (Lag om läkemedelsförmåner) for pricing and reimbursement. Before 2002, the National Social Insurance Board decided on prices for pharmaceuticals. In October 2002, the price reference system (comparing international prices) was abolished and ever since no international price reference system has been applied. The Act on Pharmaceutical benefits (2002:160) came into effect in October 2002 and contains provisions on price control mechanisms for products included in the Pharmaceutical Benefit Scheme. The national Dental and Pharmaceutical Benefits Board (TLV) makes reimbursement decisions based on the proposed price of the manufacturer, formally without price negotiation. Additionally, TLV sets the pharmacy margin and the pharmacy purchase price and thus sets the final fixed pharmacy retail price that county councils have to pay for outpatient drugs covered by the reimbursement system. Moreover, generic substitution between equivalent drugs became mandatory by law. TLV estimated that this resulted in about 15% lower prices and €700 million savings.[152]

Furthermore, drug expenditure has been contained by delisting drugs as a result of reviews of drugs admitted in the Benefit Scheme before 2002. For example, TLV estimated that the review of medicines for lowering blood pressure could potentially save 400 million SEK (≈ €40.4 million).[153]

Pharmaceuticals outside the Benefit Scheme (OTC products and hospitals drugs) have no price setting policies and can be priced freely by the manufacturer. County councils directly agree with manufacturers on prices for inpatient drugs and thus prices may vary between counties.

From 1971, the state-owned Apoteket monopoly chain of pharmacies was the sole provider of prescription and non-prescription drugs. In November 2009, the government opened the country's pharmaceutical market to competition. It is estimated that in the first two months around ten percent of the OTC drugs were sold outside Apoteket.[154] In January 2010, the first private pharmacy obtained permission to operate on the Swedish market for prescription drugs. So far, it is unclear if the privatisation of the pharmaceutical market will generate lower pharmaceutical prices as argued by the government.

Cost sharing policies

The OECD estimates that out-of-pocket expenditure is accountable for 15.6% of the total expenditure on health services in Sweden.[71] Regarding pharmaceuticals, 70% of private expenditure is related to out-of-pocket spending on prescription drugs and the remaining 30% is related to OTC drugs.[150] In 2008, consumers spend €374 million on non-prescription drugs, accounting for 9.3% of the Swedish pharmaceutical market.[137]

Cost sharing for drugs mainly applies to outpatient drugs. County councils bear the full costs for inpatient drugs, patients co-pay 80 SEK (≈ €8.09) per hospital admission day.[155] For drugs included in the (outpatients) Pharmaceutical Benefit Scheme, patients are responsible for the first 900 SEK. Thereafter, subsidies reduce costs by: a) 50% if costs are between 900 to 1,700 SEK; b) 75% if costs are between 1,700 and 3,300 SEK; c) 90% if costs are between 3,300 and 4,300 SEK.[152] The maximum co-payment during a 12 month period is thus 1,800 SEK (≈ €182). Additionally, patients are confronted with direct payments if they refuse a generic substituted product, they have to pay the price difference. There is no co-payment for insulin; drugs for other chronic diseases are not exempted from co-payments. Families are allowed to pool drug co-payments for children younger than 18 years old and thus pay maximum 1,800 SEK for all children.

DESCRIPTION OF THE REIMBURSEMENT SYSTEM

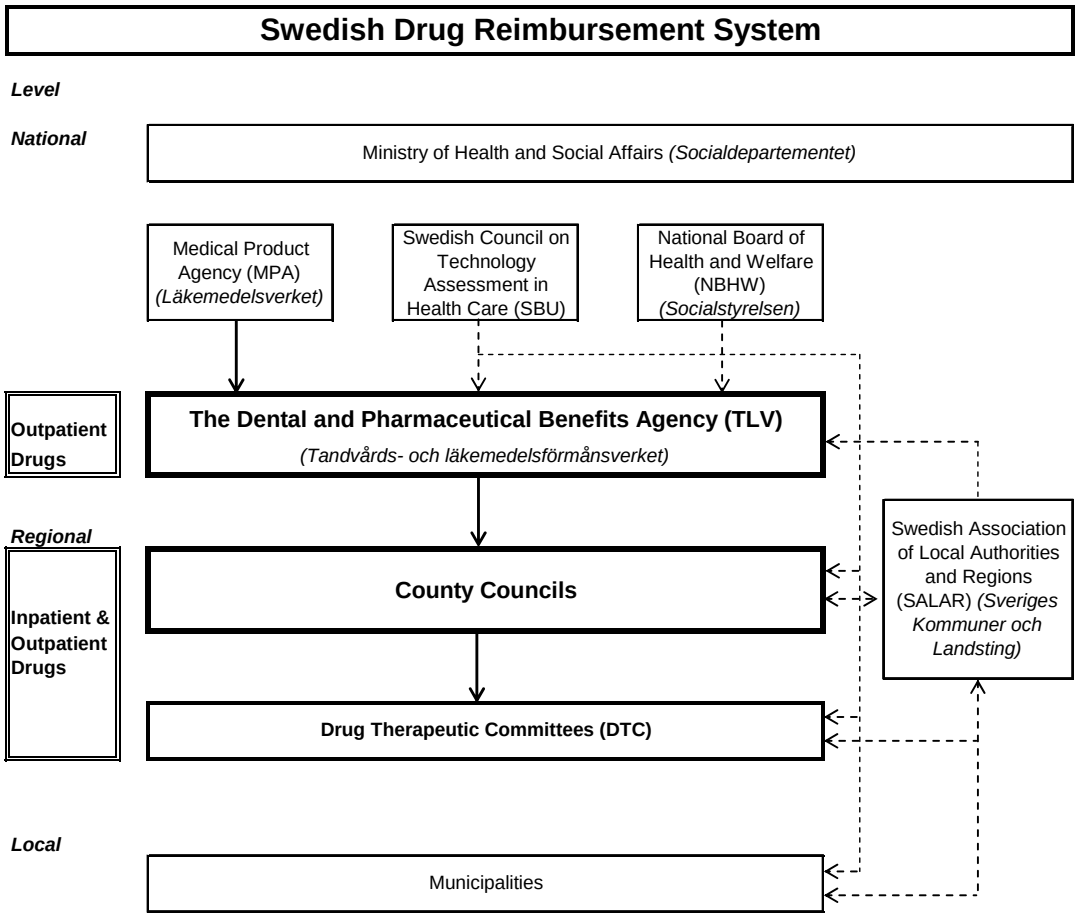
Overview drug reimbursement system

In accordance with the Medicinal Products Act (SFS 1992:859) and the Medicinal Products Ordinance (SFS 1992:1752), pharmaceuticals can enter the national market after a national market authorisation has been issued by the Medical Products Agency (MPA) or when a Community authorisation has been granted by the European Medicines Agency (EMA).

After market approval, medicines do not automatically qualify for reimbursement. Before 2002, all pharmaceuticals with an approved price by the National Social Insurance Board were reimbursed.156 In October 2002 the Act on Pharmaceutical benefits (2002:160) came into effect. As consequence, only drugs assessed by the Dental and Pharmaceutical Benefits Agency (TLV) are admitted on the positive list of the national Pharmaceutical Benefit Scheme and entitled for reimbursement. Manufacturers have to submit evidence on effectiveness and cost-effectiveness for a reimbursement application. TLV makes a mandatory decision at the national level in order to ensure that benefits are equally distributed through Sweden. However, the implementation of the decisions is decentralised to county councils who are responsible for health care planning and budgeting. Every county council is required by law to set up at least one Drug Therapeutic Committee (DTC) producing and disseminating guidelines for recommended drug therapy. Consequently, the degree and the rate of adoption of national reimbursement decisions may vary between counties due to budget planning mechanisms and different interpretations of TLV's decisions. If TLV decides that the drug is not included in the Pharmaceutical Benefit Scheme, county councils may still decide to reimburse the drug or patients can pay privately for these drugs. The Pharmaceutical Benefit Scheme is only applicable to outpatient drugs. Inpatient drugs are not assessed by TLV, county councils are responsible for hospital care provision including inpatient drugs assessments and expenditure.

Figure 21 gives an overview of the main actors at national and regional level of the Swedish reimbursement system. The following paragraph analyses the Swedish drug reimbursement system in detail and describes the main actors and the application of health technology assessment within this system according to the Hutton 'fourth hurdle' framework.[40]

Figure 21: Overview Swedish Drug Reimbursement System



Policy Implementation Level

Establishment

The Health and Medical Services Act (1982) and the Act on Pharmaceutical benefits (2002:160) establish the legal basis of the drug reimbursement system. The main actors in the system are the Dental and Pharmaceutical Benefits Agency (TLV; Tandvårds- och läkemedelsförmånsverket), the county councils and their Drug Therapeutic Committees (DTCs). Other involved parties are the ministry of Health and Social Affairs (Socialdepartementet), the Medical Products Agency (MPA; Läkemedelsverket), the Swedish Council on Technology Assessment in Health Care (SBU; Statens Beredning för medicinsk Utvärdering), the National Board of Health and Welfare (NBHW; Socialstyrelsen), and the Swedish Association of Local Authorities and Regions (SALAR; SKL; Sveriges Kommuner och Landsting) (see

Figure 21).

Briefly, the reimbursement pathway for outpatient drugs is as follows. Manufacturers have to submit an application for admission in the Pharmaceutical Benefits Scheme (positive list) to TLV. TLV performs the assessment and appraisal of the product and makes the final mandatory national reimbursement decision for outpatient drugs. County councils, supported by their DTCs, are responsible for the actual implementation of these decisions. In contrast, inpatients drugs are not evaluated by TLV, the 'fourth hurdle' system for inpatient drugs is confined to county councils and DTCs. The minister of health oversees and steers the system but can not overrule a decision of TLV.

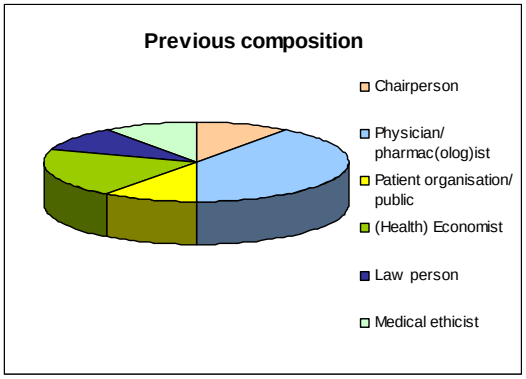
TLV was established in 2002, it was previously known as the Pharmaceutical Benefits Board (PBB = LFN). TLV has the legal responsibility to decide whether or not a pharmaceutical product will be included in Pharmaceutical Benefit Scheme and thus subsidised by the state. TLV is an independent agency funded by the government with one Director-General appointed by the minister of health and around 60 employees.

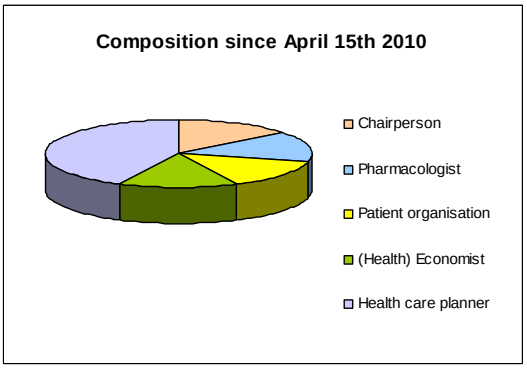
Within TLV, the Reimbursement Application unit (twelve staff members) and the Pharmaceutical Reviews unit (twelve staff members) work closely alongside each other on new reimbursement applications and on the reviews of drugs admitted under the benefit scheme before 2002. These 'technical departments' prepare reimbursement dossiers for Expert Board meetings. Staff has expertise in different medical areas, pharmac(olog)y, health economics and legislation. The Pharmacy Project unit (seven staff members) focuses on TLV's responsibilities connected with the regulation of the pharmacy market.

Finally, the Expert Board of TLV conducts the assessment, appraisal and makes the final reimbursement decision. Previously, the Expert Board consisted of one Chairperson and ten committee members, who all have a personal substitute. Expert Board members are appointed by the government for a two year period; these periods can be consecutively (no maximum). These members had expertise in a broad area of medicine, pharmacy, and health economics, one person was a representative of consumer/ patient groups (see Figure 22). Since April 15th 2010, the Expert Board has, besides the Chairperson, only six members. One member is a clinical pharmacologist, one member is a health economist, one member is representative of a patient organisation, and three members are health care planners from county councils. It is important to realise that Expert Board members are appointed for their personal capacities and expertise and do not represent any organisation.

The Expert Board meets once per month (except in July), one full day and one and a half day intermittently.

Figure 22: Composition of the Expert Board





The Swedish Association of Local Authorities and Regions (SALAR) represents the county councils and municipalities. As mentioned before, county councils are responsible for the provision and financing of both outpatient and inpatient pharmaceuticals. All county councils deliberate with the minister on their annual pharmaceutical subsidy for outpatient drugs; they bear the full responsibility on inpatient drugs. County councils are elected every four years by their residents; counties vary in size between approximately 60,000 and 2 million inhabitants.[149] The councils' chairs meet formally four times per year, but the informal network is extensively used for sharing information. On average five to ten persons within a county council work on medical affairs. Since 1997, every county council is legally required to set up at least one formulary committee (DTC), some of the large councils have more than one committee, and committees can vary enormously in size. For example, Stockholm's three DTCs recently merged to one DTC representing 20 different therapeutic areas with eight to ten representatives per area, whereas another DTC can only have ten members in total.

The background of most DTC members is foremost related to medical and pharmacological expertise. According to interviewees, there are only two health economists in all DTCs. DTCs produce guidelines for doctors and pharmacists and develop lists of recommended drugs.

Table 21 provides an overview of the key actors and their responsibilities in the reimbursement process.

Table 21: Key actors involved in the reimbursement process

Institution/ Actor	Function(s)
Medical Product Agency (MPA)	Is responsible for determining which drugs are therapeutic equivalent/ substitutable.
Dental and Pharmaceutical Benefits Agency (TLV)	Is responsible for the entire drug reimbursement process; the technical department communicates with manufacturer, prepares the assessment, drafts a memorandum, and publishes the final decision online.
Expert Board of TLV	Is responsible for making the final reimbursement decision.
County Councils	Are responsible for the implementation of the decision.
Drug Therapeutic committee	Are responsible for making drug therapeutic guidelines.
Minister of Health and Social Affairs	Is responsible for health care policy and regulations.

Besides these main actors, three other independent governmental agencies are involved in the drug reimbursement system. First, the Medical Products Agency (MPA) is the national authority responsible for market regulation and surveillance of drugs and other medicinal products. The MPA supervises all Swedish pharmacies and issues the licences for outpatient pharmacies. Additionally, the MPA decides which drugs are therapeutic equivalent and thus substitutable (Ordinance 2002:687). The MPA is mainly financed through application fees and has around 450 staff members, mostly pharmacists and doctors.

Second, the Swedish Council on Technology Assessment in Health Care (SBU) is the main Swedish producer on general health technology assessments and evaluates selected health care technologies and services by reviewing research findings.[157] SBU selects and prioritises research topics that are of major importance to public health and quality of life. TLV can ask SBU to conduct a scientific review to support reimbursement decision making. SBU produces evidence based guidelines and disseminate their scientific information to central and local governments and health care purchasers and providers in order to support decision making. The SBU was established in 1987 and is funded by the government and has around 30 staff members who are supported by an extensive external network of several hundred involved clinical and scientific experts.

Third, the National Board of Health and Welfare (NBHW) provides education, develops and distributes professional standards and guidelines, supervises the delivery of health care services and maintains health data registers and statistics. Regarding the drug reimbursement system, the NBHW develops professional disease management guidelines including recommendations on drug therapy. County councils and DTCs are obliged to take these national guidelines into account in developing their professional guidelines in more detail. The NBHW was established in 1968 and has the central units a central supervision department and six regional offices. Usually, NBHW's guidelines follow after SBU's scientific reports that follow after TLV decisions. TLV's decisions are on pharmaceuticals and dental procedures while SBU's and NBHW's reports and guidelines incorporate pharmaceuticals and non-pharmaceuticals, the latter agency also produces general clinical guidelines. Interviewees generally acknowledged that SBU reports are to be seen as scientific advice whereas NBHW's guidelines are more formal treatment recommendations (e.g. how to treat breast cancer).

Finally, all these agencies are under the responsibility of the ministry of Health and Social Affairs. The minister of Health and Social Affairs oversees the entire health care system, sets the health care policies and develops regulations and laws accordingly. It is important to realise that the minster can not overrule TLV's reimbursement decisions. At the ministry of Health and Social Affairs six staff members are responsible for the pharmaceutical market and regulations.

System objectives

The Health and Medical Services Act of 1982 emphasises a vision of equal health for all. The minister states that the objective of their welfare policy is *"to reduce the gaps between different social groups while giving people security, the opportunity to develop and an acceptable economic standard"* (Government Offices of Sweden 2008). The Act on Pharmaceutical Benefits describes that the Pharmaceutical Benefit Scheme *"should protect individuals against high costs"* of pharmaceuticals that *"appear reasonable from the medical, humanitarian an economic aspects"* and that "*there are no other drugs or treatment available that are significantly more suitable for the purpose"* (Act 2002:160). In 2002, this Act came into effect because the previous reimbursement system resulted in rapid increasing expenditures. TLV states that the aim of the pharmaceutical reimbursement system is to get *"value for money"* by using a value based pricing system that leads to "*rational and cost-effective public use of medicines"*.[152] Whereas TLV promotes cost-effectiveness from a societal perspective, county councils have responsibilities for drug expenditure and thus might have different perspectives and objectives. Furthermore, other involved parties describe similarly stated objectives of the system on their public websites. They promote efficient utilisation of resources use (SBU), aim to ensure access to safe and effective pharmaceutical products that are used in a rational and cost-effective manner (MPA) and aim to develop and improve health and medical services and ensure high quality of care equal for the entire Swedish population (NBHW).

Scope of the system

The Act on Pharmaceutical Benefits determines the scope of the system and that, in order to be entitled to reimbursement, drugs should be included in the Pharmaceutical Benefit Scheme. This scheme is only applicable to outpatient drugs. County councils have the freedom to decide on inpatient drugs. All drugs previously priced by the National Social Insurance board were initially included in the benefit scheme. New drugs need to apply to TLV to obtain a positive decision. Although TLV makes product based reimbursement decisions, meaning that the drug shall be subsidised for all authorised prescriptions, TLV can decide to restrict reimbursement to a specific area of use. For example, TLV made until July 2008 in total 352 decisions, 66% received a positive decision without restrictions, 17% with restrictions and another 17% were denied reimbursement.[158] Additionally, TLV has the remit of the ministry to review all drugs included in the Scheme before 2002 by 49 therapeutic classes, seven of these reviews were finalised at the end of 2009. While TLV assesses all new drugs, SBU selects technologies that are of major importance to public health and quality of life and are issues of great concern.[159]

Implementation

The Expert Board of TLV makes the final pricing and reimbursement decision that is mandatory at national level. Reimbursement decisions are sent within ten days to the applicant and other stakeholders. After the decision, TLV deliberates with the manufacturer on potential sensitive information and confidentiality issues and on the content of the final report that is published online on TLV's website.[160] The online publications provide a summary of TLV's assessment and may include statements from stakeholders (e.g. SALAR). It is important to realise that TLV may not publish a full report on a negative decision. Additionally, transparency can be limited due to the fact that manufacturers may withdraw their confidential submission up until TLV makes a final decision. Pharmaceuticals are admitted in the Benefit Scheme the day after TLV's notification and the final decisions are sent electronically to the National Corporation of Swedish pharmacies and pharmaceutical distributors.[160]

The actual implementation of the decision is the responsibility of the county councils. As mentioned before, every county council is required by law to set up at least one Drug Therapeutic Committee (DTC) producing and disseminating guidelines for recommended drug therapy.

> The degree and the rate of adoption of national reimbursement decisions may vary between counties due to considerably flexibility in deciding on the provision of drugs, budget planning mechanisms and dissimilar interpretations of TLV's decisions. Although TLV makes mandatory decisions to ensure equity and equal treatment of all Swedish residents, several papers report extensive variation in drug therapy between county councils.[10, 11] It has been extensively researched that guidelines and recommendations can potentially save a substantial amount of money, however, it remains unclear if differences in DTC's guidelines compromise the quality of care or have a negative impact on the health of the population.[11-15]

Accountability

The minister of Health and Social Affairs is responsible for the health care system and accountable to the Swedish Parliament. All agencies are accountable to the minister. The minister is overseeing the drug reimbursement system and sets overall health care goals and policies and can thus influence the drug reimbursement system by steering the national agencies' policies. Performance assessment of these agencies falls under the responsibility of the minister. An external committee under the parliament annually audits these agencies regarding their budget, process evaluations only occur on an ad-hoc basis.

DTCs are under the responsibility of county councils. County councils are political bodies whose representatives are accountable to the public established by elections every four year. Each county council has its own budget responsibility and has considerable flexibility in the provision of health care. Consequently, the impact of the reimbursement system is mainly monitored on pharmaceutical expenditure by county councils. Although overall health system outcomes are monitored by the NBHW, direct health effects related to the pharmaceutical reimbursement system are not evaluated.

Technology Decision Level

Assessment process

Before an application is submitted, manufacturers can deliberate with TLV on the case. From September 2009, TLV and MPA have been conducting a pilot project of joint scientific advice meetings with the pharmaceutical industry during phase II and III studies. This project will be evaluated in autumn 2010.

The report "Guidelines for Companies" describes in detail TLV's assessment procedure and application requirements.[160] Additionally, TLV published a report with general guidelines how to perform economic evaluations.[161] It should be noted that there are several different application procedures, amongst others new drugs, new dose forms, substitutable drugs, parallel imported or distributed drugs, new packaging, new strengths, and price changes. This report focuses on the applications for new drugs since this is the most extensive procedure.

The actual assessment process starts when a formal application is submitted, and should be finalised within 180 days (European Directive). The government stressed that TLV should make their final decision within 120 days, but has recently taken away this goal. On average applications are finalised within 101 days.[47] An application can be submitted before market approval has been obtained to reduce processing time. Nevertheless, it is required to have a sales approval before a positive reimbursement decision can be taken. Formal applications should include evidence on clinical effectiveness and cost-effectiveness.[160]

Less extensive evidence is required for applications for substitutable drugs, including parallel imported, new dosages and packages. The latter requirements are mainly related to justifications of the requested changes and to facilitate price comparison with (equivalent) drugs in the benefit scheme.

After submission, TLV assigns the application dossier to three persons from the technical department: one lawyer, one health economist and one pharmacist or person with a medical background. Within ten working days the applicant is informed if the application contains sufficient evidence, at this time the 'clock' starts. At any phase, if more profound investigation shows that the application lacks significant information, TLV staff members 'stop the clock' in order to give applicants time to supply additional data. This core team prepares a memorandum for the Expert Board meeting. In this preparation period, the core team members deliberate with the applicant, can ask for additional information, conduct research, assess available evidence, and may consult stakeholders and experts. Furthermore, the application file and any further obtained documents are sent during the preparation period to the Pharmaceutical Benefit Group of SALAR to provide county councils the best insight into the product and the opportunity to put forward their point of view. TLV staff of the technical department meets once per week to discuss ongoing cases.

A week before the Expert Board meeting, the complete file is sent to the Expert Board members and to the Pharmaceutical Benefit Group of SALAR. The file includes the memorandum, accumulated evidence and for designated members the pharmacoeconomic model. This memorandum is also sent to the applicant. Both the applicant and the county councils have the right to deliberate with the Expert Board. The memorandum describes the evaluation and conclusions of the technical department, and this forms the basis of the Expert Board's decision. Applicants can contact TLV staff during the entire procedure, but are only allowed one deliberation with the Expert Board. In this Board meeting, they have 30 minutes to put forward their view on the case and the memorandum and can refute factual errors. However, it is not allowed to present any new information. The Pharmaceutical Benefit Group of SALAR used this deliberation right only four times the last eight years.

In the next phase, the dossier is evaluated by the Expert Board. A dossier can be decided upon in one meeting, but in more complex cases appears at two or more Expert Board meetings. In every meeting, expert committee members have to express any conflicts of interest, in which case they have to leave the room. The meetings are not open to the public, only TLV staff including the General-Director, are attending the meeting. Additionally, the Expert Board can invite one or more experts (such as medical specialists, physician association and patient association) to the meeting to take part in the discussion, but they do not have voting rights regarding the final decision. Reimbursement dossiers are not assigned to specific Expert Board members. The core team members of the technical department first presents the case to the Expert Board, after that, the evidence and the memorandum are assessed and decided upon by expert board members.

In contrast, inpatient drugs come under the full responsibility of county councils and are not assessed by TLV. It appears more ambiguous how county councils assess inpatient drugs. County councils can deliberate with each other and with the Pharmaceutical Benefit Group of SALAR. They are supported by their DTCs and DTCs' extensive network of experts who are foremost from the medical field. Every DTC disseminates information to physicians and pharmacists, and produces professional guidelines with drug treatment recommendations. It is important to realise that prioritisation of treatments within these guidelines can differ per county council. Furthermore, county councils should adhere to the national NBHW treatment guidelines and can make use of SBU assessment reports. County councils further allocate budgets to primary care centres and hospitals at varying levels.[10] Consequently, assessments of inpatient drugs may also be further decentralised to hospitals or groups of health care providers.

Assessment and appraisal criteria

The Health and Medical Services Act (1982:763) emphasises equal access to health services on the basis of need and a vision of equal health for all. In 1997, a core section of the Act changed by including three main principles for priority setting in health care as put forward by an ethical platform appointed by the Swedish parliament.[38, 162] These principles are the human value principle, the need and solidarity principle and the cost-effectiveness principle. Consequently, these are the main prioritising principles that TLV must legally take into account in their assessment and appraisal as set out in the Act on Pharmaceutical Benefits.

The human value principle reflects the equality of all human beings and the integrity of every individual. The need and solidarity principle implies that those individuals in greatest need have the highest priority in medical care. Guidelines further divided health care into four different groups of priority, of which the first three are provided by the Swedish welfare system: 1) life threatening diseases or conditions, 2) prevention and rehabilitation, 3) less severe acute and chronic diseases and injuries, 4) other reasons than disease or injury.[38] Furthermore, TLV uses different levels of severity based on the patient's condition and risk of permanent damage or early death without treatment and taking into account all effects from a drug on people's health and quality of life.[160] The cost-effectiveness principle indicates that costs should be reasonable from a medical, humanitarian and social economic perspective.[152] However, the implication of the term 'reasonable' is not further defined. TLV does not consider budget impact or other cost containment criteria since they assess cost-effectiveness from a societal perspective and apply a value based pricing system in order to achieve as much value as possible for publicly financed drugs. Additionally, the Expert Board has to consider 'marginal utility', which is described by TLV as 'if no alternative treatment exists, cost should be reasonable'.[163]

As mentioned before, the Expert Board conducts the actual assessment and appraisal. Staff of the technical department presents the case to the Expert Board and drafts a reimbursement proposal (i.e., memorandum). The board generally first discusses the effectiveness evidence and after that the cost-effectiveness evidence. Generally, pharmacists and medical experts focus on the clinical and therapeutic evidence and health economists deliberate on the pharmacoeconomic evidence. The board does not set specific sub-criteria regarding effectiveness. It is evaluated considering all positive effects on a person's health and quality of life by mainly balancing effectiveness, efficacy and side effects and other additional evidence (e.g. ease of use). Pharmacoeconomic evidence is assessed based on the economic evaluation framework using societal perspective as described by TLV's economic evaluation guidelines. The (cost-) effectiveness is compared with the most appropriate alternative and QALYs are the most preferred outcome measures. However, interviewees acknowledge that often only surrogate end-points are available. TLV's guidelines state that manufacturers should provide evidence on phase II and III and ongoing studies, direct comparative studies with a relevant comparator are the best studies, and full references should be enclosed.[160] Besides that, TLV maintains that published articles in peer reviewed scientific journal have undergone a form of quality control whereas unpublished articles require greater demand on possibilities for quality control and transparency.[160, 161] It should be mentioned that if the application concerns therapeutic equivalent drugs (as determined by MPA), TLV only requires a cost minimisation analysis. Furthermore, if the expected sales volume/ budget impact is very low (e.g. orphan drugs), TLV states that a more rough estimation of effects and costs may be sufficient.[160] If there is much uncertainty around the evidence, manufacturers can be asked to provide more evidence or more advanced economic models. Uncertainty can lead to a negative decision, but also to a decision with restrictions, such as restricted use for a specific group or a temporary reimbursement decision requiring additional data collection on for example prescription volumes or real word effectiveness at a prefixed time.

It is then up to the Expert Board to balance and appraise all evidence considering the prioritisation principles. Need is mainly interpreted as severity of illness and, according to the law, the people in greatest need should be prioritised. TLV evaluates the evidence from a societal perspective. Although cost-effectiveness is a crucial aspect, TLV does not set a threshold value.[152]

Interviewees generally acknowledged that their 'implicit' threshold depends on the severity of illness or the patient in the greatest need. For illustration, TLV has accepted a cost-effectiveness ratio up to €90,000 per QALY for some severe conditions. In 2008, TLV denied reimbursement to Tyverb®, a drug for breast cancer, and considered €120,000 per QALY gained as to expensive.[7] Hugosson and Engstrom estimated an average accepted cost-effectiveness of €36,000 per QALY for all 216 decisions from 2002 up until 2007.[8]

As mentioned before, county councils are responsible for the assessments of inpatient drugs. All county councils establish measures to enhance rational utilisation of pharmaceuticals such as production of professional guidelines, academic detailing, benchmarking and incentivised prescribing targets.[12] It is generally acknowledged that although county councils are interested in health economics, they lack health economic knowledge and budget responsibility may force a narrower budget perspective. Furthermore, variation in recommendations of first choice drugs in guidelines suggests that different criteria are applied across county councils. It remains unclear to what extent county councils and DTCs use health economics in their assessments.[32, 33, 164] Bergström and Karlberg (2007) identified two different incentive models applied by county councils: prescriber based and population based model. They found that the former model was mainly applied as a tool for cost containment whereas the latter model focused on the quality of services.[165] To illustrate an example of assessment criteria, the recommendations of Stockholm county council's "Wise Drug List" are based on: medical efficacy and safety, pharmaceutical suitability (e.g. strengths and pharmacokinetic properties), efficiency (e.g. cheapest drug if identical efficacy and safety), experience (e.g. at least two year on the market), and environmental aspects.[12, 14, 166, 167]

Decision Process

From April 15th 2010, the composition of the Expert Board has changed. So far, it is not clear if any consequences will arise from this and if decisions will be different in such that other considerations might play a role in decision making. Because of no remaining medical expertise in the Expert Board, it seems that the importance and workload of the technical department might have been increased. Although budget impact is not a formal reimbursement criterion, it might be possible that the expertise of health care planners within the Expert Board will make it more likely to discuss budgetary considerations. On the other hand, the fact that three healthcare planners are members of the Expert Board might improve collaboration between TLV and county councils and might enhance synergy between the national and regional level.

The Expert Board of TLV makes the final pricing and reimbursement decision for new licensed (original and substitutable) drugs. TLV's national decisions are mandatory. It should be noted that the General-Director makes direct decisions without an assessment of the Expert Board on request for price changes, new packages and parallel imported pharmaceuticals. The majority of TLV's decisions concern price changes; approximately 1% involves new original drugs.[38] As mentioned before, dossiers can appear at one or more Board meetings depending on the complexity of the case. In the last meeting, decision making is based on voting; majority voting determines the final reimbursement decision. The chairperson and at least half of the committee members should be present to form a quorum.

In principle, reimbursement decisions are product based, which means that the drug is reimbursed (or not) for all authorised prescriptions. In exceptional cases, such as different levels of patient benefit and/ or different cost-effectiveness ratios, the Expert Board can decide to limit reimbursement to a specific area of use (section 11 Act on Pharmaceutical Benefits 2002:160). TLV can use several conditions for reimbursement such as time restrictions, obligation to state any restrictions or conditions in all marketing activities, obligation to provide prescription volumes, data collection requirement.[33, 158, 160, 168] As mentioned before, 17% of TLV's cases until July 2008 received a conditional reimbursement decisions.[158]

After the Expert Board meeting, minutes are published online within two days. Minutes show whether a decision has been taken or that the case needs further preparation. The actual content of the decision is not included in the minutes. TLV sends this documentation to the manufacturer within ten working days. After that, TLV deliberates with the manufacturer on confidentiality issues regarding the content of the final reimbursement document that will be published online. This online document provides a summary of the decision and its rationale, votes are not recorded. Manufacturers can withdraw their application at any time up until a final decision has been made. All information on withdrawn dossiers remains confidential and thus no information is publicly available.

Furthermore, decisions on county councils' assessments can be found in the recommendations put forward in the professional guidelines that are disseminated and promoted by DTC's to health care providers, pharmacists and the public.

Outputs and implementation

The day after a final positive decision has been notified, the drug is included in the Pharmaceutical Scheme and thus patients are entitled to reimbursement. However, decisions on price changes and on excluding drugs from the Scheme come into effect one month after the decision has been issued.[169] Applicants can appeal to TLV's decisions at a public administrative court. They must send TLV the appeal within three weeks after notification; TLV forwards the appeal to the administrative court. Since 2007, TLV's decisions are valid even if appealed against until otherwise decreed by court. Manufacturers can resubmit an application at a lower price or when new evidence has become available.

Implementation follows after the final reimbursement decision. TLV informs the National Corporation of Swedish Pharmacies and pharmaceutical distributors on their decisions.[160] County councils are responsible for the actual implementation and financing of outpatient drugs reimbursement decisions. Consequently, the implementation of both inpatient and outpatient drugs are county councils' responsibility. The only notable difference is that TLV's price and reimbursement decisions for outpatient drugs are mandatory to county councils and thus county councils cannot refuse reimbursement and cannot make price agreements for outpatient drugs. However, the diffusion of drugs may vary per county council due to considerable flexibility in deciding on the provision of drugs, budget planning mechanisms and dissimilar interpretations of TLV's decisions. County councils are supported by DTCs and an extensive network of experts. Additionally, county councils and DTCs collaborate with the MPA, TLV, SBU and the NBHW and use their expert knowledge, guidelines and (Alert, Yellow and White) report as input into decision making regarding drug recommendations. This extensive and widespread implementation system can either speed up or limit the diffusion of drugs.

TLV has the remit to conduct a review of all drugs previously included in the Benefit Scheme under the old scheme. They divided all drugs into 49 different therapeutic classes, overall sales determines the sequence of the reviews. The reviews can take up to 15 months and are confirmed with a final public report describing how the review was performed and conclusions regarding cost-effectiveness estimations and decisions on which drugs will continue to be entitled for reimbursement. TLV indicates in every report the estimated savings of implementation of the review. During the review process, manufacturers are requested to submit information on clinical use and cost-effectiveness of pharmaceuticals under review. Additionally, TLV collaborates with the MPA, NBHW and the SBU on these reviews. For example, two exemptions were made on the review sequence since the NBHW was producing national guidelines on two diseases. TLV can ask SBU to conduct a scientific review and request a yellow or white report for the designated disease area.

An assigned project team of the technical department (pharmac(olog)ist, health economist and a lawyer) conducts the review, supported by external experts appointed by the Director-General, such as user groups, SALAR's Pharmaceutical Benefit Group, chairpersons of Medical Committees, the Swedish Association of the Pharmaceutical industry (LIF), Swedish Society of Medicine and the Swedish Medical Association.[170] The external experts neither take part in producing the memorandum nor are involved in decision making. Similar to new drugs, the project team prepares a draft (more extensive) memorandum that will be evaluated and decided upon in the Expert Board meeting by applying the same assessment and appraisal criteria. The draft memorandum is sent to the manufacturer and SALAR's Pharmaceutical Benefit Group. Generally, they have 5 weeks time to put forward their comments and they have the opportunity to deliberate with the Expert Board before the members make a final decision.[170] The decisions come into effect immediately, however, actual delisting of drugs will not occur for at least another three months after the report has been published. At the end of 2009, seven of these reviews were conducted. The minister of Health and Social Affairs has recently asked TLV to speed up the reviews. In April 2010, TLV published a report on developing the pricing system as requested by the minister. In this report, TLV identifies several opportunities to improve the value based pricing system such as more effective reviews and closer collaboration with county councils to improve rational and cost-effective drug usage.[47, 171]

Besides this comprehensive review, TLV reappraises drugs that obtained a conditional reimbursement decision (e.g. time limited decisions requiring additional data). Manufacturers have to submit data at least six months before the reimbursement period expires otherwise the subsidy will cease on the pre-fixed date as determined by TLV at the time of the initial reimbursement decision. The evidence is reviewed and decided upon by the Expert Board, decisions on drugs that are excluded from the scheme come into effect after one month. Furthermore, TLV has the right to initiate an ad hoc review on any of the drugs within the scheme (e.g. drugs that go off-patent). Decisions emanating from any of these reviews are implemented by county councils and their DTCs as previously described.

Key points Sweden

- **The Dental and Pharmaceutical Benefits Agency (TLV) is the national reimbursement agency for outpatient drugs.**
- **The Expert Board of TLV makes the final pricing and reimbursement decision.**
- **Stakeholder involvement is formally implemented.**
- **Since April 2010, the Expert Board of TLV consists of a chairperson, a pharmacologist, a patient representative, a health economist and three health care planners. The minister of health appoints Expert Board members. Expert Board meetings are not open to the public.**
- **The reimbursement decision is based on majority voting.**
- **The three main principles for priority setting in health care are the human value, need and solidarity, and cost-effectiveness principle.**
- **Therapeutic value and cost-effectiveness are the main assessment criteria. Budget impact is not a formal reimbursement criterion.**
- **There is no formal hierarchy in assessment and appraisal criteria.**
- **There is no formal cost-effectiveness threshold (range).**
- **A summary decision report (memorandum) is publicly available. The decision-making process is often not documented.**
- **A manufacturer can withdraw the application until a final decision has been made, in this case the memorandum remains confidential.**
- **TLV has been conducting a review of all drugs enlisted before 2002 based on therapeutic classes, delisting is a possible outcome.**
- **County councils are responsible for the implementation of the decision and bear financial responsibility. They are required to set up at least one drug therapeutic committee (DTC).**
- **DTCs produce and disseminate drug guidelines.**
- **The manufacturer can appeal to a decision at an administrative court based on procedural grounds.**

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