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ORIGINAL RESEARCH

Role of centralized review processes for making reimbursement decisions on new health technologies in Europe

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Background: The purpose of this study was to compare centralized reimbursement/coverage decision-making processes for health technologies in 23 European countries, according to: mandate, authority, structure, and policy options; mechanisms for identifying, selecting, and evaluating technologies; clinical and economic evidence expectations; committee composition, procedures, and factors considered; available conditional reimbursement options for promising new technologies; and the manufacturers' roles in the process.

Methods: A comprehensive review of publicly available information from peer-reviewed literature (using a variety of bibliographic databases) and gray literature (eg, working papers, committee reports, presentations, and government documents) was conducted. Policy experts in each of the 23 countries were also contacted. All information collected was reviewed by two independent researchers.

Results: Most European countries have established centralized reimbursement systems for making decisions on health technologies. However, the scope of technologies considered, as well as processes for identifying, selecting, and reviewing them varies. All systems include an assessment of clinical evidence, compiled in accordance with their own guidelines or internationally recognized published ones. In addition, most systems require an economic evaluation. The quality of such information is typically assessed by content and methodological experts. Committees responsible for formulating recommendations or decisions are multidisciplinary. While criteria used by committees appear transparent, how they are operationalized during deliberations remains unclear. Increasingly, reimbursement systems are expressing interest in and/or implementing reimbursement policy options that extend beyond the traditional "yes," "no," or "yes with restrictions" options. Such options typically require greater involvement of manufacturers which, to date, has been limited.

Conclusion: Centralized reimbursement systems have become an important policy tool in many European countries. Nevertheless, there remains a lack of transparency around critical elements, such as how multiple factors or criteria are weighed during committee deliberations.

Keywords: reimbursement, centralized review, health technologies, Europe

Introduction

The past decade has seen unprecedented growth in the number of new, often high-cost, health technologies and consumer demand for access to them. It has also seen increased public awareness and scrutiny of decisions about which technologies to include in the basket of publicly insured services.[1–3] To improve the legitimacy of such decisions and optimize health outcomes through the effective use of increasingly strained health care resources, many payers, particularly those in Europe, have established centralized systems for determining the reimbursement status of new health technologies.[4,5]

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In this invited review, we compare these systems across selected countries in Northern, Southern, Western, Eastern, and Central Europe, examining:

- Their mandate, authority, organizational structure, and policy options
- Mechanisms for identifying, selecting, and evaluating technologies
- Clinical and economic evidence expectations
- Review committee composition, procedures, and key factors considered during deliberations
- Use of conditional reimbursement options for enabling access to promising new technologies around which considerable uncertainty related to clinical and/or economic value exists
- The role of manufacturers in steps comprising the reimbursement review process.

Methods

This review is based upon findings from a comprehensive search for publicly available information on centralized reimbursement systems in selected European countries. Peer-reviewed literature published in English over the past decade (ending in January 2011) was located using a structured search strategy that combined relevant controlled vocabulary terms, ie, MeSH and EMTREE (eg, "technology, medical," "reimbursement mechanisms," "decision-making," "technology assessment," "health policy") and free text terms (eg, "pharmaceuticals," "medical devices," "coverage," "funding," "centralized review," "health technology assessment," and "reimbursement," the full search strategy being available from the authors). Such terms were identified through an analysis of words used to index references familiar to the authors. The strategy was applied to several health-related electronic bibliographic databases, including PubMed, MEDLINE, EMBASE, HealthSTAR, CINAHL, EconLit, PASCAL, SCOPUS, International Pharmaceutical Abstracts, Web of Science, and the UK Centre for Reviews and Dissemination databases (Database of Abstracts of Reviews of Effects, National Health Service Economic Evaluation Database, and Health Technology Assessment). For comprehensiveness, reference lists of retrieved papers and the most recent issues of health policy-related journals were hand-searched.

A search for gray (unpublished) literature (eg, working papers, conference abstracts, reports, presentations, government documents) was also performed using the Google® search engine and terms from the main search strategy. In addition, the following dedicated gray literature databases were scanned: the New York Academy of Medicine's Gray Literature database, Knowledge Utilization database, Systematic Reviews for Management and Policy Making, and National Health Service Evidence in Health and Social Care. Separate searches for information on centralized reimbursement processes within health care systems of the top 30 European countries ranked according to gross domestic product per capita by the World Bank were also conducted. This number was considered sufficient to capture the full spectrum of such processes. For each country, the websites of relevant ministries (eg, health, social affairs, economics), translated into English with Google Translate®, were scanned for documents describing legislation and other policies and processes for making reimbursement decisions on new health technologies, including pharmaceuticals, medical devices, diagnostic tests, and procedures.

Documents retrieved from the various searches were reviewed independently by two of the authors. Published papers unrelated to the introduction of individual health technologies (eg, those on macrolevel priority setting) were excluded. Because the purpose of this review was to examine current actual processes, papers proposing specific decision-making tools or discussing one component of decision-making were also excluded. Information on process-related characteristics of the centralized reimbursement systems, including perceived strengths and weaknesses, was extracted using a standardized, pretested data abstraction form. To ensure it reflected the current policy environment, the following individuals were consulted: corresponding authors of published papers, contacts listed on organizations' websites, and European policy experts with whom the authors were already acquainted.

Extracted information was tabulated to facilitate the identification of patterns or trends across country-specific reimbursement processes, and subsequently analyzed qualitatively using content analysis and constant comparison techniques.

Results

Of the 30 European countries initially identified for the review, information on centralized reimbursement processes could only be found for 23. Therefore, the review included the following 23 countries: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Norway, Poland, Portugal, Scotland, Slovakia, Spain, Sweden, Switzerland, the Netherlands, the United Kingdom, and Wales.

Mandate of centralized reimbursement systems

The majority (18/23) of countries have established centralized reimbursement processes to support coverage decision-making for either pharmaceuticals or pharmaceuticals and devices needed for their delivery. In general, eligible pharmaceuticals comprise those requiring a prescription. Two-thirds of such processes review both inpatient and outpatient pharmaceuticals (12/18), while one-third (6/18) considers those administered in outpatient settings only (Table 1). The remaining five countries have invested in centralized reimbursement systems that span medical devices, procedures, and pharmaceuticals (Table 1). Despite differences in the scope of technologies included, such processes share a similar mandate to determine the reimbursement status of new technologies. In most of the countries, this amounts to a decision on whether to add the technology to a "positive list" (ie, list of insured services). However, a small proportion of the countries also maintain a "negative list" (ie, a list of nonreimbursable services), broadening the mandate of their centralized reimbursement systems to include decisions resulting in active exclusion of some technologies from the benefit plan (Table 1). In legislation governing most systems (13/23), decisions are authoritative (ie, must be implemented), rather than advisory (ie, recommendations). Given that the price of a technology can significantly influence assessments of value for money and affordability, many of the countries have also incorporated pricing into the mandates of such systems (discussed in detail later). Finally, all consider at least three funding decision options, ie, provide, do not provide, and provide with restrictions or conditions (ie, restrict use to specific providers or patients meeting certain criteria, Table 1). In addition, approximately one-third have introduced a fourth option, ie, provide while additional evidence is collected. The latter comprises a provisional funding arrangement in which the technology is reimbursed in the interim while information needed to reduce uncertainties in existing evidence is collected to support a definitive decision.

Assessment of health technologies in centralized reimbursement systems

Approaches to the identification of technologies for review by centralized reimbursement systems vary across countries (Table 2). Broadly, there are three strategies: technologies may be submitted by manufacturers seeking coverage for newly licensed pharmaceuticals (13/23); they may be referred by potential payers (eg, government, sickness funds) or users (eg, hospitals, providers, patients), as well as manufacturers (8/23); or they may be identified by payers or users only (2/23). Systems limited to consideration of reimbursement applications from manufacturers alone typically review submissions in order of receipt, unless a technology is eligible for "fast tracking," which moves it to the front of the queue. In countries with such mechanisms (eg, the Netherlands), eligibility criteria include technologies (mainly pharmaceuticals) used to treat rare or life-threatening conditions for which no alternatives beyond best supportive care exist. Some countries (eg, Scotland and Norway) have more closely linked centralized regulatory and reimbursement processes in order to reduce overall inefficiencies in technology policy. Specifically, pharmaceuticals are automatically sent to the centralized reimbursement system for review upon market approval. In systems that accept referrals from multiple stakeholders, technology selection and/or prioritization criteria have been established. For example, Germany's Federal Joint Committee, which determines which technologies to review, takes into account clinical relevance, cost implications, and potential "risks" related to the technology and its introduction into the health care system.[6] In the UK, the topic selection panel of the National Institute of Health and Clinical Excellence, whose members include health care providers and patient representatives, formulate recommendations following consideration of: the burden of disease for which the technology targets; anticipated clinical impact (ie, whether the technology represents a significant medical advance that could yield substantial health benefits); potential impact on National Health Service costs and resources; alignment of the technology with broader government priority areas; concerns over appropriateness of use in practice; and potential for national guidance to add value.[7] Recommendations are forwarded to the Department of Health, which makes the final decision.

Across centralized reimbursement systems, technology identification and selection is followed by some form of health technology assessment (Table 2). This involves collection and synthesis of evidence (clinical and, in most cases, economic), the findings of which are presented in an assessment report, and critical appraisal of the relevance, quality, and generalizability of that evidence. The results of the latter are summarized in an evaluation report. Responsibility for the preparation of these reports varies. In systems where a manufacturer's submission initiates the reimbursement review process, the assessment report is part of the submission (Table 2). Therefore, its preparation rests with the

Table 1 Centralized reimbursement system and mandate

Country	Centralized reimbursement review/decision-making body (role)	Technology scope	Decision problem
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board/ Austrian Medicines Evaluation Commission (recommendations)[21,56–58]	• Pharmaceuticals – Outpatient[55]	• Provide as publicly insured service (reimbursable)[55] • Do not provide as publicly insured service (nonreimbursable)[55]
Belgium	• Minister of Social Affairs (decisions) • Commission on reimbursement of medicines/Drug Reimbursement Committee (recommendations)[9,60–63]	• Pharmaceuticals – Outpatient – Inpatient[21,64]	• Provide as publicly insured service (reimbursable)[21]
Czech Republic	• State Institute for Drug Control (decisions)[65–67]	• Pharmaceuticals – Outpatient[65]	• Provide as publicly insured service (reimbursable)[65]
Denmark	• Danish Medicines Agency (decisions).[68–70] Reimbursement Committee (recommendations)[68,70]	• Pharmaceuticals – Outpatient[71]	• Provide as publicly insured service[38,46,69,71]
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	• Pharmaceuticals – Outpatient[72]	• Provide as publicly insured service (reimbursable)[72]
Finland	• Pharmaceuticals Pricing Board (decisions)[64,73,74] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	• Pharmaceuticals – Outpatient[76]	• Provide as publicly insured service (reimbursable)[76] • Do not provide as publicly funded service (nonreimbursable)[76]
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	• Pharmaceuticals – Outpatient – Inpatient[79] • Devices[79] • Procedures[79]	• Provide as publicly insured service (reimbursable)[80]
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19]	• Pharmaceuticals – Outpatient – Inpatient[81,82] • Devices[18] • Procedures[83]	• Provide as publicly insured service (reimbursable)[55] • Do not provide as publicly funded service (nonreimbursable)[55] Note: Must not exclude technologies for which there is no alternative[18,81]
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85,86]	• Pharmaceuticals – Outpatient[85]	• Classify pharmaceutical into therapeutic category[85]
Hungary	• Ministers of Health and Finance (decisions) • National Health Insurance Fund Administration Health Technology Assessment Committee (recommendations)[88,89]	• Pharmaceuticals – Outpatient – Inpatient[90]	• Provide as publicly insured service[88] • Do not provide as publicly funded service (nonreimbursable)[26]
Ireland	• Health Service Executive (decisions)[91,92]	• Pharmaceuticals – Outpatient – Inpatient • Devices • Procedures[91,92]	• Provide as publicly insured service (reimbursable)[92]
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	• Pharmaceuticals – Outpatient – Inpatient[21]	• Provide as publicly insured service (reimbursable)[21]
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmacoeconomics (recommendations)[98]	• Pharmaceuticals – Outpatient – Inpatient[34]	• Provide as publicly insured service (reimbursable)[98]

Decision "scope"		Available decision options			
Reimbursement	**Linkage to pricing**	**Provide**	**Do not provide**	**Provide with restrictions**	**Provide while additional evidence is collected**
Yes[56,59]	Yes[21,56,59]	Yes[56]	Yes[56]	Yes[56]	Not specified
Yes[21]	Yes[21]	Yes[21]	Yes[21]	Yes[21]	Yes[21]
Yes[67]	Yes[67]	Yes[65]	Yes[65]	Yes[65]	Not specified
Yes[68]	No[68]	Yes[38,69]	Yes[38,69]	Yes[38,69]	Not specified
Yes[72]	Yes[72]	Yes[72]	Yes[72]	Yes[72]	No[67]
Yes[76]	Yes[76]	Yes[77]	Yes[73]	Yes[73]	No[74]
Yes[16,20,22,78]	Yes[16,20,22,78]	Yes[20]	Yes[20]	Yes[20]	Yes[16,20]
Yes[19]	Yes[82,84]	Yes[19]	Yes[19]	Yes[19]	Yes[19]
Yes[85]	Yes[87]	N/A	N/A	N/A	N/A
Yes[88]	Not specified	Yes[90]	Yes[90]	Yes[90]	Not specified
Yes[91]	No[91]	Yes[91]	Yes[91]	Yes[91]	No[93]
Yes[96,97]	Yes[96,97]	Yes[96]	Yes[96]	Yes[96]	Yes[96]
Yes[98]	Yes[98]	Yes[98]	Yes[98]	Yes[98]	Not specified

(*Continued*)

Table 1 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Technology scope	Decision problem
Poland	• Ministry of Health (decisions)[99]	• Pharmaceuticals – Outpatient – Inpatient[100]	• Provide as publicly insured service (reimbursable)[100]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[44,101]	• Pharmaceuticals – Outpatient – Inpatient[102]	• Provide as publicly insured service (reimbursable)[44]
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	• Pharmaceuticals – Outpatient – Inpatient[30]	• Provide as publicly insured service (reimbursable)[30]
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105–107]	• Pharmaceuticals – Outpatient – Inpatient[102]	• Provide as publicly insured service (reimbursable)[102] • Do not provide as publicly funded service (nonreimbursable)[102]
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products (decisions)[21,108]	• Pharmaceuticals – Outpatient – Inpatient[108]	• Provide as publicly funded service (reimbursable)[108] • Do not provide as publicly funded service (non-reimbursable)[108]
Sweden	• Dental and Pharmaceutical Benefits Board (decisions)[15,109,110]	• Pharmaceuticals – Outpatient • Devices (for administration of pharmaceuticals)[15,21,33,109]	• Provide as publicly funded service (reimbursable)[15]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113–115]	• Pharmaceuticals – Outpatient – Inpatient[113]	• Provide as publicly funded service (reimbursable)[113]
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Medicinal Products Reimbursement Committee of the Dutch Healthcare Insurance Board (recommendations)[116]	• Pharmaceuticals – Outpatient – High cost Inpatient[49] • Procedures[117]	• Provide as publicly funded service (reimbursable)[49]
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	• Pharmaceuticals – Outpatient – Inpatient[7] • Devices[7] • Procedures[7]	• Provide as publicly funded service (reimbursable)[7]
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[120]	• Pharmaceuticals – Outpatient – Inpatient[120]	• Provide as publicly funded service (reimbursable)[120]

manufacturer. Most systems have developed a standard template/structure for the report and submission guidelines to which manufacturers must adhere. These guidelines largely include content/information requirements and internationally accepted methods for synthesizing and analyzing evidence. In two of the countries, responsibility for the assessment depends upon the type of review ("appraisal"). Both France and the UK have created "single technology appraisal" and "multiple technology appraisal" processes. "Single technology appraisals" compare the candidate technology with a limited number of alternatives for a specific, well-defined indication (eg, disease stage). Their scope most closely resembles processes based upon manufacturers' submissions. "Multiple technology appraisals" consider either several indications for a candidate technology or several technologies (along with the candidate technology) for a condition at one or more points in its course, taking a disease management approach. The assessment report for a single technology appraisal is prepared by the manufacturer. For a multiple technology appraisal, the report is drafted either internally with support

Decision "scope"		Available decision options			
Reimbursement	**Linkage to pricing**	**Provide**	**Do not provide**	**Provide with restrictions**	**Provide while additional evidence is collected**
Yes[100]	Yes[100]	Yes[100]	Yes[100]	Yes[100]	Not specified
Yes[103]	Yes[99]	Yes[99]	Yes[99]	Yes[99]	No[99]
Yes[104]	No[104]	Yes[104]	Yes[104]	Yes[99]	No[99]
Yes[106]	Yes[106]	Yes[102]	Yes[102]	Yes[102]	Not specified
Yes[21]	Yes[21]	Yes[21]	Yes[21]	Yes[21]	No[21]
Yes[111]	Yes[112]	Yes[109]	Yes[109]	Yes[109]	Yes[109]
Yes[113,114]	Yes[113,114]	Yes[113,114]	Yes[113,114]	Yes[113,114]	Not specified
Yes[117,118]	No[31]	Yes[31]	Yes[31]	Yes[119]	Yes[119]
Yes[7]	No[7]	Yes[7]	Yes[7]	Yes[7]	Yes[7]
Yes[120]	No[120]	Yes[120]	Yes[120]	Yes[120]	Yes[120]

from external content and methodological experts (France) or by an independent academic group (the UK). Finally, in some countries, technical staff of a dedicated health technology assessment body or the centralized reimbursement system itself undertake the assessment report, regardless of the scope (eg, Germany).

With one exception (the UK), responsibility for preparing the evaluation report that accompanies each assessment also lies with technical staff and, if necessary, external experts. The National Institute of Health and Clinical Excellence commissions independent academic groups to evaluate assessments submitted by manufacturers as part of its single technology appraisal process.

Clinical and economic evidence expectations of centralized reimbursement systems

Centralized reimbursement systems have issued their own guidelines or endorsed internationally recognized published ones specifying clinical and economic evidence

Table 2 Comparison of processes for identifying, selecting, and assessing technologies

Country	Centralized reimbursement review/ decision-making body (role)	Technologies to be considered for review Technology identification
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[58]
Belgium	• Minister of Social Affairs (decisions) • Commission on reimbursement of medicines/Drug Reimbursement Committee (CRM) (recommendations)[9]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[17]
Czech Republic	• State Institute for Drug Control (decisions)[65]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[66]
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[84]
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[72]
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[76]
France	• Ministry for Health and Social Security (decisions)[21,78] • French National Authority for Health (recommendations)[78]	*Depends on type of appraisal I*[6,20] *Single technology appraisal* Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals and devices • Health care professional associations seeking reimbursement for procedures *Multiple technology appraisals* *Typically classes of pharmaceuticals or categories of devices* *Referred by:* • Health care professional associations • Ministry of Health • National Union of Health Insurance Funds • Patient and/or carer organizations[120]
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19]	Referred by: • Associations represented by Federal Joint Committee • Ministry of Health • Institute for Quality and Efficiency in Health Care • Federal commissioner of patient affairs • Patient and/or carer organizations[18]
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[85]
Hungary	• Ministers of Health and Finance (decisions) • National Health Insurance Fund Administration (recommendations)[88,89]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals • National Health Insurance Fund Administration[88]

	Health technology assessment	
Technology selection	**Synthesis and analysis of evidence (assessment report)**	**Evaluation of evidence provided (evaluation report)**
• Typically considered in order received[58]	• Manufacturer through submission requirements[55] • Methods should comply with internationally recognized systematic review and economic guidelines[55]	• Technical staff within Association of Austrian Social Security Institutions (Department of Pharmaceutical Affairs – pharmacological and medical-therapeutic assessment; Health Economics Team – economic assessment)[55]
• Typically considered in order received[17]	• Manufacturer through submission requirements[9] • Methods should comply with internationally recognized systematic review guidelines[9]	• Technical staff within CRM supported by external experts[9]
• Typically considered in order received[65]	• Manufacturer through submission requirements[66]	• Technical staff within State Institute for Drug Control[65]
• Typically considered in order received[84]	• Manufacturer through submission requirements[68] • Methods must comply with "Danish guidelines for the socioeconomic analysis of medicines"[68]	• Technical staff within Danish Medicines Agency supported by external experts, if necessary[68]
• Not specified	• Manufacturer through submission requirements[72]	• Technical staff within Estonian Health Insurance Fund and State Agency of Medicines[72]
• Typically considered in order received[73]	• Manufacturer through submission requirements[122] • Methods must comply with guidelines of the Ministry of Social Affairs and Health[122]	• Technical staff within Pharmaceuticals Pricing Board supported by external experts[122]
Single technology appraisals • Typically considered in order received[16] *Multiple technology appraisals* • Selection criteria not specified	*Single technology appraisals* • Manufacturer through submission requirements[20] *Multiple technology appraisals* • Technical staff within Health and Social Security supported by external experts[20] • Methods should comply with internationally recognized systematic review and economic guidelines[20]	*Single technology appraisals* • Technical staff within Health and Social Security supported by external experts[20] *Multiple technology appraisals* • Technical staff within Health and Social Security or independent academic group[20]
• Determined by Federal Joint Committee • Selection criteria: 1. Clinical relevance 2. Cost implications 3. "Risks"[6]	• Technical staff within Institute for Quality and Efficiency in Health Care supported by external experts[123,124] • Methods must comply with Institute for Quality and Efficiency in Health Care systematic review and economic guidelines[124]	• Technical staff within Institute for Quality and Efficiency in Health Care supported by external experts[123,124]
• Not specified	• Manufacturer through submission requirements[85]	• Technical staff within Transparency Committee in the Reimbursement and Medicinal Products[85]
• Not specified	• Technical staff within National Technology Assessment Office of the National Institute for Strategic Health Research[90]	• Technical staff within National Technology Assessment Office of the National Institute for Strategic Health Research[90]

(*Continued*)

Table 2 (*Continued*)

Country	Centralized reimbursement review/ decision-making body (role)	Technologies to be considered for review Technology identification
Ireland	• Health Service Executive (decisions)[91,92]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[91] Referred by: • Department of Health and Children of the Health Services Executive for new and existing devices and diagnostic tests that might "incur a high cost or have a significant budget impact"[91]
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[27]
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmacoeconomics (recommendations)[98]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[34]
Poland	• Ministry of Health (decisions)[99]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[99]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[36,45]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[36]
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[104] • Automatic within 12 weeks of market launch[104]
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,107,129,106]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[104]
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products • Inter-Ministerial Pricing Commission (decisions)[21,108]	Referred by: • Ministry of Health (newly approved pharmaceuticals)[108]
Sweden	• Dental and Pharmaceutical Benefits Board (decisions)[15,109,110]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[104] • Dental and Pharmaceutical Benefits Board (for pharmaceuticals approved prior to 2002)[133,134]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[114,115]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[114] • Patients and carers • Hospitals and hospital groups • Health care professional associations • Federal Office of Public Health[114,137]
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Medicinal Products Reimbursement Committee of the Dutch Healthcare Insurance Board (recommendations)[116]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[31] • University hospital federations, health care professional associations, and Dutch Healthcare Insurance Board for high-cost inpatient pharmaceuticals

	Health technology assessment	
Technology selection	**Synthesis and analysis of evidence (assessment report)**	**Evaluation of evidence provided (evaluation report)**
• Not specified	• Manufacturer through submission requirements[93,125] • Methods must comply with Irish Health Technology Assessment Guidelines[93]	• Technical staff within National Centre for Pharmacoeconomics, supported by external clinical experts[93]
• Typically considered in order received[27]	• Manufacturer through submission requirements[126] • Methods must comply with Italian submission guidelines[27]	• Members of Technical Scientific Committee[126]
• Not specified	• Manufacturer through submission requirements[34] • Methods should comply with internationally recognized systematic review guidelines[34]	• Technical staff within Norwegian Medicines Agency and Department of Pharmacoeconomics[98]
• Not specified	• Manufacturer through submission requirements[99]	• Technical staff within Ministry of Health[99] • Agency for Health Technology Assessment[127]
• Not specified	• Manufacturer through submission requirements[36]	• Technical staff within INFARMED supported by external experts[36]
• Exclusion criteria: Already appraised by National Institute of Health and Clinical Excellence through its multiple technologies appraisal process[104]	• Manufacturer through submission requirements[128] • Methods must comply with Scottish Medicines Consortium systematic review and economic guidelines[34]	• Technical staff within Scottish Medicines Consortium supported by external experts[128]
• Not specified	• Manufacturer through submission requirements[131]	• Working group for pharmacoeconomics and outcomes research[131]
• Not specified	• Manufacturer through invitation to submit information to Inter-Ministerial Pricing Commission[21] • Technical staff within Ministry of Health[132]	• Inter-Ministerial Pricing Commission[21]
• For new pharmaceuticals: typically considered in order received • For older pharmaceuticals: Overall sales volume[134,135]	• For new pharmaceuticals: Manufacturer through submission requirements[136] • For older pharmaceuticals: Technical staff within Dental and Pharmaceutical Benefits Board supported by external experts[136] • Methods must comply with Dental and Pharmaceutical Benefits Board systematic review and economic guidelines[10]	• For new pharmaceuticals: Technical staff within Dental and Pharmaceutical Benefits Board[136] • For older pharmaceuticals: Technical staff within Dental and Pharmaceutical Benefits Board supported by external experts[136]
• Not specified	• Manufacturer through submission requirements[113]	• Federal Drug Commission[114]
• Not specified	• Manufacturer through submission requirements[31] • Technical staff within Dutch Healthcare Insurance Board[117] • Methods must comply with internationally recognize systematic review guidelines and Dutch Healthcare Insurance Board economic guidelines[117]	• Technical staff within Dutch Healthcare Insurance Board[117]

(*Continued*)

Table 2 (*Continued*)

Country	Centralized reimbursement review/ decision-making body (role)	Technologies to be considered for review Technology identification
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals • Patients and carers • Health care providers • Health care professional associations • General Public • National Horizon Scanning Centre[120]
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[28]	Referred by: • Manufacturers seeking reimbursement for newly approved pharmaceuticals[28] • Welsh Medicines Partnership horizon scanning process for identifying pharmaceuticals expected to receive market approval within 18 months[28]

requirements for assessment reports (Tables 3 and 4). These guidelines state topics to be addressed and the types of information accepted for addressing them. In most cases (16/23), specified clinically-related topics are similar and include: burden of illness and/or characteristics of the target patient population; therapeutic claim of the candidate technology; safety; efficacy; and effectiveness (preferably comparative effectiveness) across relevant patient subgroups (Table 3). Additionally, several require information on current management or the place of the candidate technology within existing treatment pathways (eg, France and the UK), and its proposed frequency and duration of use (eg, Austria). Across systems and where reported, there is a shared preference for information on health outcomes that represent final clinical endpoints related to mortality, morbidity, and quality of life. Less frequently, information on adverse events/complications is also required. This may be explained by the fact that a prerequisite for reimbursement review is typically regulatory approval. Therefore, systems may view reconsideration of adverse events, which relate to the safety of a technology, unnecessary. In systems proposing or stipulating the use of quality-adjusted life-years (7/23), change in health-related quality of life is to be measured in patients and then valued in the public or general population (eg, the UK). Surrogate outcomes are discouraged or not accepted unless well validated (eg, Germany). Lastly, some systems elicit the views of patients and or carers in identifying topic specific outcomes and their relative importance (eg, Germany).

In general, centralized reimbursement systems state a preference for head-to-head randomized controlled trials comparing the candidate technology with standard care, no active treatment/best supportive care, or placebo (if no alternatives exist, Table 3). However, increased interest in evidence of "comparative effectiveness" over "comparative efficacy" among most reimbursement systems has led to requests for inclusion of head-to-head randomized controlled trials conducted in "naturalistic settings" (ie, pragmatic trials, in the UK) and other direct comparative studies (observational and experimental in design), the collective findings of which may offer a more accurate prediction of the behavior of the technology in general clinical practice (eg, France, Germany, and Sweden). Also, there appears to be emerging recognition of the need for flexibility in evidence expectations under certain circumstances. Recently, Germany's Institute for Quality and Efficiency in Health Care, which conducts

	Health technology assessment	
Technology selection	**Synthesis and analysis of evidence (assessment report)**	**Evaluation of evidence provided (evaluation report)**
Selection criteria: • Burden of disease (population affected, mortality, and morbidity) • Resource impact (on National Health Service costs and resources) • Clinical importance • Policy importance (alignment with government priority areas) • Inappropriate variations in practice • Likelihood of national guidance adding value[7] Technology selection panel composition: • Health care providers (specialists, general practitioners, and public health professionals) • Patient representatives Technology selection panel makes recommendations. Final decisions made by Department of Health[7]	*Single technology appraisals* • Manufacturer through submission requirements[120] Multiple technology appraisals • Independent academic group[120] • Methods must comply with National Institute for Health and Clinical Excellence systematic review and economic guidelines[120]	*Single technology appraisals* • Independent academic group[120] Multiple technology appraisals • Independent academic group[120]
• Typically considered in order received[28]	• Manufacturer through submission requirements[28] • Welsh Medicines Partnership[28] • Methods must comply with All Wales Medicines Strategy Group systematic review and economic guidelines[28]	• Welsh Medicines Partnership[28]

health technology assessments and makes reimbursement recommendations on selected health technologies to the Federal Joint Committee, issued methodological guidelines suggesting that when no active alternative treatment exists, well designed case series would be deemed adequate.[8]

While across systems, the preferred source of such clinical evidence is published, peer-reviewed studies, many encourage, and in several cases require if available, inclusion of unpublished or ongoing studies (eg, Austria, Belgium, Norway, Poland, Slovakia, Sweden, the Netherlands, and the UK), commercial in-confidence data (eg, Austria, France, Sweden, and the UK) and/or current national and international clinical practice guidelines (eg, France) in assessment reports. In recent years, some systems have incorporated submissions from patient and/or carer organizations into their processes (eg, Scotland, Sweden, and the UK). Such submissions are increasingly viewed as an important source of information regarding the relative value of outcome measures employed in clinical studies and the meaningfulness or significance of findings to patients and carers. Finally, while systems tend not to explicitly exclude sources of information, Belgium's Drug Reimbursement Committee states that abstracts are not accepted.[9]

Most centralized reimbursement systems (20/23) have made mandatory the inclusion of a formal economic evaluation/analysis for either some (ie, those for which alternative(s) exist(s), eg, Germany, or those offering "added therapeutic value," eg, Austria and Belgium, or all candidate technologies to inform deliberations around "value for money" and/or "efficiency." In the latter case, the type of evaluation is rarely stipulated, because options available depend, in part, on the magnitude of the incremental benefit of the technology over its comparators. However, a rationale must be presented, and methods adopted must comply with economic guidelines developed or endorsed by the centralized reimbursement system (Table 4). For technologies that appear to offer "added therapeutic value" (ie, are more effective), some systems indicate a preference for certain types of evaluations, such as cost-utility analysis by Ireland's Health Service Executive.[10] Others state explicitly which types will not be accepted, such as cost-benefit analysis by Belgium's Drug Reimbursement Committee.[11] In addition to a formal economic evaluation, the Institute for Quality and Efficiency in Health Care in Germany requires an efficiency frontier analysis, which assesses the relative value of different technologies within a given therapeutic area.[12] Regarding the perspective to be taken for

Table 3 Comparison of clinical evidence requirements

Country	Centralized reimbursement review/decision-making body (role)	Clinical evidence requirements
		Topic
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	• Target patient population and indications (therapeutic claim) • Pharmacology • Safety • Efficacy • Effectiveness (across population subgroups) • Frequency and duration of treatment[55]
Belgium	• Minister of Social Affairs (decisions) • Commission on reimbursement of medicines/Drug Reimbursement Committee (recommendations)[9,60]	• Target patient population and indications (therapeutic claim) • Safety • Efficacy • Effectiveness (across population subgroups)[11]
Czech Republic	• State Institute for Drug Control (decisions)[65]	• Safety • Efficacy • Effectiveness[66]
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	• Target patient population and indications (therapeutic claim) • Safety • Efficacy • Effectiveness (across population subgroups)[38]
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[67]	• Safety • Efficacy • Effectiveness[139]
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Effectiveness (across population subgroups)[76]
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[20,78]	• Target patient population and indications (therapeutic claim) • Current management • Place of technology in care pathway • Safety • Efficacy • Effectiveness (across population subgroups)[16]
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19,141]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Safety • Efficacy • Effectiveness (across population subgroups)[8]
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85]	• Safety • Efficacy • Effectiveness[145]

Preferred clinical outcomes	Type	Source
• Not specified	Preference for: • Double-blind randomized controlled trials • Systematic reviews and meta-analyses of randomized controlled trials complying with internationally recognized guidelines[55]	• Published, peer-reviewed studies • Unpublished reports and studies may be accepted in exceptional circumstances[55] • Commercial, in-confidence data[55]
• Morbidity • Adverse events/complications • Quality of life • Overall survival/mortality (life-years gained) • Quality-adjusted life years (QALYs) – measured in patients but valued by public/society • Other relevant disease-specific outcomes[4] • Final endpoints[11]	Preference for: • Randomized controlled trials • Observational head-to-head comparative studies[11,17] • Effectiveness studies (over efficacy studies)[17] • Minimum of one positive superiority trial on primary endpoints against active control or placebo (if no alternative treatments exist)[17]	• Published, peer-reviewed studies • Unpublished reports and studies[17] • Abstracts not accepted[9]
• Not specified	• All clinical trials[138]	• Not specified
• Not specified	Preference for: • Randomized controlled trials comparing pharmaceutical to standard care[38]	• Not specified
• Adverse events/complications • Side effects • Overall survival/mortality[139,140]	Preference for: • Randomized controlled trials[84]	• Published, peer-reviewed studies[84]
• Not specified	Preference for: • Randomized controlled trials comparing pharmaceutical to standard care[76] *Evidence from other available direct comparative experimental and observational studies, as well as meta-analyses, should be included*[76]	• Published, peer-reviewed studies[76]
• Morbidity • Overall survival/mortality • Quality of life[16]	Preference for: • Head-to-head, double-blind randomized controlled trials • Other direct comparative studies • Post-market studies • Systematic reviews and meta-analyses of randomized controlled trials complying with internationally recognized guidelines[16]	• Published, peer-reviewed studies • Current national and international clinical practice guidelines • Expert opinion • Surveys of practice • Commercial, in-confidence data[16]
• Morbidity • Overall survival/mortality • Quality of life • Adverse events/complications • Side effects • Duration of illness • Health status[8,83,142–144] • Topic specific outcomes identified in consultation with patient organizations[18] • Validated surrogate outcomes[83]	Preference for: • Randomized controlled trials comparing pharmaceutical to placebo, standard care, or no active treatment[8] *Evidence from other available direct comparative experimental and observational studies, as well as systematic reviews and meta-analyses complying with internationally recognized guidelines, should also be included*[8] • If no treatment alternative exists, well-documented case series acceptable[8]	• Published, peer-reviewed studies • Commercial, in-confidence data not accepted unless it can be published[18]
• Not specified	• Not specified	• Not specified

(*Continued*)

Table 3 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Clinical evidence requirements
		Topic
Hungary	• Ministers of Health and Finance (decisions) • National Health Insurance Fund Administration (recommendations)[88]	• Severity and burden of illness • Current management • Safety • Efficacy • Effectiveness (across population subgroups)[90]
Ireland	• Health Service Executive (decisions)[91,92]	• Safety • Efficacy • Effectiveness (across population subgroups)[146]
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Safety • Efficacy • Effectiveness (across population subgroups)[148]
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmacoeconomics (recommendations)[98]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Place of technology in care pathway • Safety • Efficacy • Effectiveness (across population subgroups)[34,149]
Poland	• Ministry of Health (decisions)[99,100]	• Severity and burden of illness • Current management • Safety • Efficacy • Effectiveness (across population subgroups)[151]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[44]	• Safety • Efficacy • Effectiveness (across population subgroups)[101]
Scotland	• National Health Service Scotland (decisions)[50] • Scottish Medicines Consortium (recommendations)	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Place of technology in care pathway • "Comparative" safety • Efficacy • Effectiveness (across population subgroups)[128]
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,107,130]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Patient acceptance • Safety • Efficacy • Effectiveness • Frequency and duration of treatment[106]
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Safety • Efficacy • Effectiveness[132]

Preferred clinical outcomes	Type	Source
• Not specified	Preference for: • Randomized controlled trials[84]	• Published, peer-reviewed studies[90]
• Morbidity • Overall survival/mortality • Quality of life • QALYs – measured in patients but valued by public/society[146] • All other health benefits accrued by individuals[147]	Preference for: • Randomized controlled trials[147] *Evidence from other available direct comparative experimental and observational studies, as well as systematic reviews and meta-analyses complying with Irish Health Technology Assessment Guidelines, should also be included*[146]	• Not specified
• Morbidity • Overall survival/mortality • Quality of life[149]	Preference for: • Randomized controlled trials comparing pharmaceutical to standard care[97] • Evidence from other available direct experimental and observational studies comparing pharmaceutical with standard care[148]	• Not specified
• Morbidity • Overall survival/mortality • Quality of life[144]	Preference for: • Head-to-head, double-blind randomized controlled trials • Other direct comparative studies • Systematic reviews and meta-analyses complying with internationally recognized guidelines[149,150]	• Published, peer-reviewed studies • Unpublished reports and studies[149,150]
• Morbidity • Overall survival/mortality • Quality of life[151]	Preference for: • Randomized controlled trials[151]	• Published, peer-reviewed studies • Unpublished reports and studies[151]
• Morbidity • Overall survival/mortality • Quality of life[101]	Preference for: • Effectiveness studies of target population (over efficacy studies)[101] • Comparative clinical trials • Other study designs accepted, but rationale must be provided[101]	• Not specified
• Morbidity • Overall survival/mortality • Quality of life • QALYs (strongly preferred)[50]	• Randomized controlled trials required • Comparative observational studies accepted[50] • If no head-to head studies available, indirect comparison required[50]	• Published, peer-reviewed studies • Unpublished reports and studies • Expert opinion • Submissions from patient and carer organizations[128]
• Morbidity • Overall survival/mortality • Adverse events/complications • Quality of life[106]	Preference for: • Comparative studies[84]	• Published, peer-reviewed studies • Unpublished reports and studies with negative findings[152]
• Morbidity • Overall survival/mortality • Quality of life • QALYs[132]	Preference for: • Randomized controlled trials *Evidence from other available direct comparative experimental and observational studies should also be included*[132]	• Not specified

(*Continued*)

Table 3 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Clinical evidence requirements
		Topic
Sweden	• Dental and Pharmaceutical Benefits Board (decisions)[15,109]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Safety • Efficacy • Effectiveness[153]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113–115]	• Safety • Efficacy • Effectiveness[113]
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Medicinal Products Reimbursement Committee of the Dutch Healthcare Insurance Board (recommendations)[116]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Safety • Efficacy • Effectiveness[154]
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Place of technology in care pathway • "Comparative" safety • Efficacy • Effectiveness (across population subgroups)[29]
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[120]	• Target patient population and indications (therapeutic claim) • Severity and burden of illness • Current management • Place of technology in care pathway • "Comparative" safety • Efficacy • Effectiveness (across population subgroups)[28]

the economic evaluation, the proportion of systems adopting a "payer," "societal," or both "payer" and "societal" perspective is similar. Among systems considering a payer's perspective only, costs to be captured are often restricted to those directly related to care associated with the use of the candidate technology throughout the course of a disease or condition (ie, direct costs to the health care system). One exception is the National Institute of Health and Clinical Excellence, which specifies inclusion of direct and indirect costs to the National Health Service and Personal Social Services.[13] In systems requiring a societal perspective, costs specified comprise direct costs to not only the health care system, but also services beyond health care and indirect (lost productivity) costs. However, they must be reported separately (eg, Finland, Portugal, and the Netherlands). In Sweden, The Dental and Pharmaceutical Benefits Board has taken a wider view on indirect costs, requesting that time lost by patients and carers be considered, along with lost productivity.[14,15] Thus, its methods broadly resemble those of "holistic" economic analysis, a technique initially developed for economic evaluations of public programs, the costs and benefits of which are often complex. Nevertheless, considerable debate over the valuation of items such as "time lost" within academic and policy communities remains. This may be why other systems employing a societal perspective have assumed a narrower position on eligible indirect costs. With respect to the choice of comparator for the economic evaluation, almost all systems specify use of one of the following: "standard care," "the most commonly used alternative," or "alternative most likely to be replaced." France also requires separate analyses with two additional comparators, ie, the most recently reimbursed alternative and the least expensive alternative.[16] In Belgium, if the candidate technology represents an "addon" treatment, the comparator must constitute current treatment without the candidate technology.[17] Further, the use of "offlabel" treatments as the comparator is not permitted.[11] All systems rely upon sensitivity analyses to assess the stability of estimates generated through the economic evaluation, but few stipulate the type. Among those that do, probabilistic sensitivity analysis is the most commonly prescribed (eg, Belgium, Germany, Scotland, Slovakia, the UK, and Wales).

Preferred clinical outcomes	Type	Source
• Morbidity • Overall survival/mortality • Quality of life • QALYs (preferred)[109]	Preference for: • Randomized controlled trials comparing pharmaceutical to standard care[109] *Evidence from other available direct comparative experimental and observational studies should also be included*[15]	• Commercial, in-confidence data[109] • Published, peer-reviewed studies • Unpublished reports and studies • Ongoing studies • Submissions from patient and carer organizations[51]
• Not specified	• Not specified	• Not specified
• Morbidity • Overall survival/mortality • Quality of life[36,155]	Preference for: • Head-to-head randomized controlled trials • Systematic reviews or meta-analyses complying with internationally recognized guidelines[35,156]	• Published, peer-reviewed studies • Unpublished reports and studies • Commercial, in-confidence data • Expert opinion[154]
• Morbidity • Overall survival/mortality (life years) • Quality of life[157] • QALYs – measured in patients but valued by public/society[29,158]	Preference for: • Head-to-head randomized controlled trials conducted in "naturalistic" settings • Effectiveness studies of target population (over efficacy studies) • Systematic reviews or meta-analyses complying with internationally recognized guidelines[159] *Evidence from other available direct comparative experimental and observational studies should also be included*[159] *Registries, case series, and follow-up studies also accepted*[159]	• Published, peer-reviewed studies • Unpublished reports and studies • Commercial, in-confidence data[159] • Submissions from patient and carer organizations[159] • Information from health care professional associations, administrators, government, and manufacturers[157]
• Morbidity • Overall survival/mortality • Quality of life • QALYs (preferred)[28]	• All types of clinical studies accepted, but greater importance given to high quality ones[28]	• Published, peer-reviewed studies • Unpublished reports and studies • Expert opinion • Submissions from patient and carer organizations describing experiences of those who have taken the pharmaceutical[28]

In recent years, affordability has become an increasingly important consideration for centralized reimbursement systems, with almost all of those included in this review (where information could be found) requiring a budget impact analysis (Table 4). However, some waive this analysis in certain circumstances, eg, when no alternative treatment exists (Belgium).[17] Although information describing the specific costs to be included appears scarce, based on that available, they mirror those for the economic evaluation of the same technology. Specifically, if the economic evaluation is limited to direct costs, so must the budget impact analysis, eg, Hungary and Ireland.

Reimbursement decisions: review committee composition, procedures, and key factors

In most of the centralized reimbursement systems, the assessment and evaluation reports are sent to and scrutinized by a review committee (sometimes referred to as an appraisal committee). While the composition of this committee varies across systems, it is usually multidisciplinary, with members representing payers, administrators, health care providers, and academia (eg, health economists, Table 5). Approximately one-third have also appointed patient representatives to their respective committees (eg, Sweden, Switzerland, and the UK), although not always as voting members (Germany),[18,19] and one-fifth include manufacturers (Belgium, Switzerland, the UK, and Wales). In most systems, the authority of the review committee is advisory (ie, makes recommendations). Aside from lists of factors/criteria considered (Table 6), publicly available procedural information on committee deliberations is often limited to conditions under which presentations/testimonials from external experts (including patients) are sought or accepted and whether an incremental cost-effectiveness ratio threshold is employed. Among the exceptions is France. There, review committees (the Commission d'Evaluation des Medicaments (CEM), followed by the Transparency Commission) adhere to a two stage process. First, the CEM assigns a "medical benefit" or "SMR" level/

Table 4 Comparison of economic evidence requirements

Country	Centralized reimbursement review/decision-making body (role)	Economic analysis		
		Required	Economic analysis types accepted	Perspective/ costs included
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	Yes for: • "innovative products providing substantial therapeutic benefit • "where no comparable medical preparation exists"[21]	• Any type, but rationale for selection must be provided[21] • Should comply with internationally recognized pharmacoeconomic guidelines[21]	• Payer[21] • Costs not specified
Belgium	• Minister of Social Affairs (decisions) • Commission on reimbursement of medicines/ drug reimbursement committee (recommendations)[9,60]	Yes for: • Pharmaceuticals with added therapeutic value relative to existing alternatives (Class I)[11,17] Not required for orphan pharmaceuticals[62]	• Cost effectiveness • Cost utility • Cost benefit not accepted[11] • Should comply with Belgium pharmacoeconomic guidelines[17]	• Payer (includes patient copayments and government)[11,17] • Direct costs only[11,17]
Czech Republic	• State Institute for Drug Control (decisions)[65]	Yes[66]	• Cost effectiveness[138]	• Payer[66] • Direct costs[138]
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	No, but often included to justify high price[68,71,160]	• Cost effectiveness • Cost utility[68] If included, methods should comply with Danish Guidelines for the Socio-economic Analysis of Medicines[68]	• Societal (if included) • Direct, indirect, and intangible; to be reported separately[71]
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	Yes[84,139]	• Cost effectiveness • Cost utility • Cost minimization rationale for selection must be provided[139]	• Payer[139] • May present separate analysis from societal perspective[84] • Direct costs within and outside of the health care system (should be reported separately)[139]
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	Yes for: Pharmaceuticals considered for reimbursement in one of the special refund categories[74,76]	• Any type, but rationale for selection must be provided[76] • Methods must comply with Ministry of Social Affairs and Health guidelines[76]	• Societal[76] • Direct and indirect costs – presented separately[76]
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	Yes for: • Multiple technology appraisals of pharmaceuticals[20]	• Any type, but rationale for selection must be provided[22] • Methods must comply with French economic guidelines[20]	• Varies, but should take the widest possible perspective – rationale for selection must be provided [84] • Direct costs; may include indirect costs, but must be presented separately[22]

Comparator	Sensitivity analysis	Systematic review of economic analysis studies	Budget impact analysis		Other economic information
			Required	Costs included	
• Most commonly used alternative[21]	Yes – type not specified[21]	Yes	No information found	N/A	• 3 year market sales forecast • Price in other European Union countries • Reimbursement status in other European Union countries[55]
• Most commonly used alternative OR • Alternative most likely to be replaced • If add-on: current treatment without add-on[17] • Off-label treatments not acceptable[11] Rationale must be provided	Probabilistic[17]	Yes[17]	Yes[11]	• Direct costs only[11,17]	• Price • Reimbursement status in other European Union countries[11,17]
No information found	Method not specified	No information found	Yes[138]	No information found	No information found
• Most commonly used alternative[38]	Method not specified, but key parameters associated with uncertainty should be explored[38]	No information found	Yes[38]	No information found	• Reimbursement status in other European Union countries • Estimated consumption (number of patients and utilization)[38]
• Most commonly used alternative OR • Standard care[139] Rationale must be provided	Method not specified	No information found	No information found	No information found	No information found
• Alternative most likely to be replaced OR • Most commonly used alternative OR • Most effective alternative OR • Minimum management[76] Rationale must be provided	Method not specified	Yes[76]	Yes[161]	No information found	• Market sales forecast • Reimbursement status in other European Union countries • Estimated consumption (number of patients and utilization)[161]
Following 3 comparators required: • Most commonly used alternative • Most recently reimbursed alternative • Least expensive alternative[16]	Method not specified	Yes for pharmaceuticals[22]	Yes[20]	No information found	• Market sales forecast • Reimbursement status in other European Union countries • Breakdown of costs for manufacturing and distribution[22,162]

(*Continued*)

Table 4 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Economic analysis		
		Required	**Economic analysis types accepted**	**Perspective/ costs included**
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19,24,144]	Yes for: • Technologies where alternative treatment exists[8,18]	Any one of: • Cost effectiveness • Cost utility • Cost minimization/ cost comparison[18] Efficiency frontier analysis[12]	• Payer • Patient[83] • Direct and indirect costs[8]
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85,160]	Yes for: • Pharmaceuticals eligible for reference price system[85]	No information found	No information found
Hungary	• Ministers of Health and Finance (decisions) • National Health Insurance Fund Administration (recommendations)[86,90,102]	Yes[84]	Preference for: • Cost effectiveness • Cost utility[163]	• Payer • Societal (also recommended) Report results from each perspective separately[163]
Ireland	• Health Service Executive (decisions)[91,92]	Yes[146]	Preference for: • Cost utility[10] Any one of the following may be acceptable if rationale is provided: • Cost benefit • Cost effectiveness • Cost minimization/ cost comparison[147,165] • Methods must comply with Irish Healthcare Technology Assessment Guidelines[146]	• Payer[147] • Direct costs only[147]
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	Yes for: • Pharmaceuticals with a favorable "risk/benefit profile"[97,148]	Preference for: • Cost utility • Cost effectiveness[148] • Methods must comply with Italian pharmacoeconomic guidelines[148]	• Societal AND • Payer[148] • Direct and indirect costs[148]
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmaco economics (recommendations)[98]	Yes for: • Pharmaceuticals with added therapeutic value relative to existing alternatives[34]	Preference for: • Cost-value analysis[150] Any one of the following may be acceptable if rationale is provided: • Cost benefit • Cost effectiveness • Cost utility • Cost consequence • Cost minimization/ cost comparison[34] • Methods must comply with Norwegian pharmacoeconomic guidelines[34]	• Societal AND • Payer[150]

Comparator	Sensitivity analysis	Systematic review of economic analysis studies	Budget impact analysis		Other economic information
			Required	Costs included	
• Most commonly used alternative OR • Most effective alternative OR • Minimum standard care[8]	One-way and multi-way (performed as probabilistic)[24]	Yes[84]	Yes, except when no alternative exists[18]	No information found	No information found
No information found	No information found	No information found	Yes[85]	No information found	• Cost of daily treatment • Reimbursement status in other European Union countries[85]
• Standard care[163]	Yes, but type not specified[163]	No information found	Yes[84]	• If payer perspective, include direct costs only • If societal perspective, include indirect costs (productivity)[163]	No information found
• Standard care[125]	Probabilistic and deterministic[125]	No information found	Yes	• Direct costs only[91,147]	No information found
• Most commonly used alternative[148]	Methods not specified, but should involve multi-way analysis[148]	No information found	Yes[148]	No information found	• Cost of treatment compared to those in same therapeutic class • Market sales forecast • Price in other European Union countries • Reimbursement status in other European Union countries • Estimated consumption (number of patients and utilization) • Industrial implications[97]
• Most commonly used alternative OR • Least expensive alternative[150]	Probabilistic preferred[150]	No information found	Yes[149] Aggregate added expense to health service for first 5 years[149]	No information found	• Market sales forecast • Price in other European Union countries • Reimbursement status in other European Union countries • Estimated consumption (number of patients and utilization)[149,150]

(*Continued*)

Table 4 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Economic analysis		
		Required	Economic analysis types accepted	Perspective/ costs included
Poland	• Ministry of Health (decisions)[99,166]	Yes for: • Pharmaceuticals with added therapeutic value relative to existing alternatives[84]	• Cost effectiveness • Cost utility[84]	• Societal AND • Payer[167]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[64,160]	Yes[44,160]	Any one of : • Cost benefit • Cost effectiveness • Cost utility • Cost minimization/ cost comparison; rationale for selection must be provided[101]	• Societal[101] • Direct costs • Indirect costs: only those related to lost productivity[101]
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	Yes[168]	Any one of : • Cost benefit • Cost effectiveness • Cost utility • Cost minimization/ cost comparison; rationale for selection must be provided[168] • Methods must comply with SMC economic guidelines[168]	• Payer[30]
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,107]	Yes[105,106]	• Cost effectiveness • Cost utility (if pharmaceutical has impact on quality of life) • Cost minimization/ cost comparison • Cost benefit not accepted[169] Methods should comply with national economic guidelines[170]	• Payer[169] • Direct costs[169]
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108,171]	No[21]	Preference for: • Cost effectiveness • Cost utility[10,21] Any one of the following may be acceptable if rationale is provided: • Cost benefit • Cost effectiveness • Cost utility • Cost consequence • Cost minimization/ cost comparison[10]	• Societal AND • Payer[10] Presented separately

Comparator	Sensitivity analysis	Systematic review of economic analysis studies	Budget impact analysis		Other economic information
			Required	Costs included	
• Alternative most likely to be replaced OR • Most commonly used alternative OR • Least expensive alternative OR • Standard care compliant with clinical practice guidelines[151]	Methods not specified	No information found	Yes[84]	No information found	No information found
• Most commonly used alternative • Standard care[101]	Methods not specified	No information found	No[101]	N/A	No information found
• Alternative most likely to be replaced OR • Most commonly used alternative[30]	Probabilistic[168]	No information found	Yes[30]	No information found	• National Health Service resource implications[30]
• Alternative most likely to be replaced • If add-on: current treatment without add-on[152]	Probabilistic[106,152]	Yes[152]	Yes Estimated over first 5 years[84]	No information found	No information found
• Most commonly used alternative • Standard care[10] Rationale must be provided	Multi-way[10]	No information found	Yes, comparing "corresponding products"[10]	No information found	No information found

(*Continued*)

Table 4 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Economic analysis		
		Required	Economic analysis types accepted	Perspective/ costs included
Sweden	• Dental and Pharmaceutical Benefits Board (decisions)[15,109]	Yes, if requested[21]	Any one of: • Cost effectiveness • Cost utility • Cost minimization/ cost comparison; rationale for selection must be provided[15] • Methods must comply with Swedish economic guidelines[15]	• Societal • Direct costs • Indirect costs: lost productivity and lost time for patients and carers[14,15]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113,114]	No, but should be included if available[115,172]	No information found	No information found
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Medicinal Products Reimbursement Committee of the Dutch Healthcare Insurance Board (recommendations)[116]	Yes for pharmaceuticals with added therapeutic value (Annex 1B), except for orphan pharmaceuticals with small budget impact or absence of active alternative[154]	• Cost effectiveness • Cost utility • Methods must comply with Dutch Healthcare Insurance Board economic guidelines[36,84,173]	• Societal • Direct costs[154] • Indirect costs may be included but must be reported separately[154]
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	Yes[7]	• Cost effectiveness • Cost utility • Methods must comply with National Institute for Health and Clinical Excellence economic guidelines[13,157]	• Payer[13,157] • Direct and indirect costs to National Health Service and Personal Social Services
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[28]	Yes[174]	Any one of: • Cost effectiveness • Cost utility • Cost minimization/ cost comparison; rationale for selection must be provided[28,174] • Methods must comply with economic guidelines[28,174]	• Societal[28]

score to the candidate technology (a new pharmaceutical). The score is based on a five-point scale, with "I" representing "major medical benefit" and "V" representing "insufficient to justify reimbursement."[16,20–23] Upon approval of the score by the Minister, the CEM then compares the technology with already reimbursed alternatives in order to formulate an opinion on the "improvement in medical benefit" or "ASMR" level. Six possible levels exist, ranging from I (major innovation) to VI (negative opinion regarding inclusion on the benefit list). Therefore, "innovativeness" is viewed as the size of the incremental clinical benefit achieved by the candidate technology. The opinion of the CEM is forwarded to the Transparency Commission, who makes a formal recommendation on the ASMR classification. This classification is, in turn, used to negotiate price and reimbursement rate. In Germany, the "innovativeness" of a technology is also based on whether it offers "added therapeutic value." Moreover, it plays an important role in determining the content of subsequent committee deliberations, because "cost-benefit" analyses are only taken into account when a technology has been deemed

Comparator	Sensitivity analysis	Systematic review of economic analysis studies	Budget impact analysis		Other economic information
			Required	Costs included	
• Most commonly used alternative[15]	Not specified	No information found			• Estimated average duration of use • Estimated consumption (number of patients and utilization) • Estimated cost of use per day[15]
No information found	No information found	No information found	Yes[115,172]	No information found	• Price in other European Union countries • Reimbursement status in other European Union countries • Estimated cost of use per day[115,172]
• Most commonly used alternative OR • Most relevant reimbursed alternative[84,173]	One-way, multi-way, and probabilistic[35]	No information found	Yes[154]	No information found	• Anticipated substitution effects • Price • Estimated consumption (number of patients and utilization)[154]
• Most commonly used alternative OR • Best practice alternative[13,157]	Probabilistic[157]	Yes[13,157]	Yes[13,157]	No information found	• National Health Service resource implications[13,157]
• Most commonly used alternative[28]	Probabilistic[28]	Yes[28]	Yes[28,174]	No information found	• National Health Service resource implications[28,174]

innovative.[18–24] The review committee of the Italian Medicines Agency, ie, the Technical Scientific Committee, explicitly weighs both the availability of existing treatments and the extent of clinical benefit in its assessment of a new pharmaceutical's innovativeness. The two attributes are scored separately and then combined to determine whether it represents an "important," "moderate," or "modest" innovation.[25] This rating, along with the category of clinical value to which the pharmaceutical has been assigned, is sent to a second review committee, ie, the Pricing and Reimbursement Committee, which negotiates price and reimbursement status with the manufacturer.[26,27]

Regardless of the reimbursement system, one of the main goals of the review committee is to determine the "therapeutic value" of a candidate technology. Broadly, its assessment combines consideration of clinical benefit with that of clinical need, taking into account key factors related to each dimension. For clinical need, they comprise, at a minimum, burden of illness (prevalence of severity) of the target condition and availability of alternatives. For clinical benefit,

Table 5 Comparison of decision-making processes

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	20 voting members: • 3 academics • 10 from sickness funds • 2 from physicians associations • 2 from economic chamber • 2 from federal chamber of labour • 1 from Austrian chamber of pharmacists	1. Manufacturer submits application for reimbursement to Association of Austrian Social Security Institutions 2. Internal staff (Department of Pharmaceutical Affairs) prepare evaluation of application (pharmacological and therapeutic) based on evidence presented in application, and assigns pharmaceutical to 1 of 6 categories of therapeutic value – pharmaceuticals classified into categories 5 or 6 can request price above average European Union price 3. Health economics team evaluates cost effectiveness of pharmaceutical relative to comparable alternatives 4. Pharmaceutical Evaluation Board deliberates over both evaluation reports and prepares report 5. Pharmaceutical Evaluation Board sends report to manufacturer for comment 6. Pharmaceutical Evaluation Board prepares reimbursement recommendation, taking into account responses received from manufacturer 7. Deputy director of Association of Austrian Social Security Institutions reviews recommendations and makes final decision[21,56,58]	No[21]	180 days (includes pricing and reimbursement decision)[58]	• Decision may be appealed to Independent Pharmaceuticals Commission[58]
Belgium	• Minister of Social Affairs (decisions) • Drug Reimbursement Committee (recommendations)[9,60]	31 members (23 voting including chair): • 7 academics • 8 from sickness funds • 4 physicians • 3 from pharmacist associations Nonvoting: • 2 from pharmaceutical industry • 1 from generic pharmaceutical industry • 4 from Ministries of Public Health, Social Affairs, and Economic Affairs, and Federal Public Service Budget	1. Manufacturer submits application for reimbursement to Secretariat of Drug Reimbursement Committee Includes incremental cost-effectiveness ratio (ICER) if Class I claim (added therapeutic value compared to existing alternatives) and simultaneously submits pricing dossier to Federal Public Service economy 2. Brief overview report of product characteristics prepared 3. Staff within Bureau of Drug Reimbursement Committee, supported by experts, prepare evaluation of pharmaceutical's safety, efficacy, effectiveness, applicability, and convenience based on evidence submitted by manufacturer; pricing commission simultaneously examines pricing dossier, determines maximum price, and notifies manufacturer 4. Drug Reimbursement Committee discusses and approves evaluation report 5. Drug Reimbursement Committee sends report to manufacturer	No[62]	150 days (includes pricing and reimbursement)[21]	• Decision may be appealed on procedural grounds only • Heard by administrative court

		• 1 from National Institute for Health and Disability Insurance[62]	6. Staff prepare draft recommendations, taking into account evaluation report, price from manufacturer, and responses received from manufacturer 7. Drug Reimbursement Committee discusses and approves (by 2/3 majority vote) draft recommendations 8. Drug Reimbursement Committee sends draft recommendations to manufacturer, who must reply within 10 days; manufacturer may request a hearing 9. Drug Reimbursement Committee prepares final recommendations, taking into account responses received from manufacturer 10. Minister receives recommendations, seeks advice from Minister of Budget and financial administration, and makes final decision[9,17,21,62,175]			
Czech Republic	• State Institute for Drug Control (decisions)[65,170]	No information found	1. Manufacturer submits application for reimbursement to State Institute for Drug Control 2. Internal staff (Department for Price and Reimbursement Regulation) consult with medical experts, health economists, and patient groups, and prepare evaluation report; assess safety, efficacy, and clinical use first, and then financial aspects 3. State Institute for Drug Control makes decision on price and level of reimbursement, based on evaluation report[176–180]	No[138]	75 days (includes pricing and reimbursement decision)	• Decision may be appealed to Ministry of Health
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	Maximum of 7 members: Must include: • 2 general practitioners • 1 representative of the regions[69]	1. Manufacturer submits application for reimbursement to Danish Medicines Agency 2. Internal staff, supported by external experts (if necessary) prepare evaluation report based on evidence submitted by manufacturer; clinical effect and safety profile compared to already reimbursed pharmaceutical and non-pharmaceutical products for same indication 3. Danish Medicines Agency simultaneously prepares price survey 4. Health economics expert(s) evaluate(s) economic analysis, if submitted 5. Reimbursement Committee reviews evaluation report, price survey, and review of economic analysis and makes reimbursement recommendation to Danish Medicines Agency 6. If negative, Danish Medicines Agency sends draft recommendations to manufacturer 7. Danish Medicines Agency Board makes final decision [21,68,69]	No[68]	90 days after receipt of "adequate application"[38]	• Decision may be appealed to Ministry of Health and Prevention[38,68]

(*Continued*)

Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	No information found	No information found	No information found	No information found	No information found
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	7 members of Pharmaceuticals Pricing Board: • 2 from Ministry of Social Affairs and Health • 2 from Social Insurance Institution (Kela) • 1 from Ministry of Finance • 1 from National Agency for Medicines • 1 from National Research and Development Centre for Welfare and Health 7 members of Expert Group: • Includes individuals with medical, pharmacological, health economics, and social insurance expertise[75,181]	1. Manufacturer submits application for reimbursement to Pharmaceuticals Pricing Board secretariat 2. Internal staff, with support from Expert Group, prepare evaluation report based on evidence submitted by manufacturer 3. Expert Group reviews report and formulates opinions 4. Pharmaceuticals Pricing Board Secretariat presents summary of report and opinions, along with written statement regarding the potential impact of the pharmaceutical on its budget provided by Kela, to Pharmaceuticals Pricing Board 5. Pharmaceuticals Pricing Board formulates recommendations 6. If negative, Pharmaceuticals Pricing Board sends recommendations to manufacturer, who may choose to lower price or provide additional evidence 7. Pharmaceuticals Pricing Board makes final decision[74,122,181,182]	No[181]	180 days (includes pricing and reimbursement decision)[181]	• Decision may be appealed to Supreme Court[181]
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	Transparency Committee within French National Authority for Health: 20 voting members (includes chair): • 4 from "public institutions"	*Single technology appraisals* 1. Manufacturer submits application for reimbursement to French National Authority for Health secretariat 2. Internal staff prepare evaluation report based on evidence submitted by manufacturer (focuses on clinical effectiveness, target population, conditions of use, and already reimbursed technologies)	No[20]	• 90 days for inpatient pharmaceuticals (includes pricing and reimbursement)	• May appeal recommendation to French National Authority for Health, requesting a hearing or providing written comments

• 3 from main health insurance fund • 1 from pharmaceutical industry • 12 with medical and pharmacological expertise[78,184] 7 Specialist subcommittees of clinical experts	3. External clinical and methodological experts review evaluation report 4. Commission d'Evaluation des Medicaments reviews evaluation report and expert opinions to appraise the "medical benefit" of the pharmaceutical (on a 5 point scale; I – major to V – insufficient to justify reimbursement) 5. Minister makes final decision on the medical benefit level/score 6. Commission d'Evaluation des Medicaments then performs comparative assessment of pharmaceutical with already reimbursed alternatives to appraise the "improvement in medical benefit" (on a 6 point scale; I – major innovation to VI – negative opinion regarding inclusion on benefit list) 7. Transparency Commission considers advice received from Commission d'Evaluation des Medicaments and assigns an "improvement in medical benefit" classification to the pharmaceutical 8. Once positive reimbursement recommendation is received, the Comite Economique des produits de Sante = negotiates price with manufacturer and the Union Nationale des Caisses d'Assurance Maladie fixes the reimbursement rate 9. Minister for Health and Social Security makes final decision on reimbursement level and price[16,20–23] Multiple technology appraisals 1. French National Authority for Health approves technology topic for multiple technology appraisals 2. French National Authority for Health conducts consultations with relevant stakeholders and the Interdisciplinary Economic Evaluation and Public Health Committee to define scope and protocol for multiple technology appraisals 3. Internal staff and/or independent academic group prepares assessment report (includes clinical review and economic analysis) 4. Interdisciplinary Economic Evaluation and Public Health Committee and external experts review assessment report 5. Stakeholders receive assessment report for comment 6. Stakeholders also consulted through working group meetings 7. Appropriate health technology assessment specialist subcommittee appraises report and comments and formulates recommendations 8. French National Authority for Health Board reviews and approves recommendations[21,185]	• 180 days for outpatient pharmaceuticals (includes pricing and reimbursement)[20]	• Once decision has been made, may appeal to administrative court[20]

(*Continued*)

Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19]	13 members including representatives from: • Associations of physicians, dentists, and physiotherapists • Hospital associations • Sickness funds • Patient organizations (nonvoting)[18,19]	1. Federal Joint Committee makes decision to assess technology and notifies Institute for Quality and Efficiency in Health Care 2. Institute for Quality and Efficiency in Health Care appoints internal staff to manage and/or conduct assessment 3. Institute for Quality and Efficiency in Health Care carries out consultations with external clinical experts and patient/carer organizations to define assessment scope and protocol 4. Institute for Quality and Efficiency in Health Care posts draft scope and protocol on website for public comment 5. Internal staff, supported by external experts, prepare assessment, first considering clinical benefit or innovativeness (ie, is the first active ingredient or offers therapeutic improvement); if deemed noninnovative, technology is assigned to 1 of 3 groups (1: identical active ingredient; 2: therapeutically comparable and one active ingredient; 3: therapeutically comparable and two active ingredients); technologies with similar efficacy/effectiveness must demonstrate comparable efficiency through findings from efficiency frontier analysis[119]; if deemed innovative (ie, offers added therapeutic value over already reimbursed alternatives), "cost-benefit" analysis is performed to set maximum reimbursable amount; if technology treats life-threatening condition for which there are no alternatives, cost must not be considered[18,19] 6. Institute for Quality and Efficiency in Health Care steering committee reviews draft report and recommendations for quality assurance 7. Institute for Quality and Efficiency in Health Care posts draft report and recommendations on website for public comment 8. Staff prepare final report, incorporating comments received and recommendations, and submit it to the Institute for Quality and Efficiency in Health Care steering committee for final quality assurance review and then to the Board for final approval 9. Board sends recommendations to Federal Joint Committee, who makes final decision[19,24,124,144]	No[18]	No information found	• May not appeal recommendations • Decision may be appealed to administrative court[18]

Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85,86]	7 members including representatives from: • Ministry of Health • Ministry of Finance • Ministry of Employment and Social Protection • Merchant Marine[85]	1. Manufacturer submits application for reimbursement to Transparency Committee in the Reimbursement and Medicinal Products 2. Transparency Committee in the Reimbursement and Medicinal Products recommends classification of pharmaceutical into pre-existing therapeutic category based on "therapeutic and pharmacoeconomic effectiveness" 3. Transparency Committee in the Reimbursement and Medicinal Products sends classification recommendation to Ministry of Health and Social Security for approval 4. Price set taking into account products already included in assigned category or average of the 3 lowest European prices[186]	No information found	90 days (includes pricing and reimbursement decision)[186]	No information found
Hungary	• Ministers of Health and Finance • National Health Insurance Fund Administration Technology Appraisal Committee (recommendations)[88,89]	Technology Appraisal Committee: includes members delegated by stakeholder groups[102]	1. Manufacturer submits application for reimbursement to Transparency Secretariat of National Health Insurance Fund Administration (pharmaceutical division) 2. Transparency Secretariat registers and checks application for completeness and then determines whether application should undergo simplified procedure or normal procedure; normal procedure applies to new agents, indications, routes of administration, and combinations 3. National Health Insurance Fund Administration Department of Pharmaceuticals prepares a preliminary evaluation 4. If application is assigned to normal procedure, Transparency Secretariat transfers it to Technology Assessment Office of the National Institute for Strategic Health Research 5. Assessment Office prepares assessment report comprising a systematic review of clinical evidence and economic analysis 6. Technology Appraisal Committee deliberates over report, preliminary evaluation of pharmaceutical department, and advice from professional colleges, and formulates a recommendation 7. Director of pharmaceutical division approves recommendation and forwards it to the Ministers of Health and Finance[90,102,187]	No information found	No information found	Decision may be appealed to Appeals Committee Includes representatives from: • Ministry of Health • Ministry of Finance • Ministry of Economy • National Institute of Pharmacy • Prime Minister's office[90]
Ireland	• Products Committee of Corporate Pharmaceuticals Unit of Health Service Executive (decisions)[91,92]	No information found	1. Products Committee of Health Service Executive selects technology for assessment OR manufacturer submits application for reimbursement to Health Service Executive 2a. If Products Committee selects technology, Health Service Executive notifies manufacturer of referral to National Centre for Pharmacoeconomics	No fixed threshold, but €45,000/QALY used as a guide[91,125,165]	90 days (for reimbursement decision)[93]	Decision may be appealed to designated expert committee[91]

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Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
			2b. If manufacturer submits application, staff prepare preliminary evaluation report based on evidence from manufacturer 3a. Staff within National Centre for Pharmacoeconomics appointed to comprise review group 3b. Products Committee reviews evaluation report and decides whether to refer technology to National Centre for Pharmacoeconomics for formal pharmacoeconomic evaluation or recommend reimbursement 4a. Review group meets with manufacturer to determine scope and requirements for evaluation 4b. If referred, National Centre for Pharmacoeconomics conducts pharmacoeconomic evaluation 5a. Manufacturer prepares pharmacoeconomic submission, which includes cost-effectiveness and budget impact analyses 5b. National Centre for Pharmacoeconomics sends pharmacoeconomic evaluation to manufacturer for comment 6a. Review group prepares evaluation report based on manufacturer's submission 6b. National Centre for Pharmacoeconomics prepares final pharmacoeconomic evaluation, incorporating manufacturer's comments 7a. National Centre for Pharmacoeconomics sends report to manufacturer for comment 7b. National Centre for Pharmacoeconomics sends evaluation to Products Committee, who makes reimbursement decision 8a. Review group prepares final evaluation report, incorporating manufacturer's comments 9a. National Centre for Pharmacoeconomics sends report to Products Committee, who makes reimbursement decision[91,93,125,147]			
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94]	Technical Scientific Committee: Includes 17 members: • Health care providers • Pharmacists	1. Manufacturer submits application for reimbursement to Italian Medicines Agency 2. Technical Scientific Committee reviews submission and formulates advice on clinical value, assigning it to one of three reimbursement classes: A – fully reimbursable – essential	No[126]	180 days (includes pricing and reimbursement decision)[188]	No information found

	• Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	• Pharmacologists Pricing and Reimbursement Committee: Includes 12 members: • Academics • Health care providers • Administrators responsible for managing pharmaceutical services[95]	products and those intended for chronic diseases; H – Fully reimbursable in hospitals; and C – non-reimbursable. Pharmaceuticals in classes A and H are further assigned to one of three classes: I – treatments for serious diseases; II – treatments to reduce or eliminate risk of serious diseases; and III – treatments for non-serious diseases 3. Technical Scientific Committee then assesses the degree of innovation offered by the technology, considering 2 factors: 1) availability of existing treatments and 2) extent of therapeutic benefit; scores on each factor are combined to determine if pharmaceutical represents "important," "moderate," or "modest therapeutic innovation" 4. Submission and Technical Scientific Committee evaluation are sent to Pricing and Reimbursement Committee 5. Pricing and Reimbursement Committee reviews advice and contacts manufacturer to negotiate reimbursement status and price 6. Pricing and Reimbursement Committee submits report containing negotiation outcomes to Technical Scientific Committee, who makes final decision [26,27,126]			
Norway	• Norwegian Medicines Agency (recommendations/ decisions)[34,98] • Ministry of Health and Care Services (recommendations/ decisions) • Department of Pharmacoeconomics (recommendations)[98]	No information found	Process depends on anticipated budget impact of pharmaceutical: If < 5 million Krone/year: 1. Manufacturer submits application for reimbursement to Norwegian Medicines Agency 2. Norwegian Medicines Agency Department of Pharmacoeconomics staff prepare evaluation report based on evidence submitted by manufacturer 3. Norwegian Medicines Agency reviews evaluation report and makes reimbursement decision If > 5 million Krone/year: 1. Manufacturer submits application for reimbursement to Norwegian Medicines Agency 2. Norwegian Medicines Agency Department of Pharmacoeconomics staff prepare evaluation report based on evidence submitted by manufacturer 3. Norwegian Medicines Agency reviews evaluation report and consults with National Advisory Committee for Drug Reimbursement 4. Norwegian Medicines Agency sends evaluation report to Ministry of Health and Care Services 5. Ministry consults with National Council for Health Care Priorities to determine whether pharmaceutical would be viewed as" money well spent"	No[34]	180 days (includes pricing and reimbursement decision)[34]	No information found

(Continued)

Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
			6. Ministry formulates recommendation; if positive, it is sent to Parliament for approval[34,98,189]			
Poland	• Ministry of Health (decisions)[99] • Agency for Health Technology Assessment Consultative Council and Drug Management Team (recommendations)[99]	Consultative Council: 12 voting members including representatives from: • Ministry of Health (7) • Polish Chamber of Physicians (1) • Chief Pharmaceutical Council (1) • Supreme Council of Nurses and Midwives • National Health Fund[127] Drug Management Team: Includes representatives of: • Minister of Finance • Minister of Economy and Labour • Minister of Social Policy • National Health Fund[99]	1. Manufacturer submits application for reimbursement to Ministry of Health 2. Ministry of Health sends application to the Agency for Health Technology Assessment 3. Agency for Health Technology Assessment staff prepare evaluation report based on evidence from the submission and information received from invited experts 4. Agency for Health Technology Assessment Consultative Council meets to review report, hear from experts, and formulate recommendations 5. Director of Agency for Health Technology Assessment issues reimbursement recommendation to Minister of Health 6. Drug Management Team within Ministry of Health negotiates maximum reimbursement price 7. Ministry of Health makes final decision on reimbursement and price[100,127,190]	No information found	180 days (includes pricing and reimbursement decision)[100]	None[127]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[44]	No information found	1. Manufacturer submits application for reimbursement to INFARMED following approval of maximum price by Directorate General of Economic Activities 2. External experts prepare evaluation report based on evidence submitted by manufacturer (includes pharmacotherapeutic and pharmacoeconomic information demonstrating added therapeutic value and proposed reimbursement price) and assigns "grade" of innovation and added therapeutic value (compared to already reimbursed alternatives) 3. Economists analyze pharmacotherapeutic information from manufacturer to determine "economic advantage"; if pharmaceutical offers added therapeutic value or treats a condition for which there are no alternative therapies, economic advantage should be demonstrated through formal economic analyses conducted by the manufacturer	No information found	90 days (includes pricing and reimbursement decision)[36]	• Decision may be appealed to administrative court[36]

			4. Using findings from both reports, INFARMED formulates reimbursement recommendation 5. If negative, INFARMED contacts manufacturer, who may present additional information 6. INFARMED submits recommendations to Minister, who makes final decision[36,101,191]			
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	No information found	1. Manufacturer submits application for reimbursement to Scottish Medicines Consortium 2. Internal staff ("assessment team"), supported by clinical and economic experts, prepare evaluation report based on evidence submitted by manufacturer 3. New Drugs Committee reviews report and prepares draft recommendations for the Scottish Medicines Consortium 4. New Drugs Committee also sends draft recommendations to manufacturer for comment 5. Manufacturer sends comments to Scottish Medicines Consortium, which also considers submissions received from patient interest groups 6. Scottish Medicines Consortium formulates final recommendations and forwards them to the National Health Service Boards, Area Drug and Therapeutics Committees, manufacturer, and competitor(s)[30,128]	No fixed threshold, but range of £20,000–£30,000/QALY used as a guide[30]	No information found	• Decisions may be appealed on process-related and scientific grounds • For process-related appeals: Manufacturer contacts Scottish Medicines Consortium secretariat, Chair, or New Drugs Committee to resolve issues through discussion • For scientific disputes: May resubmit or convene independent panel appointed by Scottish Medicines Consortium
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,107]	Reimbursement Committee: Includes 11 members representing: • Ministry of Health (3) • Slovakian medical chamber (3) • Health insurance funds (5)[101]	1. Manufacturer submits application for reimbursement, including proposed maximum retail price, to Ministry of Health 2. Staff evaluate pharmaceutical using evidence from manufacturer to determine where its ICER lies in the accepted ICER threshold range 3. One of 22 specialist working groups then evaluates the pharmaceutical according to its anatomic and therapeutic classification	No fixed threshold, but range of €20,000–€26,500/QALY used as a guide[105]	No information found	• Decision may be appealed to Ministry

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Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
			4. A separate working group evaluates pharmacoeconomic data 5. Evaluations from both working groups are forwarded to the Reimbursement Committee 6. The Reimbursement Committee reviews the reports and formulates a reimbursement decision[102,106,107,131,169]			
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108]	Inter-Ministerial Pricing Commission: Includes representatives from: • Ministry of Health • Ministry of Economy • Ministry of Industry[132]	1. Ministry of Health initiates reimbursement decision-making process upon receipt of notice of market approval for new pharmaceutical 2. Ministry of Health invites manufacturer to provide all relevant information to Inter-Ministerial Pricing Commission 3. Internal staff of Ministry of Health prepare evaluation report 4. Inter-Ministerial Pricing Commission reviews report and makes reimbursement and pricing decision[108,132]	No[132]	180 days (includes pricing and reimbursement decision)[132]	No information found
Sweden	• Dental and Pharmaceutical Benefits Board Expert Board (decisions)[15,109]	Expert Board: Includes 11 members and a chair: • Pharmacologist (1) • Health economists (4) • Patient representatives (2) • Health care providers (3)[15,109]	1. Manufacturer submits application for reimbursement 2. Internal staff (executive officer, health economist, and legal expert) review submission to determine if application contains sufficient evidence 3. Dental and Pharmaceutical Benefits Board sends copy of application to Pharmaceutical Benefits Group for County Councils for review 4. Internal staff prepare evaluation report and draft recommendations in the form of a "memorandum" 5. Dental and Pharmaceutical Benefits Board sends copy of memorandum to manufacturer for review 6. Manufacturer may request a meeting with the Board, during which it can present case, dispute arguments which form the basis of recommendations, and refute factual errors 7. Meeting of Expert Board held – memorandum, manufacturer's comments, and any feedback received from the Pharmaceutical Benefits Group are reviewed; external experts may be invited to participate in deliberations; 8. Expert Board makes final reimbursement decision[33,192]	No fixed threshold, but €45,000/ QALY used as a guide[35]	180 days (includes pricing and reimbursement decision)[192]	• Decision may be appealed on procedurals grounds only[15,33,192] • Board may reconsider decision before appeal is heard by administrative court[192]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113,114]	Federal Drug Commission: Includes 25 voting members representing: • Academics (4) • Physicians (3) • Pharmacists (3)	1. Manufacturer submits application for reimbursement 2. Federal Drug Commission reviews application and makes a classification recommendation: pharmaceutical may be classified into one of five categories of relative effectiveness: 1 – Therapeutic breakthrough; 2 – Therapeutic progress; 3 – Saving compared to other drugs; 4 – No therapeutic progress and no savings; and 5 – Not appropriate for the social health insurance	No information found	No information found	• Decision may be appealed to Federal Office of Public Health[114]

		• Health insurers (5) • Hospitals (1) • Patient organizations (2) • Manufacturers (2) • Federal Office of Social Insurance (1) • Cantons (1) • Swissmedic (1) • Army pharmacy (1)[113,114]	3. Federal Office of Public Health makes final decision, based on Federal Drug Commission's recommendation, assessment by Swiss Agency for Therapeutic Products for market authorization and internal and external price referencing 4. If Federal Office of Public Health plans to make a negative decision, the manufacturer is informed prior to issuing the final decision; manufacturer may apply for re-evaluation on the basis of price adjustments or availability of additional data[114]			
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Dutch Healthcare Insurance Board Committee (CHF) (recommendations)[26]	Committee of the Dutch Healthcare Insurance Board: Includes: • A maximum of 24 members with expertise in various medical disciplines, health sciences and economics • 2–3 nonvoting members from the Ministry[21,117] Includes: • 3 Dutch Healthcare Insurance Board board of directors • 6 members with health and social security insurance expertise[21]	For outpatient pharmaceuticals: 1. Manufacturer submits application for reimbursement to Minister of Health 2. Internal staff prepare evaluation, which includes 4 draft reports (summary, pharmacotherapeutic, pharmacoeconomic, and budget impact assessments based on evidence from manufacturer, as well as independently conducted literature review); if deemed necessary, staff may consult with manufacturer, external experts, and stakeholders 3. CHF reviews report and consults with manufacturer and other stakeholders 4. Staff revise report, incorporating results of CHF deliberations and comments from manufacturer and other stakeholders 5. Dutch Healthcare Insurance Board sends revised report to manufacturer and stakeholders for comment 6. CHF meets to discuss revised report and comments received and prepare final advice 7. Dutch Healthcare Insurance Board board of directors receives final report, which is also sent to manufacturer and stakeholders appointed by Dutch Healthcare Insurance Board for comment 8. Dutch Healthcare Insurance Board board of directors meet to discuss final report and comments received and formulate recommendations; may consult with the Appraisal Committee 9. Alternatively, Steps 7 and 8 may be skipped, with the Board chair drafting a recommendation 10. Dutch Healthcare Insurance Board sends final recommendations to the Minister of Healthcare, Welfare, and Sport	No fixed threshold, but €20,000/QALY used as a guide [31]	• 90 days for outpatient pharmaceuticals • 60 days for inpatient pharmaceutical[21]	• Decision may be appealed on procedural grounds only • Appeal is heard by administrative court[21]

(*Continued*)

Table 5 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Committee composition	Steps in review/decision-making process	Use of cost-effectiveness threshold	Timelines for review/ decision	Appeals mechanisms
			11. Minister makes final reimbursement decision, which includes classifying the pharmaceutical into one of three categories: Annex 1A – Therapeutic equivalent value; Annex 1B – Therapeutic added value; and Annex 2 – Conditional reimbursement For high-cost inpatient pharmaceuticals: 1. Dutch Federation of University Hospitals, Dutch Hospitals Association, Medical Specialists Association, and Dutch Health Insurance Organization may submit reimbursement application (in the form of additional funding) for high cost inpatient pharmaceuticals 2. Dutch Healthcare Insurance Board prepares evaluation report, which includes evidence on therapeutic value, projected budget impact, and plan for collecting pharmacoeconomic information in daily practice, and formulates recommendations (process similar to that described above) 3. Dutch Healthcare Insurance Board sends final report and recommendations to the Dutch Healthcare Authority 4. Dutch Healthcare Authority formulates recommendation on whether pharmaceutical should be provisionally added to the Expensive Drug List 5. Minister of Health, Welfare, and Sport makes final decision[21,31,49,116,117,193]			
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	Includes: • Academics (eg, health economists) • Health care providers in National Health Service • Representatives from patient and carer organizations • Manufacturers[29]	Single technology appraisal 1. Topics selection panel selects technology for review 2. National Institute for Health and Clinical Excellence invites stakeholders (ie, consultees and commentators (cannot make a submission or appeal recommendation)) to participate 3. Nonmanufacturer consultees invited to nominate clinical and/or patient experts to take part in Technology Appraisals Committee meetings 4. Manufacturer completes evidence submission (assessment) 5. Independent academic group commissioned to review submission, along with information received from consultees and nominated experts, and prepare evaluation report 6. Technology Appraisals Committee meets to review evaluation report and hear from nominated clinical and patient experts	No fixed threshold, but range of £20,000–£30,000/ QALY used as a guide[37,196,197]	Single technology appraisal approximately 39 weeks[29]	• Final recommendations may be appealed on procedural grounds only • Appeals may only be initiated by consultees identified at the beginning of the assessment and who are not representing National Health Service trusts or local boards

			7. Technology Appraisals Committee formulates draft recommendations, which are presented in appraisal consultation document 8. Appraisal consultation document made available to stakeholders for comment 9. Technology Appraisals Committee meets to consider comments and formulate final recommendations (final appraisal determination) 10. Technology Appraisals Committee submits final recommendations to Guidance Executive 11. Guidance Executive makes final reimbursement decision[29,194,195] Multiple technology appraisal Same as single technology appraisal process except: 1) Formal scoping process to develop review protocol is required; 2) Independent academic group conducts assessment (rather than the manufacturer); 3) Independent academic group attends Technology Appraisals Committee meetings[13]			• Appeal is heard by Appeals Panel appointed by National Institute for Health and Clinical Excellence board[39]
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group New Medicines Group (recommendations)[120]	Includes: • Physicians • Pharmacists • Pharmacologists • Health economist • Nurse • Patient representative • Representative from pharmaceutical industry association[28]	1. Manufacturer submits application for reimbursement ("Form A") to All Wales Medicines Strategy Group 2. All Wales Medicines Strategy Group determines whether application requires full appraisal; if yes, manufacturer must submit "Form B" 3. All Wales Medicines Strategy Group identifies and invites clinical experts and patient organizations to submit written statements 4. Internal staff prepare evaluation report, which includes Form A, Form B, and additional relevant information 5. Report sent to manufacturer for comment 6. All Wales Medicines Strategy Group New Medicines Group meets to review evaluation report and comments received and formulate draft recommendations 7. Staff prepare final report and draft recommendations (ie, preliminary appraisal), which is sent to manufacturer and posted on website 8. New Medicines Group meets to deliberate over final report, recommendations, and manufacturer's response 9. New Medicines Group formulates final recommendation, which is included in final appraisal 10. Minister makes reimbursement decision, based on final appraisal from New Medicines Group[28,120]	No fixed threshold, £20,000/ QALY used as a guide[28]	No information found	• Decisions may be appealed on process-related and scientific grounds • For process-related appeals: Appeals submitted to Welsh Medicines Partnership, who discusses case with All Wales Medicines Strategy Group Chair and senior staff • For scientific disputes: Independent review process initiated[198]

Table 6 Comparison of key factors considered during committee deliberations

Country	Centralized reimbursement review/decision-making body (role)	Clinical need			Clinical benefit/value*
		Disease burden (severity and number of patients)	Availability of alternatives	Place of technology in care pathway/ strategy	Safety (risk–benefit ratio; harm–benefit ratio)
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	Yes[55]	Yes[58]	Not specified	Not specified
Belgium	• Ministry of Health and Social Affairs (decisions) • Drug Reimbursement Committee (recommendations)[9,60]	Yes[11,17]	Yes[21]	Not specified	Yes[9]
Czech Republic	• State Institute for Drug Control (decisions)[65,176]	Yes[84]	Yes[84]	Not specified	Yes[84]
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	Not specified	Not specified	Not specified	Yes[21,68]
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	Yes[84]	Yes[84]	Not specified	Not specified
Finland	• Pharmaceuticals Pricing Board (decisions)[74,76,77] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	Yes[181]	Yes[181]	Not specified	Not specified
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	Yes[35]	Yes[35]	Yes[35]	Yes[80]
Germany	• Federal Joint Committee (decisions)[24] • Institute for Quality and Efficiency in Health Care (recommendations)[19,24]	Yes[19]	Yes[19]	Not specified	Yes[19]
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85]	Yes[186]	Yes[186]	Not specified	Yes[186]
Hungary	• Ministers of Health and Finance • National Health Insurance Fund Administration (recommendations)[88]	Yes[186]	Yes[84]	Not specified	Not specified
Ireland	• Health Service Executive (decisions)[91,92,147]	Yes[125,165]	Yes[125,165]	Not specified	Not specified

Efficacy/ effectiveness	Side effects	Acceptability (tolerance, convenience)	Cost-benefit ratio (cost-effectiveness; efficiency; "value for money")†	Impact on health resources/ affordability (budget impact)	Innovativeness	Other
Yes[55]	Not specified	Not specified	Yes ("pharmaco-economic evidence")[58]	Yes[55]	Yes[50]	• Price in other European Union countries[58]
Yes (across patient subgroups)[9]	Yes[9]	Yes[11,17]	Yes[11,17]	Yes[11,17]	Yes[35]	• Feasibility of implementation[11,17] • Market price[11,17] • Social needs[11,17,21]
Yes[84]	Not specified	Yes[66]	Yes[84]	Yes[84]	Not specified	• Clinical practice guidelines[138] • Public interest[35]
Yes (across patient subgroups)[21,68]	Yes[21,68]	Not specified	Yes[21,68]	Not specified	Not specified	• Reasonableness of price relative to therapeutic value[21,68]
Yes[84]	Not specified	Not specified	Yes[84]	Yes[84]	Not specified	• "Cost efficiency"§[140]
Yes (across patient subgroups)[181]	Not specified	Not specified	Yes[181]	Yes[181]	Not specified	• Research and development[35] • Level of uncertainty in supporting evidence[181] • Price in other European Union countries[181] • Market forecast and share[75] • Daily cost of treatment per day[75]
Yes[35]	Yes[80]	Yes[80]	Not specified	Yes[80]	Yes[35]	• Public health impact[16,35] • Costs relative to current treatment[199]
Yes[19]	Not specified	Not specified	Yes‡[19]	Yes[113]	Yes[19]	
Yes[186]	Not specified	Not specified	Yes ("pharmaco-economic effectiveness")[186]	Not specified	Not specified	• Daily cost of treatment[186] • Reimbursement status in other European Union countries[186]
Yes[84]	Not specified	Not specified	Yes[186]	Yes[84]	Not specified	• Equity[26]
Yes[125,165]	Not specified	Not specified	Yes[125,165]	Yes[125,165]	Yes[125,165]	• Level of uncertainty in supporting evidence[125] • Wider societal costs and benefits[165]

(*Continued*)

Table 6 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Clinical need			Clinical benefit/value*
		Disease burden (severity and number of patients)	Availability of alternatives	Place of technology in care pathway/ strategy	Safety (risk–benefit ratio; harm–benefit ratio)
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	Yes[27]	Yes[27]	Not specified	Yes[96]
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmacoeconomics (recommendations)[98]	Yes[34]	Not specified	Not specified	Yes[149]
Poland	• Ministry of Health (decisions)[99]	Yes[84]	Not specified	Not specified	Yes[84]
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[36,44]	Yes[36]	Yes[36]	Not specified	Yes[36]
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	Yes[104]	Yes[30]	Not specified	Yes[104]
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,107,169]	Yes[106]	Yes[84]	Not specified	Yes[106]
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108]	Yes[132]	Yes[132]	Not specified	Yes[10]
Sweden	• Dental and Pharmaceutical Benefits Board Expert Board (decisions)[15,109,110]	Yes[21]	Yes[109]	Not specified	Yes[21]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113,114]	Not specified	Not specified	Not specified	Not specified

Efficacy/ effectiveness	Side effects	Acceptability (tolerance, convenience)	Cost-benefit ratio (cost-effectiveness; efficiency; "value for money")†	Impact on health resources/ affordability (budget impact)	Innovativeness	Other
Yes (across patient subgroups)[27]	Not specified	Yes[27]	Yes[27]	Yes[27]	Yes[20]	• Daily cost of treatment[27] • "Special medical needs"[96] • Price in other European Union countries[200] • Market forecast and share[96]
Yes (across patient subgroups)[34]	Not specified	Not specified	Yes[34]	Yes[34]	Not specified	• Equity[35] • "Solidarity"[34] • "Rationality"[34]
Yes[84]	Not specified	Not specified	Yes[84]	Yes[84]	Not specified	
Yes[36]	Not specified	Not specified	Yes[36]	Not specified	Not specified	• Equity[36] • "Universality"[36] • "Accessibility"[36]
Yes[104]	Not specified	Not specified	Yes[104]	Yes[104]	Yes[30]	• Whether pharmaceutical reverses rather than stabilizes condition or bridges a gap to curative therapy[104] • Level of uncertainty in supporting evidence[30] • Wider societal costs and benefits[30]
Yes[106]	Yes[106]	Yes[106]	Yes[84,105]	Yes[84,106]	Not specified	• Price of other pharmaceuticals within reference category[106]
Yes (across patient subgroups)[132]	Not specified	Not specified	Not specified	Yes[132]	Yes[108]	• "Social utility"[132] • Rationalization of public expenditures on pharmaceuticals[132] • Specific needs of certain groups of people[132] • Research and development[132] • Price in other European Union countries[132] • Market forecast[132]
Yes (across patient subgroups)[15,21]	Not specified	Not specified	Yes[21]	No[21]	Not specified	• Equity[35] • "Reasonableness of cost from medical, humanitarian, and socio-economic perspective"[33] • Solidarity[21]
Yes[108]	Not specified	Not specified	Yes ("value for money")[109]	Not specified	Yes[108]	• Research and development[109]

(*Continued*)

Table 6 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Clinical need			Clinical benefit/value*
		Disease burden (severity and number of patients)	Availability of alternatives	Place of technology in care pathway/ strategy	Safety (risk–benefit ratio; harm–benefit ratio)
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Dutch Healthcare Insurance Board Committee of the Dutch Healthcare Insurance Board (recommendations)[31]	Yes[35]	Yes[21]	Not specified	Yes[35]
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	Yes[202]	Yes[202]	Yes[202]	Yes[202]
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[120]	Yes[28]	Not specified	Not specified	Not specified

they include at least safety (risk–benefit ratio) and efficacy/effectiveness, on the basis of which an overall estimate of the ratio of the benefits to harms of a candidate technology is estimated (Table 6). While a further goal shared by most review committees is to formulate an opinion on whether the candidate technology represents "value for money" or an efficient use of resources, their approach to accomplishing this differs. Approximately one-third are guided by, but not compelled to adhere to, a predefined incremental cost-effectiveness threshold or threshold range.[28,29] Typically, if the incremental cost-effectiveness for a candidate technology lies below the threshold, it is deemed cost-effective or good value for money. If it lies above the threshold, additional factors are taken into account when judging acceptability (eg, uncertainties in estimates of outcomes, the severity of condition, and wider societal benefits).[30,31] Across systems whose committees do not refer to an incremental cost-effectiveness threshold, approaches to operationalizing "value or money" appear vague, with information largely limited to statements such as "reasonableness of cost relative to therapeutic value" (Table 6).[32] Similarly, although all but one of the systems (Sweden[21]) list "affordability" or "impact of the candidate technology on health system resources" among factors/criteria considered by their respective review committees, no information describing processes for deciding whether or not a technology is affordable could be found.

Equity or ethical implications comprise decision-making factors/criteria (explicitly or implicitly) in one-third of

Efficacy/ effectiveness	Side effects	Acceptability (tolerance, convenience)	Cost-benefit ratio (cost-effectiveness; efficiency; "value for money")†	Impact on health resources/ affordability (budget impact)	Innovativeness	Other
Yes[35,117]	Yes[35]	Yes[35]	Yes[35,117]	Yes¥[21,201]	Yes[35]	• Rarity • Feasibility of implementation[117] • Accessibility • Level of uncertainty in supporting evidence[115] • Individual versus collective responsibility[201] • Public health impact[35]
Yes (across patient subgroups)[202]	Not specified	Not specified	Yes[202]	Not specified	Yes[35,197]	• Level of uncertainty in supporting evidence[196] • Whether technology represents life-extending, end of life treatment[37] • Wider societal costs and benefits[196] • Public health impact[35,197] • Alignment with broad government priorities[202] • ICERs of already funded programmes[13,157]
Yes (across patient subgroups)[28]	Not specified	Not specified	Yes[28]	Yes[174]	Yes[28]	• Level of uncertainty in supporting evidence[174] • Wider societal costs and benefits[28] • Alignment with broad government priorities[28] • ICERs of funded programmes[28]

Notes: *In a well-defined population; †price proportionate to effect; §cost efficiency takes into account costs of treatment per patient, as well as costs of compensatory allowance due to lost income and costs of restoring patients' capacity to work; ‡efficiency of resource use within a single therapeutic area relative to existing interventions; ¥not a formal criterion.

systems. For example, Sweden's Dental and Pharmaceutical Benefits Board stipulates two principles that decisions must reflect, ie, the "need and solidarity principle" (patients in the greatest need or "worse off" must be given priority) and the "human value principle" (sociodemographic characteristics of patient populations cannot influence decisions).[21,33] Along with "solidarity," the Norwegian Medicines Agency explicitly takes into account "equity," as do review committees in Hungary and Poland.[26,34–36] However, the way in which this is accomplished during deliberations is not clear. Committees using an incremental cost-effectiveness threshold to guide decisions implicitly incorporate equity by virtue of the assumptions underpinning the incremental cost-effectiveness calculation (ie, each quality-adjusted life-year [QALY] carries the same weight, regardless of the characteristics of the patients receiving it (eg, age, gender, social status, income). Consideration of additional, often competing ethical principles by these committees is operationalized through "exception" conditions under which the normal "efficiency" expectations do not need to be met (eg, "last chance" therapies, orphan technologies, life-extending, end-of-life treatments).[37] Under such conditions, not all QALYs are deemed equal. Rather, a form of "solidarity" premium is applied, where, for example, QALYs gained in the later stages of disease are given greater weight. While there is little disagreement over the importance of instituting "exception" conditions as a means of ensuring that reimbursement decisions embody the broader values of the population,

Table 7 Comparison of conditional reimbursement policy options for managing decision uncertainties

Country	Centralized reimbursement review/decision-making body (role)	Policy options for addressing decision-making uncertainties	
		Reassessment	Value-based pricing/ reimbursement
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	• Yes • Association of Austrian Social Security Institutions may remove pharmaceutical from benefit list in the wake of new clinical or economic evidence • Manufacturer may suggest delisting pharmaceutical[21]	No[56]
Belgium	• Minister of Social Affairs (decisions) • Drug Reimbursement Committee (recommendations)[9]	• Yes – automatic reassessment of pharmaceuticals offering added therapeutic value 1.5 to 3 years after inclusion on benefit list • Minister of Social Affairs or manufacturer may suggest delisting a pharmaceutical[41,49]	No information found
Czech Republic	• State Institute for Drug Control (decisions)[65]	• Yes – for "highly innovative" pharmaceuticals without evidence of effectiveness and "efficiency" • Granted provisional reimbursement for 1 year, after which pharmaceutical is reassessed[65]	Manufacturer may request a surcharge of up to 30% over the basic reimbursement level if evidence suggests pharmaceutical demonstrates "superior" therapeutic benefits[66]
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	• Pharmaceuticals reassessed as part of therapeutic class reviews every 5 years • Pharmaceutical may be scheduled for a separate reassessment when initial reimbursement decision is made if Reimbursement Committee considers it necessary to collect additional information about the use of the pharmaceutical in clinical practice before making a definitive decision[50]	No information found
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	No information found	No information found
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	• Yes – for all pharmaceuticals • Automatic reassessment every 3 to 5 years after inclusion on benefit list[182,203]	No information found
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	For pharmaceuticals • Yes – for all pharmaceuticals • Automatic reassessment every 5 years after inclusion on benefit list[20] For medical devices • Yes – for devices • Automatic reassessment within 5 years of inclusion on benefit list[20,162]	No information found

Reimbursement as part of a formal study	Risk-sharing schemes/ payment by results	Other
No information found	No information found	No information found
No information found	Financially or clinically based: • For pharmaceuticals offering added therapeutic value for which the Drug Reimbursement Committee formulated a negative reimbursement recommendation[49] Financially based: • Price-volume agreements – "Provision Fund" established – Advances paid by manufacturers are used to cover 75% of overrun[41]	• Creation of Special Solidarity Fund – Grants, on an individual basis, reimbursement of pharmaceuticals for rare diseases or rare indications unavailable in Belgium – Only granted if patient meets certain criteria and has exhausted all other treatment options – Must be prescribed by relevant specialist – Reimbursement decisions made by College of Medical Doctors Directors[62]
No information found	No information found	No information found
No information found	Clinically based: • Example: "No cure no pay" scheme for valsartan for high blood pressure • Individual level schemes – Patient may apply for reimbursement on an individual basis, which requires evidence of treatment effect for continued reimbursement[46] – Typically for patients who have exhausted all other options – Period of reimbursement varies[68]	No information found
No information found	Financially based: • For all new pharmaceuticals – price-volume agreements mandatory for 1 year following reimbursement decision[41]	No information found
No information found	No information found	No information found
• May provide provisional coverage for a set period during which "real-world" effectiveness and/or economic implications must be assessed through a study: – To be carried out: 1) By skilled teams in a limited number of selected centers 2) Under well-defined conditions of use 3) Using a protocol approved by French	For pharmaceuticals Financially based: • Price-volume agreements – Manufacturer must "pay back" the cost of sales exceeding those forecasted for the first 4 years [23,43] – Pharmaceuticals exempt from such schemes for various periods depending on their "improvement in medical benefit"	For pharmaceuticals for serious or rare diseases • May be granted temporary access in a hospital setting for 1 year[162] For "innovative" medical devices • May establish "innovation point of contact" and an internal multidisciplinary network[162]

(*Continued*)

Table 7 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Policy options for addressing decision-making uncertainties	
		Reassessment	Value-based pricing/ reimbursement
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19]		
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85]	No information found	No information found
Hungary	• Ministers of Health and Finance • National Health Insurance Fund Administration (recommendations)[88,89]	No information found	No information found
Ireland	• Products Committee of Corporate Pharmaceuticals Unit of Health Service Executive (decisions)[91,92]	No information found	No information found
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	No automatic/routine reassessment, with the exception of pharmaceuticals reimbursed under condition that additional studies would be conducted[25]	No information found

Reimbursement as part of a formal study	Risk-sharing schemes/ payment by results	Other
National Authority for Health Transparency Committee • Applies to pharmaceuticals that: 1) Target a large population; 2) May be prescribed outside their labeled indications; or 3) May have a significant impact on health care organizations[16,20] • Also applies to medical devices – French National Authority for Health specifies study protocol[120]	(ie, improvement in medical benefit) level: "improvement in medical benefit" I – 36 months; "improvement in medical benefit" II – 24 months; "improvement in medical benefit" III – 24 months at 50%; and "improvement in medical benefit" IV – 24 months at 25% – Also applies to "orphan drugs" (eg, eculizumab for paroxysmal nocturnal hemoglobinuria and galsulfase for mucopolysaccharidosis type VI)[41]	
For medical devices and procedures • May provide provisional coverage for a set period during which "real-world" effectiveness and/or economic implications must be assessed through a study[204]	For pharmaceuticals Financially based: • Price-volume agreements – "target agreements": if prescription volume target is exceeded by 25%, manufacturers must "pay back" sickness funds (eg, insulin analogs, olanzapine, risperidone, clopidogrel, zolendronate, mycophenolic acid, everolimus, and cyclosporine)[41]	• No reimbursement limit for potentially effective technologies used to manage life-threatening technologies for which there are no alternatives[82]
No information found	No information found	No information found
No information found	Financially based: • Price-volume agreements – 12% of reimbursed sales must be paid to the Ministry by the manufacturer – If Ministry spending on pharmaceutical exceeds agreed-to budget, the manufacturer must refund the Ministry an additional amount based on a predefined formula[41]	No information found
No information found	No information found	No information found
For pharmaceuticals classified as "potentially innovative" • May require manufacturer to conduct additional studies within 3 years • Pharmaceuticals for patients enrolled in the studies must be covered by the manufacturer[25] • Have established ongoing registries to monitor prescribing and assess "therapeutic value" in practice (real-world settings) in order to inform future management and reimbursed pricing decisions (eg, cetuximab, lenalidomide, ibritumomab, tiuxetan, palifermin, temporfin, and trastuzumab)[41]	Clinically based: • Pharmaceutical initially reimbursed by National Health Service at 50% or 100% for a fixed number of treatment cycles, after which it is only reimbursed for patients achieving predefined clinical response; manufacturer may be required to refund the cost of pharmaceutical in non-responding patients (eg, sunitinib, sorafenib, dasatinib, and nilotinib) • Registries used to track outcomes included in scheme[47] • Manufacturer initially provides pharmaceutical at no cost for a fixed period, after which National Health Service pays for pharmaceutical in patients achieving predefined clinical response (eg, donepezil)[41]	• Individual reimbursement – Patients may be granted individual reimbursement of pharmaceuticals not on the benefit list if: 1) No alternative exists 2) Requested pharmaceutical is available in other European Union states 3) Clinical trials are underway 4) Pharmaceutical is already reimbursed for a different indication[96,205] • Establishment of "innovative medicines fund" – Commits 20% of available resources to reimbursement of "innovative" pharmaceuticals, ranked from most to least innovative using the following criteria: 1) Treats serious conditions that are lifethreatening or cause hospitalization or permanent disability

(*Continued*)

Table 7 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Policy options for addressing decision-making uncertainties	
		Reassessment	**Value-based pricing/ reimbursement**
Norway	• Norwegian Medicines Agency (recommendations/decisions)[34,98] • Ministry of Health and Care Services (recommendations/decisions) • Department of Pharmacoeconomics (recommendations)[98]	• Pharmaceuticals may be reassessed as part of ongoing therapeutic class reviews[34]	No information found
Poland	• Ministry of Health (decisions)[99] • Drug Management Team (recommendations)[99]	No information found	No information found
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[44,101]	No information found	No information found
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	• Yes – for all pharmaceuticals • Automatic reassessment, but review period varies with the pharmaceutical; depends upon when additional evidence is expected to be available[128]	No information found
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105,106]	No information found	No information found
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108]	No information found	No information found
Sweden	• Dental and Pharmaceutical Benefits Board Expert Board (decisions)[15,206–209]	• Yes – for all pharmaceuticals • Automatic reassessment, but review period varies with the pharmaceutical; depends upon when additional evidence is expected to be available[51,135] • Pharmaceuticals may also be reassessed as part of ongoing therapeutic class reviews[51,135]	• Reimbursement price may be adjusted to reflect actual costs and benefits once such information becomes available (eg, continuous intraduodenal infusion of levodopa/carbidopa for advanced Parkinson's disease)[209]
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113,114]	No information found	• "Innovation premium" – Granted to innovative pharmaceuticals (ie, therapeutic breakthrough products)

Reimbursement as part of a formal study	Risk-sharing schemes/ payment by results	Other
	Financially based: • Expenditure cap – Cost per patient per year cannot exceed a certain amount (eg, bevacizumab)[41]	2) Used for risk factors for serious conditions 3) Used for nonserious conditions[25,188] – If fund is overspent, manufacturers participate in refunding the system proportional to market share[95]
No information found	No information found	• Individual reimbursement – For patients who have exhausted all reimbursed alternatives and/or have serious or rare conditions – May be requested by specialists only – Reimbursement decision made by Norwegian Labour and Welfare Organization – Pharmaceutical does not need to have obtained market approval[34]
No information found	No information found	No information found
No information found	Financially based: • Price-volume agreements – Growth rate in pharmaceutical expenditures fixed per year; if exceeded, manufacturers must refund the system up to 69.6% of the coverage up to a predetermined amount, eg, €35 million (2006)[44]	No information found
No information found	No information found	No information found
No information found	No information found	No information found
No information found	No information found	No information found
• May require submission of evidence from studies collecting "real-world" data on clinical, economic, and quality of life outcomes[205,209]	No information found	No information found
No information found	No information found	No information found

(*Continued*)

Table 7 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Policy options for addressing decision-making uncertainties	
		Reassessment	**Value-based pricing/ reimbursement**
			– Surcharge of ≤20% of external reference price is added for a maximum of 15 years[113,114,205]
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Dutch Healthcare Insurance Board Committee of the Dutch Healthcare Insurance Board (recommendations)[31]	• Yes – for all pharmaceuticals • Automatic reassessment – time period not specified[31,210,211]	No information found
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	• Yes – for all technologies • Automatic reassessment, but review period varies with the pharmaceutical; depends upon when additional evidence is expected to be available[13,29,157]	• Proposed "flexible pricing" scheme: – Manufacturers can adjust the price of a pharmaceutical in response to emerging additional evidence on actual benefit or approval of a new indication which alters the value that the pharmaceutical offers to patients – National Institute for Health and Clinical Excellence assesses whether new price and evidence represents "value for money" and may veto a new price on an existing indication[45,48]

Reimbursement as part of a formal study	Risk-sharing schemes/ payment by results	Other
New inpatient pharmaceuticals with projected costs >5% of hospital budget • Granted provisional reimbursement for 3 years, during which studies collecting "real-world" data on cost-effectiveness must be conducted[119] High-cost pharmaceuticals for rare conditions • Granted provisional reimbursement for use in an academic hospital for 4 years, during which manufacturer must sponsor studies collecting "real-world" data on cost effectiveness and budget impact[119] • "Innovation pass" – Selected "innovative" technologies are made available for 3 years, during which studies to collect data needed to inform standard National Institute for Health and Clinical Excellence processes are conducted[48]	No information found	No information found
	For pharmaceuticals "Patient access schemes"[42] Financially based: • Manufacturer proposes discounts or rebates to reduce the cost of a pharmaceutical to the National Health Service, thus improving its cost-effectiveness – Manufacturer must obtain approval for such a scheme from the Department of Health prior to National Institute for Health and Clinical Excellence review[29,212–214] • Expenditure cap – Cost per patient per year cannot exceed a certain amount (eg, ustekinumab and erlotinib)[45] Clinically based: • Manufacturer covers the cost of initial fixed number of cycle(s) of treatment, after which National Health Service pays for patients achieving predefined clinical response (eg, sunitinib)[45] • National Health Service covers the cost of initial fixed number of cycles of treatment, after which manufacturer refunds the cost of treatment in patients failing to achieve predefined clinical response (eg, bortezomib)[40] • National Health Service covers the cost of the pharmaceutical for a fixed period, after which the price is reduced or refunds are issued to achieve predefined ICER (eg, interferon β, glatiramer acetate, and azathioprine)[45]	• End-of-life medicines guidance – Pharmaceuticals used to extend life by at least 3 months for patients with less than 24 months to live may be reimbursed, even if ICER exceeds threshold range[37–48] • Pharmaceuticals for rare conditions guidance – May be reimbursed when ICER exceeds threshold range if: – Target conditions in which incidence <7000 patients/year in the UK – There is sufficient evidence demonstrating that pharmaceutical offers substantial average increase in life expectancy over alternatives[205]

(*Continued*)

Table 7 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Policy options for addressing decision-making uncertainties	
		Reassessment	Value-based pricing/ reimbursement
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group New Medicines Group (recommendations)[120]	• Yes – for all pharmaceuticals • Automatic reassessment, but review period varies with the pharmaceutical; depends upon when additional evidence is expected to be available[174]	No information found

considerable debate around definitions/qualifiers (eg, what constitutes "last chance"? or by what period of time must a technology lengthen survival in order to be regarded as "life-extending"?) remains. Finally, the following factors are simply listed as criteria/factors by a small proportion of committees: alignment with government priorities; feasibility; and/or risk of off-label use of the technology (Table 6).

In general, systems aim to complete single technology reviews within 180 days of submission/identification of candidate technology, the time period prescribed by the European Union Transparency Directive. Based on tracking data, the actual time required appears to depend primarily on whether the assessment report accompanies a reimbursement application (eg, Belgium) or is undertaken (internally or externally) by the system once a technology is identified for review (eg, the UK, Table 5). In the latter case, review times can be 90 days or less (eg, Denmark and France).[20,38]

The majority of systems have established mechanisms for appealing recommendations or decisions. Briefly, there are two main types of disputes, ie, those related to process and those amounting to disagreements over the interpretation of the evidence. In approximately one-third of systems, acceptable grounds for appeals are those of the first type only ("failed to act in accordance with processes"[39]). For the most part, appeals are heard by an expert panel appointed by the respective health care organization or "payer" (eg, Ministry of Health, Table 5). Alternatively, they must be filed in an administrative court (eg, Germany and Sweden).

Conditional reimbursement enabling access to new technologies

Increasingly, reimbursement systems are expressing interest in and/or implementing reimbursement policy options that extend beyond the traditional "yes," "no," or "yes with restrictions" options. Such policy options take the form of provisional reimbursement arrangements, in which funding for a technology is provided in the interim while evidence needed to make a definitive decision is collected.[40] Collectively referred to as "Access with Evidence Development" (AED) schemes, they have emerged in response to calls for mechanisms that balance access to new technologies with the need to ensure their safe, effective, and efficient introduction and use in the health care system. In recent years, these calls have heightened, as tension between payers and manufacturers, patients, and providers has intensified. Many new high-cost technologies are supported by limited, albeit promising, evidence. Therefore, reimbursement decisions are made under conditions of considerable uncertainty, with significant risks and consequences of "getting it wrong" (wasted scarce resources and poor health outcomes). AED schemes attempt to reduce such risks through "managed entry" of new technologies into everyday clinical practice. There are three main types, ie, coverage linked to an outcomes guarantee, coverage as part of a study, and automatic reassessment (Table 7). Often referred to as "risk-sharing" schemes, "patient access schemes," and "payment by results," the first type consists of contractual arrangements between payers and manufacturers, where payment is tied to the achievement of an outcome, be it financial or health-related.[41,42] Such schemes have been employed in approximately one-third of the systems in this review (Table 7). They include financially-based price-volume agreements, where manufacturers must "pay back" the cost of sales exceeding those forecasted (eg, Belgium, France, Germany, Hungary, Portugal),[41,43,44] and expenditure caps, in which manufacturers cover the cost of "treatment" in patients for whom costs over a fixed time period exceed a prespecified amount (eg, Italy, the UK).[41,45] Health-related risk sharing arrangements, also called "no cure no pay" schemes, have been implemented by a smaller proportion of systems (Belgium, Denmark, Italy, the UK).[41,45–47] Under such schemes, continued reimbursement of a technology (usually a pharmaceutical for a rare disorder or cancer) requires evidence of a predefined treatment effect. The second type, "coverage as part of a study," involves provision of interim funding by payers in order to conduct studies designed to collect specific information needed to fill key evidence gaps.

Reimbursement as part of a formal study	Risk-sharing schemes/ payment by results	Other
No information found	No information found	No information found

Typically, such evidence gaps relate to the effectiveness and/or cost implications of the technology in "real world" settings. Funding may be partial (costs of the technology and/or health care associated with its use) or full (all health care and research costs). This type of scheme constitutes a policy option in approximately one quarter of the reimbursement systems, the majority of which have mandates that span pharmaceutical and nonpharmaceutical technologies (eg, France, Germany, the UK, Table 7). Eligible technologies vary across systems, but often include those defined as "innovative" (eg, granted an "innovation pass" in the UK) and those anticipated to significantly impact health care organization budgets (eg, the Netherlands).[25,48] The third type of AED scheme, "automatic reassessment," comprises a programmed review of a reimbursement decision following a fixed period on the "benefit list" or when additional evidence is available.[49–51] It has become a part of the policy framework in half of the reimbursement systems included in this review, with most requiring reassessments of all technologies within their decision-making scope (Table 7). Despite the appeal of AED schemes, evidence of their effectiveness is both limited and mixed. Recent reviews have highlighted the challenges involved in both their design and implementation.[52,53] Such challenges primarily stem from the need to reach consensus among stakeholders on the terms of the scheme. Often, considerable time and resources have been required to resolve disagreements over elements such as the value proposition, outcomes to be measured and for what period, how the scheme should be funded, and to whom its oversight should be handed. Further, negotiations have, in some cases, resulted in complex arrangements that failed to generate the evidence needed to support a policy decision and/or created a significant administrative burden on payers and providers involved in its implementation. In an effort to address these issues, guidelines for conducting AED schemes, derived from international experiences to date, were recently published.[53,54] Moreover, some systems have proposed alternative approaches to dealing with decision uncertainties. For example, earlier this year, National Institute of Health and Clinical Excellence announced a new form of value-based reimbursement termed "flexible pricing."[45–48] Under this approach, manufacturers adjust the price of a technology (pharmaceutical) in response to additional evidence of actual benefit to patients as it emerges. The National Institute of Health and Clinical Excellence subsequently assess this evidence, along with the proposed price, and determines whether the technology represents "value for money." If a negative opinion is reached, the National Institute of Health and Clinical Excellence may veto the proposed price. Given the potential benefits of such an approach (eg, reduced administrative burden and system resource requirements) it has already sparked interest among the National Institute of Health and Clinical Excellence's counterparts across Europe.

Role of manufacturers in steps comprising the reimbursement review process

Few reimbursement systems have established roles for manufacturers beyond referral of a technology for review and the opportunity to comment on draft reports and/or preliminary recommendations (Table 8). Where "multiple technology appraisal" processes exist and assessment reports are commissioned or undertaken by the reimbursement system, manufacturers may participate in defining the scope or protocol of the assessment (France, Germany, the UK) or submit information to the group preparing such reports (Germany, Ireland, Spain, the UK). Among systems that prepare the evaluation report only, about half invite manufacturers to contribute information (Scotland, Italy, Sweden, the UK, Wales). Involvement of manufacturers otherwise appears limited to single examples, eg, able to participate in consultations during the assessment (France) or attend review committee meetings (Wales).

Conclusion

Centralized reimbursement systems have become an important policy tool in many European countries. Their introduction has, inarguably, brought greater consistency to

Table 8 Comparison of the role of manufacturers in centralized reimbursement processes

Country	Centralized reimbursement review/decision-making body (role)	Refer technology topics for reimbursement consideration	Participate in defining scope and/or protocol of assessment	Comment on draft protocol	Participate in consultations during assessment	Submit information to group preparing assessment report
Austria	• Association of Austrian Social Security Institutions (decisions)[55] • Pharmaceutical Evaluation Board (recommendations)[56]	Yes	N/A	N/A	N/A	N/A
Belgium	• Minister of Social Affairs (decisions) • Drug Reimbursement Committee (recommendations)[9,60]	Yes	N/A	N/A	N/A	N/A
Czech Republic	• State Institute for Drug Control (decisions)[65,176]	Yes	N/A	N/A	N/A	N/A
Denmark	• Danish Medicines Agency (decisions)[68,69,121] • Reimbursement Committee (recommendations)[68,121]	Yes	N/A	N/A	N/A	N/A
Estonia	• Ministry of Social Affairs (decisions)[72] • Pharmaceuticals Committee (recommendations)[72]	Yes	N/A	N/A	N/A	N/A
Finland	• Pharmaceuticals Pricing Board (decisions)[73,74,76] • Pharmaceuticals Pricing Board Expert Group (recommendations)[75]	Yes	N/A	N/A	N/A	N/A
France	• Ministry for Health and Social Security (decisions)[20,78] • French National Authority for Health (recommendations)[78]	Yes	Yes (multiple technology appraisals) N/A (single technology appraisals)	No	Yes (multiple technology appraisals) N/A (single technology appraisals)	No (multiple technology appraisals) N/A (single technology appraisals)
Germany	• Federal Joint Committee (decisions)[19] • Institute for Quality and Efficiency in Health Care (recommendations)[19]	No	Yes	Yes	No	Yes
Greece	• Transparency Committee in the Reimbursement and Medicinal Products (makes decisions)[85]	Yes	N/A	N/A	N/A	N/A

Submit information to group preparing evaluation report	Present views during committee meetings	Nominate clinical and/or patient experts to make oral presentation to committee	Attend committee meeting	Comment on report and/or draft recommendations	Appeal recommendations or decisions
No	No	No	No	No	Yes
No	No	No	No	Yes	Yes
No information found	No information found	No information found	No information found	No information found	Yes
No	No	No	No	Yes, if recommendation is negative	Yes
No information found	No information found	No information found	No information found	No information found	No information found
No	No	No	No	Yes, if recommendation is negative	Yes
No	No	No	No	Yes	Yes
No	No	No	No	Yes	Yes (decisions only)
No information found	No information found	No information found	No information found	No information found	No information found

(*Continued*)

Table 8 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Refer technology topics for reimbursement consideration	Participate in defining scope and/or protocol of assessment	Comment on draft protocol	Participate in consultations during assessment	Submit information to group preparing assessment report
Hungary	• Ministers of Health and Finance • National Health Insurance Fund Administration (recommendations)[88]	Yes	N/A	N/A	N/A	N/A
Ireland	• Health Service Executive (decisions)[91,92,147]	Yes	N/A	N/A	N/A	Yes
Italy	• Italian Medicines Agency Technical Scientific Committee (decisions)[94] • Italian Medicines Agency Pricing and Reimbursement Committee (recommendations)[95]	Yes	N/A	N/A	N/A	No
Norway	• Norwegian Medicines Agency (decisions)[98] • Department of Pharmacoeconomics (recommendations)[98]	Yes	N/A	N/A	N/A	No information found
Poland	• Ministry of Health (decisions)[99,166]	Yes	N/A	N/A	N/A	No information found
Portugal	• Ministry of Health (decisions) • INFARMED (recommendations)[36,44]	Yes	N/A	N/A	N/A	No information found
Scotland	• National Health Service Scotland (decisions)[30] • Scottish Medicines Consortium (recommendations)	Yes	N/A	N/A	N/A	No
Slovakia	• Ministry of Health (decisions) • Reimbursement Committee for Medicinal Products (recommendations)[105–107]	Yes	N/A	N/A	N/A	No information found
Spain	• Ministry of Health Directorate General of Pharmacy and Health Products; Inter-Ministerial Pricing Commission (decisions)[21,108]	No	No	No	Yes	Yes
Sweden	• Dental and Pharmaceutical Benefits Board Expert Board (decisions)[10,104,105]	Yes	N/A	N/A	N/A	N/A

Submit information to group preparing evaluation report	Present views during committee meetings	Nominate clinical and/or patient experts to make oral presentation to committee	Attend committee meeting	Comment on report and/or draft recommendations	Appeal recommendations or decisions
No information found	No information found	No information found	No information found	No information found	Yes
No	No	No	No	Yes	Yes
Yes	No	No	No	Yes	No
No information found	No information found	No information found	No information found	No information found	Yes
No information found	No information found	No information found	No information found	No information found	No information found
No information found	No information found	No information found	No information found	No information found	Yes
Yes	No	No	No	Yes	Yes
No information found	No information found	No information found	No information found	No information found	No
No	No	No	No	No	No
Yes	Yes	No	No	Yes	Yes

(*Continued*)

Table 8 (*Continued*)

Country	Centralized reimbursement review/decision-making body (role)	Refer technology topics for reimbursement consideration	Participate in defining scope and/or protocol of assessment	Comment on draft protocol	Participate in consultations during assessment	Submit information to group preparing assessment report
Switzerland	• Swiss Federal Office of Public Health (decisions) • Federal Drug Commission (recommendations)[113,114]	Yes	N/A	N/A	N/A	N/A
The Netherlands	• Ministry of Health, Welfare and Sport (decisions) • Dutch Healthcare Insurance Board Committee of the Dutch Healthcare Insurance Board (recommendations)[31]	Yes	N/A	N/A	N/A	N/A
United Kingdom	• National Institute for Health and Clinical Excellence (decisions) • Technology Appraisals Committee (recommendations)[7]	Yes	Yes (multiple technology appraisals) N/A (single technology appraisals)	No (multiple technology appraisals) N/A (single technology appraisals)	No (multiple technology appraisals) N/A (single technology appraisals)	Yes (multiple technology appraisals) N/A (single technology appraisals)
Wales	• Ministry for Health and Social Services (decisions) • All Wales Medicines Strategy Group (recommendations)[120]	Yes	N/A	N/A	N/A	N/A

processes and an improved sense of legitimacy to decisions. Nevertheless, there remains a lack of transparency around critical elements, such as how multiple factors or criteria are weighed during committee deliberations. Further, empirical studies evaluating the extent to which centralized reimbursement systems with advisory as opposed to decision-making authority are able to reduce inequities in access to new technologies within jurisdictions appear sparse.

Given the rapid pace with which new technologies that appear promising are now entering the market and the need to work alongside broader government industrial policies for encouraging innovation in an economic climate that demands prudent use of strained health care resources, the adoption of AED schemes by reimbursement systems seems inevitable. However, until more information on the outcomes of initiatives such as flexible pricing in the UK becomes available, their implementation should be approached with caution.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Mitton C, Donaldson C. Health care priority setting: Principles, practice and challenges. *Cost Eff Resour Alloc*. 2004;2:3–8.
2. The health of Canadians: The federal role. Final report. Volume 6: Recommendations for reform. Ottawa, ON: Government of Canada, Standing Senate Committee on Social Affairs, 2002. Available from: http://www.parl.gc.ca/Content/SEN/Committee/372/soci/rep/repoct02vol6-e.htm. Accessed July 22, 2011.
3. Wilking N, Jonsson B. A pan-European comparison regarding patient access to cancer drugs. Stockholm, Sweden: Karolinska Institutet, 2006. Available from: http://ki.se/content/1/c4/33/52/Cancer_Report.pdf. Accessed March 13, 2011.
4. Stafinski T, Menon D, Philippon DJ, McCabe C. Health technology funding decision-making processes around the world the same, yet different. *Pharmacoeconomics*. 2011;29:1–21.
5. Organization for Economic Cooperation and Development. *Health Technologies and Decision Making*. Paris, France: Organization for Economic Cooperation and Development; 2005.
6. von der Schulenburg J, Vauth C, Mittendorf T, Greiner W. Methods for determining cost-benefit ratios for pharmaceuticals in Germany. *Eur J Health Econ*. 2007;8 Suppl 1:S5–S31.
7. Chalkidou K. Comparative effectiveness review within the UK's National Institute for Health and Clinical Excellence. *Issue Brief (Commonw Fund)*. 2009. Available from: http://www.commonwealthfund.org/~/media/Files/Publications/Issue%20Brief/2009/Jul/Chalkidou/1296_Chalkidou_UK_CER_issue_brief_717.pdf. Accessed July 18, 2011.

Submit information to group preparing evaluation report	Present views during committee meetings	Nominate clinical and/or patient experts to make oral presentation to committee	Attend committee meeting	Comment on report and/or draft recommendations	Appeal recommendations or decisions
No information found	No information found	No information found	No information found	No information found	Yes
No	No	No	No	No	Yes
Yes (single technology appraisals) N/A (single technology appraisals)	No	Yes	No	Yes	Yes
Yes	No	No	Yes	Yes	Yes

8. Institute for Quality and Efficiency in Health Care. General methods. Cologne, Germany: Institute for Quality and Efficiency in Health Care; 2008. Available from: http://www.iqwig.net/methods-procedures.926.en.html. Accessed July 15, 2011.
9. Van Wilder PB, Dupont AG. Reimbursement of medicines in Belgium: Role of evidence-based medicine. *Acta Clin Belg*. 2009;64:120–128.
10. International Society for Pharmacoeconomics and Outcomes Research. Pharmacoeconomic guidelines around the world: Spain. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from: http://www.ispor.org/PEguidelines/countrydet.asp?c=20&t=4. Accessed July 22, 2011.
11. Cleemput I, Van WP, Huybrechts M, Vrijens F. Belgian methodological guidelines for pharmacoeconomic evaluations: Toward standardization of drug reimbursement requests. *Value Health*. 2009;12:441–449.
12. Greiner W, Kuhlmann A, Schwarzbach C. An economic evaluation of the IQWiGs efficient frontier. *Gesundheitsokonomie und Qualitatsmanagement*. 2010;15:241–250. German.
13. Guide to the multiple technology appraisal process. London, UK: National Insitute for Health and Clinical Excellence; 2009. Available from: http://www.nice.org.uk/media/916/6B/Guide_to_the_MTA-proof_8-26-10-09.pdf. Accessed July 15, 2011.
14. Faulkner E, Matuszewski K, Niziol C. ISPOR global health care systems road map: Sweden. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/HTARoadMaps/Sweden.asp. Accessed July 15, 2011.
15. Guidelines for companies: The Swedish Pharmaceutical Benefits Board (LFN). Stockholm, Sweden: Swedish Pharmaceutical Benefits Board; 2008. Available from: http://www.tlv.se/Upload/English/Guidelines-for-Companies.pdf. Accessed July 15, 2011.
16. Le Pen C. Pricing and reimbursement policies in France: Current and future trends. In: Garau M, Mestre-Ferrandiz J, editors. European Medicines Pricing and Reimbursement. Milton Keynes, UK: Radcliffe Publishing; 2007. Available from: http://www.radcliffe-oxford.com/books/samplechapter/184X/Garau_CHPT1-5e62f200rdz.pdf. Accessed July 22, 2011.
17. Cleemput I, van Wilder PV, Vrijens F, Huybrechts M, Ramaekers D. Guidelines for Pharmacoeconomic Evaluations in Belgium [KCE Reports 78C]. Brussels, Belgium: Belgian Health Care Knowledge Centre. 2008. Available from: www.kce.fgov.be/Download.aspx?ID=1081. Accessed July 15, 2011.
18. Nasser M, Sawicki P. Institute for quality and efficiency in health care: Germany. *Issue Brief (Commonw Fund)*. 2009;57:1–12. Available from: http://www.commonwealthfund.org/~/media/Files/Publications/Issue%20Brief/2009/Jul/Chalkidou/1294_Nasser_CER_Germany_issue_brief_724.pdf. Accessed July 15, 2011.
19. The Federal Joint Committee: About us. Berlin, Germany: Gemeinsamer Bundesausschuss, Institut fur Qualitat und Wirtschaftlichkeit in Gesundheitswesen; 2010. Available from: http://www.g-ba.de/downloads/17-98-2804/2010-01-01-Faltblatt-GBA_engl.pdf. Accessed July 15, 2011.
20. Rochaix L, Xerri B. National Authority for Health: France. *Issue Brief (Commonw Fund)*. 2009;58]. New York: The Commonwealth Fund; 2009. Available from: http://www.commonwealthfund.org/Content/Publications/Issue-Briefs/2009/Jul/National-Authority-for-Health-France.aspx. Accessed July 15, 2011.

21. Habl C, Antony K, Arts D, et al. Surveying, assessing and analysing the pharmaceutical sector in the 25 EU member states: Country profiles. Vienna: European Commission; Osterreichisches Bundesinstitut fur Gesundheitswesen; 2006. Available from: http://ec.europa.eu/competition/mergers/studies_reports/oebig.pdf. Accessed July 15, 2011.
22. Chicoye A, Levesque K. ISPOR global health care systems road map: France – Medical devices. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from : http://www.ispor.org/htaroadmaps/FranceMD.asp. July 15, 2011.
23. Sermet C, Andrieu V, Godman B, Van GE, Haycox A, Reynier JP. Ongoing pharmaceutical reforms in France: Implications for key stakeholder groups. *Appl Health Econ Health Policy*. 2010;8:7–24.
24. General methods for the assessment of the relation of benefits to costs. Version 1.0. Cologne, Germany: Institute for Quality and Efficiency in Health Care; 2009. Available from: http://www.iqwig.de/download/General_Methods_for_the_Assessment_of_the_Relation_of_Benefits_to_Costs.pdf. Accessed July 15, 2011.
25. Criteria for ranking therapeutic innovation of new drugs and elements for supplementing the dossier for admission to the reimbursement system. Rome, Italy: AIFA – Italian Medicines Agency. Working Group on Innovative Drugs; 2007. Available from: http://www.agenziafarmaco.gov.it/allegati/integral_document.pdf. Accessed July 15, 2011.
26. Sorenson C. Use of comparative effectiveness research in drug coverage and pricing decisions: a six-country comparison. *Issue Brief (Commonw Fund)*. 2010;91. New York: The Commonwealth Fund; 2010. Available from: http://www.commonwealthfund.org/~/media/Files/Publications/Issue%20Brief/2010/Jul/1420_Sorenson_Comp_Effect_intl_ib_71.pdf. Accessed July 15, 2011.
27. Lo Scalzo A, Donatini A, Orzella L, Cicchetti A, Profili S, Maresso A. Italy: Health system review [Health Systems in Transition]. Copenhagen, Denmark: European Observatory on Health Care Systems, World Health Organization Regional Office for Europe; 2009. Available from: http://www.euro.who.int/__data/assets/pdf_file/0006/87225/E93666.pdf. Accessed July 15, 2011.
28. All Wales Medicines Strategy Group. Vale of Glamorgan (Wales): Welsh Medicines Partnership; 2010. Available from: http://www.wales.nhs.uk/sites3/home.cfm?orgid=371. Accessed July 15, 2011.
29. Guide to the single technology appraisal (STA) process. London, UK: National Insitute for Health and Clinical Excellence (NICE); 2009. Available from: http://www.nice.org.uk/media/913/06/Guide_to_the_STA-proof_6–26–10–09.pdf. Accessed July 15, 2011.
30. Guidance to manufacturers for completion of new product assessment form (NPAF). Revised June 2010. Glasgow, Scotland: Scottish Medicines Consortium; 2010. Available from: http://www.scottishmedicines.org.uk/files/submissionprocess/New_Product_Assessment_Form_NPAF_Guidance_Notes_updated_February_2011_Final.doc. Accessed July 22, 2011.
31. Zuidberg C, editor. Pharmaceutical Pricing and Reimbursement Information. The pharmaceutical system of the Netherlands. Vienna, Austria: 2010. Available from: http://ppri.oebig.at/Downloads/Publications/The%20pharmaceutical%20system%20of%20the%20Netherlands_FINAL.pdf. Accessed July 15, 2011.
33. Daniels N, Sabin JE. Last chance therapies and managed care. Pluralism, fair procedures, and legitimacy. *Hastings Cent Rep*. 1998;28:27–41.
34. Sjogren E. Deciding subsidy for pharmaceuticals based on ambiguous evidence. *J Health Organ Manag*. 2008;22:368–383.
35. Pharmaceutical pricing and reimbursement information: Norway. Vienna, Austria: Pharmaceutical Pricing and Reimbursement Information; 2008. Available from: http://ppri.oebig.at/Downloads/Results/Norway_PPRI_2008.pdf. Accessed July 15, 2011.
36. Sorenson C, Drummond M, Kanavos P. Ensuring value for money in health care: the role of health technology assessment in the European Union [European Observatory on Health Systems and Policies. Observatory Studies Series No. 11]. Copenhagen, Denmark: World Health Organization Regional Office for Europe; 2008. Available from: http://www.euro.who.int/__data/assets/pdf_file/0011/98291/E91271.pdf. Accessed July 15, 2011.
36. Teixeira I, Agostinho I. Pharmaceutical pricing and reimbursement information: Lisbon, Portugal: Pharmaceutical Pricing and Reimbursement Information; 2008. Available from: http://www.infarmed.pt/portal/page/portal/INFARMED/MONITORIZACAO_DO_MERCADO/OBSERVATORIO/Projectos_Internacionais/Portugal_PPRI_2008.pdf. Accessed July 15, 2011.
37. Appraising life-extending, end of life treatments. London, UK: National Institute for Health and Clinical Excellence (NICE); 2009. Available from: http://www.nice.org.uk/aboutnice/howwework/devnicetech/endoflifetreatments.jsp. Accessed July 15, 2011.
38. Guidelines for application for general reimbursement of medicinal products. Copenhagen, Denmark: The Danish Medicines Agency; 2008. Available from: http://laegemiddelstyrelsen.dk/~/media/31C93DCD939A43FBB9E20070B5548337.ashx. Accessed July 22, 2011.
39. 2000/030 summary of the appeals process. London, UK: National Insitute for Health and Clinical Excellence (NICE); 2000. Available from: http://www.nice.org.uk/newsroom/pressreleases/pressreleasearchive/pressreleases2000/2000_030_summary_of_the_appeals_process.jsp. Accessed January 7, 2010.
40. Stafinski T, McCabe CJ, Menon D. Funding the unfundable: Mechanisms for managing uncertainty in decisions on the introduction of new and innovative technologies into healthcare systems. *Pharmacoeconomics*. 2010;28:113–142.
41. Adamski J, Godman B, Ofierska-Sujkowska G, et al. Risk sharing arrangements for pharmaceuticals: Potential considerations and recommendations for European payers. *BMC Health Serv Res*. 2010;10:153. Available from: http://www.biomedcentral.com/1472-6963/10/153. Accessed July 15, 2011.
42. Garner S. How does NICE value innovation? *Drug Dev Res*. 2010;71:449–456.
43. Grandfils N. Drug price setting and regulation in France [Working paper no. 16]. Paris, France: Institut de recherche et documentation en economie de la sante (IRDES); 2008. Available from: http://www.irdes.fr/EspaceAnglais/Publications/WorkingPapers/DT16DrugPriceSettingRegulationFrance.pdf. Accessed July 15, 2011.
44. Barros PP, de Almeida Simoes J. Allin S, Mossialos E, editors. Portugal: Health system review [Health Systems in Transition 2007;9(5)]. Copenhagen, Denmark: World Health Organization Regional Office for Europe. European Observatory on Health Systems and Policies; 2007. Available from: http://www.euro.who.int/data/assets/pdf_file/0004/107842/E90670.pdf. Accessed July 15, 2011.
45. Briggs A, Ritchie K, Fenwick E, Chalkidou K, Littlejohns P. Access with evidence development in the UK: Past experience, current initiatives and future potential. *Pharmacoeconomics*. 2010;28:163–170.
46. The Danish Medicines Agency: Reimbursement. Copenhagen, Denmark: The Danish Medicines Agency; 2010. Available from: http://laegemiddelstyrelsen.dk/en/topics/statistics,-prices-and-reimbursement/reimbursement-of-medicines. Accessed July 22, 2011.
47. Tonarelli L. Italy: Pioneering pay for performance in the age of austerity. InPharm News(InPharm com) 2011. Available from: http://www.inpharm.com/news/110104/italy-drug-price-cuts. Accessed July 22, 2011.
48. Towse A. Value based pricing, research and development, and patient access schemes. Will the United Kingdom get it right or wrong? *Br J Clin Pharmacol*. 2010;70:360–366.
49. Le Polain M, Franken M, Koopmanschap M, Cleemput I. Drug reimbursement systems: International comparison and policy recommendations. Brussels, Belgium: Belgian Health Care Knowledge Centre; 2010. Available from: http://www.kce.fgov.be/index_en.aspx?SGREF=5211&CREF=18732. Accessed July 22, 2011.
50. Guidelines on procedure for reassessment of reimbursement status. Copenhagen, Denmark: Danish Medicines Agency; 2005. Available from: http://laegemiddelstyrelsen.dk/en/topics/statistics,-prices-and-reimbursement/reimbursement-of-medicines/general-reimbursement/reassessment-of-reimbursement-status-for–l-products/guidelines/guidelines-on-procedure-for-reassessment–ent-status. Accessed July 22, 2011.

51. Welcome to TLV [the Dental and Pharmaceutical Benefits Agency]. Stockholm, Sweden: Dental and Pharmaceutical Benefits Agency; 2008. Available from: http://www.tlv.se/in-english-old/in-english/. Accessed July 22, 2011.
52. McLaughlin N. Of problems and solutions. Issues with variable-rate bonds, medical errors led our recent coverage. *Mod Healthc*. 2009;39:18.
53. McCabe CJ, Stafinski T, Edlin R, Menon D. Access with evidence development schemes: A framework for description and evaluation. *Pharmacoeconomics*. 2010;28:143–152.
54. Menon D, McCabe CJ, Stafinski T, Edlin R. Principles of design of access with evidence development approaches: A consensus statement from the Banff Summit. *Pharmacoeconomics*. 2010;28:109–111.
55. Buchholz P. ISPOR global health care systems road map: Austria – Pharmaceuticals. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/htaroadmaps/Austria.asp. Accessed July 23, 2011.
56. Godman B, Bucsics A, Burkhardt T, Haycox A, Seyfried H, Wieninger P. Insight into recent reforms and initiatives in Austria: Implications for key stakeholders. *Expert Rev Pharmacoecon Outcomes Res*. 2008;8:357–371.
57. Wild C. Austria: History of health technology assessment during the past 20 years. *Int J Technol Assess Health Care*. 2009;25 Suppl 1:74–81.
58. Pharmaceutical pricing and reimbursement information: Austria. [Pharmaceutical Pricing and Reimbursement Information]. Vienna, Austria: European Commission, Health and Consumer Protection Directorate-General and Austrian Ministry of Health, Family and Youth; 2008. Available from: http://ppri.oebig.at/Downloads/Results/Austria_PPRI_2008_Englih_Version.pdf. Accessed July 23, 2011.
59. Hofmarcher MM, Rack HM, Rohrling G. Austria: Health system review [Health Systems in Transition]. Copenhagen, Denmark: European Observatory on Health Care Systems, World Health Organization Regional Office for Europe; 2006. Available from: http://www.euro.who.int/__data/assets/pdf_file/0009/96435/E89021.pdf. Accessed July 23, 2011.
60. Van Wilder PB, Dupont AG. Reimbursement of medicines in Belgium: Role of evidence-based medicine. *Acta Clin Belg*. 2009;64:120–128.
61. Cleemput I, van WP, Huybrechts M, Vrijens F. Belgian methodological guidelines for pharmacoeconomic evaluations: Toward standardization of drug reimbursement requests. *Value Health*. 2009;12:441–449.
62. Belgium. In: Policies for rare diseases and orphan drugs [KCE reports 112C]. Brussels, Belgium: Belgian Health Care Knowledge Centre; 2009. Available from: http://www.kce.fgov.be/Download.aspx?ID=2161. Accessed July 23, 2011.
63. Arrete royal portant modification de l'arrete royal du 3 juillet 1996 portant execution de la loi relative a l'assurance obligatoire soins de sante et indemnites, coordonnee le 14 juillet 1994. [Brussels]: Ministere des Affaires Sociales de la Sante Publique et de l'Environnement; 2001. Available from: http://www.inami.fgov.be/drug/fr/drugs/reglementation/legal-texts/pdf/arkb20011221.pdf. Accessed July 23, 2011.
64. Corens D. Belgium: Health system review [Health Systems in Transition 2007;9(2)]. Copenhagen, Denmark: World Health Organization Regional Office for Europe. European Observatory on Health Care Systems; 2007. Available from: http://www.euro.who.int/__data/assets/pdf_file/0007/96442/E90059.pdf. Accessed July 23, 2011.
65. Prices and reimbursements of medicinal products and foods for special medical purposes. Prague, Czechoslovakia: State Institute for Drug Control; 2010. Available from: http://www.sukl.eu/sukl/prices-and-reimbursements-of-medicinal-products-and-foods. Accessed July 23, 2011.
66. Bryndova L, Pavlokova K, Roubal T, Rokosova M, Gaskins M. Czech Republic: Health system review [Health Systems in Transition 2009;11(1)]. Copenhagen, Denmark: World Health Organization. Regional Office for Europe. European Observatory on Health Systems and Policies; 2009. Available from: http://www.euro.who.int/__data/assets/pdf_file/0010/97633/E92968.pdf. Accessed July 23, 2011.
67. Praznovcova L, Suchopar J, Wertheimer AI. Drug policy in the Czech Republic. In: Wertheimer AI, Smith MC, editors. *International Drug Regulatory Mechanisms*. Binghamton, NY: Haworth Press; 2003.
68. Pricing and reimbursement in Denmark. Copenhagen, Denmark: The Danish Association of the Pharmaceutical Industry; 2007. Available from: http://parno1.ipapercms.dk/LIF/Notater/PricingandreimbursementinDenmark/. Accessed July 23, 2011.
69. Strandberg-Larsen M, Knudsen MS. ISPOR Global Health Care Systems Road Map: Denmark. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/htaroadmaps/Denmark.asp. Accessed July 23, 2011.
70. High quality care for all. NHS next stage review final report. London, UK: Department of Health; 2008. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_085828.pdf. Accessed July 23, 2011.
71. Pedersen KM, Christiansen T, Bech M. The Danish health care system: Evolution – not revolution – in a decentralized system. *Health Econ*. 2005;14 Suppl 1:S41–S57.
72. Kanavos P, Vandoros S, Habicht J, de Joncheere K. Review of the Estonian pharmaceutical sector: towards the development of a national medicines policy. Copenhagen, Denmark: World Health Organization Regional Office for Europe; 2009. Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/96448/E93049.pdf. Accessed July 15, 2011.
73. Decree of the Ministry of Social Affairs and Health on the priced services of the Pharmaceuticals Pricing Board. Helsinki, Finland: Finland Ministry of Social Affairs and Health; 2010. Available from: http://www.stm.fi/c/document_library/get_file?folderId=71837&name=DLFE-14601.pdf. Accessed July 23, 2011.
74. Decree of the Ministry of Social Affairs and Health on applications and price notifications made to the Pharmaceuticals Pricing Board. Helsinki, Finland: Finland Ministry of Social Affairs and Health; 2009. Available from: http://www.ispor.org/PEguidelines/source/GuidelinesinFinland_EnglishVersion.pdf. Accessed July 23, 2011.
75. Pharmaceuticals Pricing Board: The expert group of the Pharmaceuticals Pricing Board. Helsinki, Finland: Ministry of Social Affairs and Health; 2010. Available from: http://www.stm.fi/en/ministry/boards/pharmaboard/expert. Accessed July 23, 2011.
76. Ministry of Social Affairs and Health, Finland. Decree of the Ministry of Social Affairs and Health on applications and price notifications made to the Pharmaceuticals Pricing Board. Helsinki, Finland: Ministry of Social Affairs and Health, Finland; 2009. Available from: http://www.ispor.org/PEguidelines/source/GuidelinesinFinland_EnglishVersion.pdf. Accessed July 23, 2011.
77. Becker C. Few details on DRG revamp. The CMS may reveal portions of new system in April. *Modern Healthc*. 2006;11:12.
78. Falissard B, Izard V, Xerri B, Bouvenot G, Meyer F, Degos L. Relative effectiveness assessment of listed drugs (REAL): A new method for an early comparison of the effectiveness of approved health technologies. *Int J Technol Assess Health Care*. 2010;26:124–130.
79. Weill C, Banta D. Development of health technology assessment in France. *Int J Technol Assess Health Care*. 2009;25 Suppl 1:108–111.
80. Chicoye A, Chhabra A. ISPOR global health care systems road map: France – Pharmaceuticals. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research (ISPOR); 2009. Available from: http://www.ispor.org/htaroadmaps/France.asp. Accessed July 23, 2011.
81. Pharmaceutical pricing and reimbursement information: Germany. Vienna, Austria: Pharmaceutical Pricing and Reimbursement Information; 2008. Available from: http://ppri.oebig.at/Downloads/Results/Germany_PPRI_2008.pdf. Accessed July 23, 2011.
82. Paris V, Docteur E. Pharmaceutical pricing and reimbursement policies in Germany [OECD Health Working Papers No. 39]. Paris, France: Organisation for Economic Co-operation and Development; 2008. Available from: http://www.oecd.org/dataoecd/6/57/41586814.pdf. Accessed July 23, 2011.

83. Fricke FU, Dauben HP. Health technology assessment: A perspective from Germany. *Value Health*. 2009;12 Suppl 2:S20–S27.
84. Sorenson C. The role of HTA in coverage and pricing decisions: A cross-country comparison. Euro Observer: The Health Policy Bulletin of the European Observatory on Health Systems and Policies. 2009;11:1–12. Available from: http://www.euro.who.int/__data/assets/pdf_file/0019/80335/EuroObserver_spring2009.pdf. Accessed July 23, 2011.
85. Pricing [Greece]. In: Surveying, assessing and analysing the pharmaceutical sector in the 25 EU member states. Luxembourg: Osterreichisches Bundesinstitut fur Gesundheitswesen for the European Commission; 2006. Available from: http://ec.europa.eu/competition/mergers/studies_reports/oebig.pdf. Accessed July 23, 2011.
86. National Organization for Medicines. Athens, Greece: National Organization for Medicines; 2011. Available from: http://www.eof.gr/web/guest/structure. Accessed July 23, 2011.
87. International Society for Pharmacoeconomics and Outcomes Research global health care systems road map: Greece. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2008. Available from: http://www.ispor.org/HTARoadMaps/Greece.asp. Accessed July 23, 2011.
88. Gaal P. Health care systems in transition: Hungary. Brussels, Belgium: European Observatory on Health Care Systems; 2004. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/80783/E84926.pdf. Accessed July 23, 2011.
89. Gulacsi L, David T, Dozsa C. Pricing and reimbursement of drugs and medical devices in Hungary. *Eur J Health Econ*. 2002;3:271–278.
90. Gulacsi L, Brodszky V, Pentek M, Varga S, Vas G, Boncz I. History of health technology assessment in Hungary. *Int J Technol Assess Health Care*. 2009;25 Suppl 1:120–126.
91. Tilson L, O'Leary A, Usher C, Barry M. Pharmacoeconomic evaluation in Ireland: A review of the process. *Pharmacoeconomics*. 2010;28:307–322.
92. Barry M. Economies in drug usage in the Irish healthcare setting. Dublin, Ireland: Department of Health and Children; 2009. Available from: http://www.dohc.ie/publications/pdf/economies_drug_usage.pdf?direct=1. Accessed July 23, 2011.
93. Coughlan JJ, Fortescue-Webb D, Heaney R, Judge G, Tilson L, Barry M. ISPOR global health care systems road map: Ireland – Pharmaceutical. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/HTARoadMaps/Ireland.asp. Accessed July 23, 2011.
94. Garattini L. Pricing and reimbursement policies in Italy: Current and future trends. In: Garau M, Mestre-Ferrandiz J, editors. European Medicines Pricing and Reimbursement. Milton Keynes, UK: Radcliffe Publishing; 2007. Available from: http://www.radcliffe-oxford.com/books/samplechapter/184X/Garau_CHPT4–65cf3e00rdz.pdf. Accessed July 23, 2011.
95. Folino-Gallo P, Montilla S, Bruzzone M, Martini N. Pricing and reimbursement of pharmaceuticals in Italy. *Eur J Health Econ*. 2008;9:305–310.
96. Impact of HTA on policy: Examples from INAHTA members. Stockholm, Sweden: International Network of Agencies for Health Technology Assessment; 2001. Available from: http://www.inahta.org/upload/About%20INAHTA/Survey_HTA_Policy_Oct2001.pdf. Accessed July 23, 2011.
97. Fattore G, Jommi C. The last decade of Italian pharmaceutical policy: Instability or consolidation? *Pharmacoeconomics*. 2008;26:5–15.
98. Johnsen JR. Health systems in transition: Norway. Copenhagen: World Health Organization Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies; 2006. Available from: http://www.euro.who.int/__data/assets/pdf_file/0005/95144/E88821.pdf. Accessed July 23, 2011.
99. Kuszewski K, Gericke C. Health systems in transition: Poland [Health Systems in Transition 2005;7(5)]. Brussels, Belgium: European Observatory on Health Care Systems; 2005. Available from: http://www.euro.who.int/__data/assets/pdf_file/0011/95159/E88670.pdf. Accessed July 23, 2011.
100. ISPOR global health care systems road map: Poland – reimbursement process. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2008. Available from: http://www.ispor.org/HTARoadMaps/Poland.asp. Accessed July 23, 2011.
101. Alves da Silva E, Gouveia Pinto C, Sampaio C, Pereira JA, Drummond M, Trindade R. Guidelines for economic drug evaluation studies. Lisbon, Portugal: Autoridade Nacional do Medicamento e Produtos de Saude; 1998. Available from: http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH/PCAEC04_vering.pdf. Accessed July 23, 2011.
102. Mazag J, Segec A. Pharmaceutical pricing and reimbursement information: Slovakia [Pharmaceutical Pricing and Reimbursement Information]. Vienna, Austria. European Commission, Health and Consumer Protection Directorate-General; Austrian Ministry of Health, Family and Youth; 2007. Available from: http://ppri.oebig.at/Downloads/Results/Slovakia_PPRI_2007.pdf. Accessed July 23, 2011.
103. Hall PS, McCabe C, Brown JM, Cameron DA. Health economics in drug development: Efficient research to inform healthcare funding decisions. *Eur J Cancer*. 2010;46:2674–2680.
104. Kohli H, Tannahill A. NICE guidance in the Scottish context. *Scott Med J*. 2009;54:35–38. Available from: http://www.smj.org.uk/0209/pdfs/Original%20Kohli%20and%20Tannahill.pdf. Accessed July 23, 2011.
105. Tomek D, Psenkova M, Hanzelova M. Reimbursement of innovative drugs in Slovakia – pharmacoeconomics of agomelatin in depression. *Value Health*. 2009;12:A364–A365.
106. Kalo Z, Docteur E, Moise P. Pharmaceutical pricing and reimbursement policies in Slovakia [OECD Health Working Paper No. 31]. Paris, France: Organisation for Economic Co-operation and Development; 2008. Available from: http://www.oecd.org/dataoecd/14/40/40177050.pdf. Accessed July 23, 2011.
107. Szalay T, Pazitny P, Szalayova A, et al. Slovakia: Health system review [Health Systems in Transition 2011;13(2)]. Copenhagen, Denmark: World Health Organisation Regional Office for Europe. European Observatory on Health Systems and Policies.; 2011. Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/140593/e94972.pdf. Accessed July 23, 2011.
108. Vogler S, Espin J, Habl C. Pharmaceutical pricing and reimbursement information (PPRI) – new PPRI analysis including Spain. *Pharm Pol Law*. 2009;11:213–234. Available from: http://ppri.oebig.at/Downloads/Publications/Article_PPRI_Spain_PharmaceuticalPolicyAndLaw_2009.pdf. Accessed July 23, 2011.
109. Persson U, Willis M, Odegaard K. A case study of ex ante, value-based price and reimbursement decision-making: TLV and rimonabant in Sweden. *Eur J Health Econ*. 2010;11:195–203.
110. Moise P, Docteur E. Pharmaceutical pricing and reimbursement policies in Sweden [OECD Health Working Papers, No. 28]. Paris, France: Organisation for Economic Co-operation and Development (OECD); 2007. Available from: http://www.oecd.org/dataoecd/63/17/40699881.pdf. Accessed July 23, 2011.
111. Pharmaceutical Pricing and Reimbursement Information: Sweden. Vienna, Austria: PPRI – Pharmaceutical Pricing and Reimbursement Information; 2007. Available from: http://ppri.oebig.at/Downloads/Results/Sweden_PPRI_2007.pdf. Accessed July 23, 2011.
112. Erntoft S. ISPOR global health care systems road map: Sweden – pharmaceutical. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/HTARoadMaps/Sweden.asp. Accessed July 23, 2011.
113. Gress S, Niebuhr D, May W, Wasem J. Reform of prescription drug reimbursement and pricing in the German social health insurance market: A comparison of three scenarios. *Pharmacoeconomics*. 2007;25:443–454.
114. Paris V, Docteur E. Pharmaceutical pricing and reimbursement policies in Switzerland [OECD Health Working Papers, No. 27]. Paris, France: Organisation for Economic Co-operation and Development (OECD); 2007. Available from: http://www.oecd.org/dataoecd/54/42/38868953.pdf. Accessed July 23, 2011.

115. European Observatory on Health Care Systems. Health care systems in transition: Switzerland. Brussels, Belgium: European Observatory on Health Care Systems; 2000. Available from: http://www.euro.who.int/__data/assets/pdf_file/0003/96411/E68670.pdf. Accessed July 23, 2011.
116. van der Meijden C, Grahlmann C. Dutch assessment procedures for the reimbursement of outpatient medicines. Diemen, The Netherlands: Ministry of Health, Welfare and Sport/College voor zorgverzekeringen; 2010. Available from: http://www.cvz.nl/binaries/live/cvzinternet/hst_content/nl/documenten/rubriek+zorgpakket/cfh/assessment-outpatient-medicines.pdf. Accessed July 23, 2011.
117. Stolk EA, de Bont A, van Halteren AR, Bijlmer RJ, Poley MJ. Role of health technology assessment in shaping the benefits package in The Netherlands. *Expert Rev Pharmacoecon Outcomes Res*. 2009;9:85–94.
118. ISPOR global health care systems road map: The Netherlands. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2007. Available from: http://www.ispor.org/HTARoadMaps/Netherlands.asp. Accessed July 23, 2011.
119. Heemstra HE. Variations in access and use of orphan drugs among EU member states. *EJHP Practice*. 2010;16:25–27. Available from: http://www.eahp.eu/EJHP/EJHP-Practice/Issue-4-2010/Cover-Story/Variations-in-access-and-use-of-orphan-drugs-among-EU-Member-States. Accessed July 23, 2011.
120. ISPOR global health care systems road map: United Kingdom (England and Wales) – reimbursement process. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2008. Available from: http://www.ispor.org/htaroadmaps/UK.asp. Accessed July 23, 2011.
121. The Danish Health Act/legislation. Copenhagen, Denmark: Danish Medicines Agency; 2010. Available from: http://laegemiddelstyrelsen.dk/en/service-menu/legislation/the-danish-health-act. Accessed July 23, 2011.
122. Mossialos E, Srivastava D. Pharmaceutical policies in Finland: Challenges and opportunities [Observatory Studies Series No. 10]. Copenhagen, Denmark: World Health Organisation. Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies; 2008. Available from: http://www.euro.who.int/__data/assets/pdf_file/0020/80651/E91239.pdf. Accessed July 23, 2011.
123. Perleth M, Gibis B, Gohlen B. A short history of health technology assessment in Germany. *Int J Technol Assess Health Care*. 2009; 25 Suppl 1:112–119.
124. Holtorf AP, Matuszewski K, Nuijten M, Vauth C. ISPOR global health care systems road map: Germany. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/htaroadmaps/Germany.asp. Accessed July 23, 2011.
125. Tilson L, Barry M. Recent developments in pharmacoeconomic evaluation in Ireland. *Expert Rev Pharmacoecon Outcomes Res*. 2010;10:221–224.
126. Pricing and reimbursement. Rome, Italy: Agenzia Italiana del Farmaco; 2010. Available from: http://www.agenziafarmaco.it/en/content/pricing-and-reimbursement. Accessed July 23, 2011.
127. Agencja Oceny Technologii Medycznych. Warsaw, Poland: Agencja Oceny Technologii Medycznych; 2011. Available from: http://www.aotm.gov.pl/. Accessed July 23, 2011.
128. Scottish Medicines Consortium. Scottish Medicines Consortium; 2010. Available from: http://www.scottishmedicines.org.uk/smc/22.html. Accessed July 23, 2011.
129. Wilking N, Jonsson B. A pan-European comparison regarding patient access to cancer drugs. Stockholm, Sweden: Karolinska Institutet; 2006. Available from: http://ki.se/content/1/c4/33/52/Cancer_Report.pdf. Accessed July 23, 2011.
130. Informace k pravidelne revizi uhrad. Prague, Czechoslovakia: Statni Ustav pro Kontrolu Leciv (SUKL); 2009. Available from: http://www.sukl.cz/leciva/informace-k-pravidelne-revizi-uhrad. Accessed July 23, 2011.
131. Tomek D, Bielik J. Legislative aspects of health technology assessment in Slovakia. *Value Health*. 2009;12:A87.
132. ISPOR global health care systems road map: Spain – Pharmaceutical. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2009. Available from: http://www.ispor.org/HTARoadMaps/Spain.asp. Accessed July 23, 2011.
133. Pharmaceutical Pricing and Reimbursement Information: Sweden. Vienna, Austria: Pharmaceutical Pricing and Reimbursement Information; 2007. Available from: http://ppri.oebig.at/Downloads/Results/Sweden_PPRI_2007.pdf. Accessed July 23, 2011.
134. Working guidelines for the pharmaceutical reimbursement review. Stockholm, Sweden: Tandvards-Och Lakemedelsformansverket (TLV)/the Dental and Pharmaceutical Benefits Agency [formerly the Swedish Pharmaceutical Benefits Board]; 2008. Available from: http://www.tlv.se/Upload/Genomgangen/guidelines-pharmaceutical-reimbursement.pdf. Accessed July 23, 2011.
135. Reimbursement review. Stockholm, Sweden: Tandvards Och Lakemedelsformansverket (TLV) [The Swedish Pharmaceutical Benefits Board]; 2009. Available from: http://www.tlv.se/in-english/reimbursement-review/. Accessed July 23, 2011.
136. Glenngard AH, Hjalte F, Svensson M, Anell A, Bankauskaite V. Health systems in transition: Sweden. Copenhagen, Denmark: World Health Organisation Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies; 2005. Available from: http://www.euro.who.int/__data/assets/pdf_file/0010/96409/E88669.pdf. Accessed July 23, 2011.
137. Gress S, Niebuhr D, Rothgang H, Wasem J. Criteria and procedures for determining benefit packages in health care. A comparative perspective. *Health Policy*. 2005;73:78–91.
138. Dolezal T. Pricing and reimbursement in Czech Republic ... road to HTA? Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2008. Available from: http://www.google.ca/url?sa=t&source=web&cd=2&ved=0CBwQFjAB&url=http%3A%2F%2Fwww.isporserbia.com%2Fdocs%2Ffirst%2FMarch10%2F02.ppt&ei=QgTkTfnFDqvQiAL0l7WoBg&usg=AFQjCNEcRD0RWYovvKcnIEV-017m4bG0ow. Accessed July 23,2011.
139. Pharmacoeconomic analysis. Tallinn, Estonia: Estonian Health Insurance Fund; 2002. Available from: http://www.haigekassa.ee/eng/health-insurance-in-estonia/medicinal-products/pharmacoeconomic-analysis. Accessed July 23, 2011.
140. Aaviskoo A, Saluse J, Palm E. Scientific community leads HTA development [Health Policy Monitor]. 2009. Available from: http://www.hpm.org/survey/ee/a14/2. Accessed July 23, 2011.
141. Daniels N, Sabin J. Limits to health care: Fair procedures, democratic deliberation, and the legitimacy problem for insurers. *Philos Public Aff*. 1997;26:303–350.
142. Bekkering GE, Kleijnen J. Procedures and methods of benefit assessments for medicines in Germany. *Eur J Health Econ*. 2008;9 Suppl 1: 5–29.
143. Martikainen J, Rajaniemi S. Drug reimbursement systems in EU member states, Iceland and Norway: France. In. 54. Helsinki: The Social Insurance Institution; 2002. Available from: http://www.kela.fi/in/internet/english.nsf/NET/050303135141PN. Accessed July 23, 2011.
144. Paris V, Docteur E. Pharmaceutical pricing and reimbursement policies in Germany [OECD Health Working Papers, No. 39]. Paris: Organisation for Economic Co-operation and Development (OECD); 2008. Available from: http://www.oecd.org/dataoecd/6/57/41586814.pdf. Accessed July 23, 2011.
145. Yfantopoulos J. Pharmaceutical pricing and reimbursement reforms in Greece. *Eur J Health Econ*. 2008;9:87–97.
146. Irish healthcare technology assessment guidelines. version 1. Dublin, Ireland: National Centre for Pharmacoeconomics (NCPE) in Ireland; 2000. Available from: http://www.ncpe.ie/contact.php. Accessed July 23, 2011.
147. Guidelines for the economic evaluation of health technologies in Ireland. Dublin, Ireland: Health Information and Quality Authority; 2010. Available from: http://www.hiqa.ie/system/files/HTA_Economic_Guidelines_2010.pdf. Accessed July 23, 2011.

148. Pharmacoeconomic guidelines around the world: Italy. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from: http://www.ispor.org/PEguidelines/countrydet.asp?c=13&t=4. Accessed July 23, 2011.
149. Application standard for acceptance to the drug reimbursement scheme; pursuant to Article 9 of the regulation on reimbursement of crucial drug costs. [Oslo]: Statens legemiddelverk/Norwegian Medicines Agency; 2005. Available from: http://www.legemiddelverket.no/templates/InterPage_25665.aspx. Accessed July 23, 2011.
150. Norwegian guidelines for pharmacoeconomic analysis in connection with applications for reimbursement. Oslo, Norway: Statens legemiddelverk/Norwegian Medicines Agency; 2005. Available from: http://www.legemiddelverket.no/templates/InterPage_25644.aspx. Accessed July 23, 2011.
151. Polish guidelines for conducting pharmacoeconomic evaluations. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from: http://www.ispor.org/PEguidelines/source/Polish-Guidelines-for-Conducting-Pharmacoeconomic-Evaluations_2010.pdf. Accessed July 23, 2011.
152. Pharmacoeconomic guidelines around the world: Slovak Republic. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2011. Available from: http://www.ispor.org/peguidelines/countrydet.asp?c=35&t=1. Accessed July 23, 2011.
153. General guidelines for economic evaluations from the Pharmaceutical Benefits Board (LFNAR 2003:2). Stockholm, Sweden: Pharmaceutical Benefits Board; 2003. Available from: http://www.ispor.org/peguidelines/source/Guidelines_in_Sweden.pdf. Accessed July 23, 2011.
154. Vegter S, Rozenbaum MH, Postema R, Tolley K, Postma MJ. Review of regulatory recommendations for orphan drug submissions in The Netherlands and Scotland: Focus on the underlying pharmacoeconomic evaluations. *Clin Ther*. 2010;32:1651–1661.
155. Stolk EA, Poley MJ. Criteria for determining a basic health services package. Recent developments in The Netherlands. *Eur J Health Econ*. 2005;6:2–7.
156. Stolk EA, de BA, van Halteren AR, Bijlmer RJ, Poley MJ. Role of health technology assessment in shaping the benefits package in The Netherlands. *Expert Rev Pharmacoecon Outcomes Res* 2009;9: 85–94.
157. Single technology appraisal (STA): Specification for manufacturer/sponsor submission of evidence. London, UK: National Institute for Health and Clinical Excellence; 2009. Available from: http://www.nice.org.uk/media/59C/B3/SpecificationForManufacturerSponsorSubmissionEvidenceJune2010.doc. Accessed July 23, 2011.
158. Lloyd A, Wild D, Gallop K, Cowell W. Reimbursement agency requirements for health related quality-of-life data: A case study. *Expert Rev Pharmacoecon Outcomes Res*. 2009;9: 527–537.
159. Niemietz KPMP. A healthy market? Health technology assessment in the UK and Germany [Stockholm Network Papers on Health Technology Assessment. Paper No. 2]. Stockholm, Sweden: Stockholm Network; 2007. Available from: http://www.stockholmnetwork.org/downloads/publications/HTA3_2.pdf. Accessed July 23, 2011.
160. Barros PP. Pharmaceutical policies in European countries. *Adv Health Econ Health Serv Res*. 2010;22:3–27.
161. Annex to the decree by the Ministry of Social Affairs and Health on applications for a reasonable wholesale price, on special reimbursement status for a medicinal product, and on the documentation to be attached to the application (1393/2003). Helsinki, Finland: Finland Ministry of Social Affairs and Health; 2003. Available from: http://www.stm.fi/c/document_library/get_file?folderId=71837&name=DLFE-7603.pdf. Accessed July 23, 2011.
162. Medical device assessment in France: Guidebook. Cedex, France: Haute Autorite de Sante; 2009. Available from: http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-03/guide_dm_gb_050310.pdf. Accessed July 23, 2011.
163. Office of Health Technology Assessment of the National Institute for Strategic Health Research. Budapest, Hungary: National Institute for Strategic Health Research; 2011. Available from: http://www.eski.hu/new3/technologia_en/technologia_en.php. Accessed July 23, 2011.
164. Brodszky V, Orlewska E, Pentek M, Karpati K, Skoupa J, Gulacsi L. Challenges in economic evaluation of new drugs: Experience with rituximab in Hungary. *Med Sci Monit*. 2010;16:SR1–SR5.
165. Barry M, Tilson L. Recent developments in pricing and reimbursement of medicines in Ireland. *Expert Rev Pharmacoecon Outcomes Res*. 2007;7:605–611. Available from: http://www.expert-reviews.com/doi/pdf/10.1586/14737167.7.6.605. Accessed July 23, 2011.
166. Kozierkiewicz A, Trabka W, Romaszewski A, Gajda K, Gilewski D. Definition of the "health benefit basket" in Poland. *Eur J Health Econ*. 2005;6 Suppl 1:58–65. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1388086/?tool=pubmed. Accessed July 23, 2011.
167. Orlewska E, Mierzejewski P. Project of Polish guidelines for conducting pharmacoeconomic evaluations in comparison to international health economic guidelines. *Eur J Health Econ*. 2003;4:296–303.
168. Pharmacoeconomic guidelines around the world: Scotland. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from: http://www.ispor.org/PEguidelines/countrydet.asp?c=19&t=2. Accessed July 15, 2011.
169. Visnansky M. HTA and health care decisions in Slovakia. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2010. Available from: http://www.ispor.org/regional_chapters/Slovakia/documents/ISPOR_HTA_and_HC_Dcisions_in_SK_HTAC_112010.pdf. Accessed July 23, 2011.
170. Guideline: the Ministry of Health of the Slovak Republic no. 343/2008 Z. z. the details of pharmaco-economic analysis of drug ... the Ministry of Health of the Slovak Republic no. 210/2008 Z. laws, which provides details on the medico-economic analysis of the medical device when the decree of the Ministry of Health of the Slovak Republic no. 149/2009 Z. z. the details of medico-economic analysis of dietary food for the implementation of pharmaco-economic analysis of drug; medico-econoic analysis of the medical device and medico-economic analysis of the dietary food. Bratislava, Slovakia: Ministerstva zdravotnictva Slovenskej republiky; 2009. Available from: http://www2.health.gov.sk/redsys/rsi.nsf/0/4399FF0A33156D1CC1256FAF002B94DE?OpenDocument. Accessed July 23, 2011.
171. Duran A, Lara JL, van Waveren M. Spain: Health system review [Health Systems in Transition]. Copenhagen, Denmark: European Observatory on Health Care Systems, World Health Organization Regional Office for Europe; 2006. Available from: http://www.euro.who.int/en/home/projects/observatory/publications/health-system-profiles-hits/full-list-of-hits/spain-hit-2007. Accessed July 23, 2011.
172. Muller KR. ISPOR global health care systems road map: Switzerland – Pharmaceutical. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research (ISPOR); 2011. Available from: http://www.ispor.org/htaroadmaps/SwitzerlandPH.asp. Accessed July 23, 2011.
173. van Nooten F, van Agthoven M. Mandatory pharmacoeconomic studies in the Dutch reimbursement setting. Institute for Medical Technology Assessment newsletter. 2005;3:1–3. Available from: http://www.bmg.eur.nl/fileadmin/ASSETS/bmg/english/iMTA/Publications/Newsletter/imta_newsletter_3_1.pdf. Accessed July 23, 2011.
174. All Wales Medicines Strategy Group: Structure of appraisal. Vale of Glamorgan, Wales: All Wales Medicines Strategy Group; 2007. Available from: http://www.wales.nhs.uk/sites3/home.cfm?orgid=371. Accessed July 23, 2011.
175. INAMI – medicaments. Brussels, Belgium: I National Institute for Health and Disability Insurance; 2011. Available from: http://www.inami.fgov.be/drug/fr/drugs/index.htm#2. Accessed July 23, 2011.

176. Sandmann FG. Framework of decision making regarding the benefit package in the Czech Republic. In: Decision making on the inclusion of new provisions in the benefit package: A comparative study between the Netherlands and the Czech Republic (with a focus on the role of value for money considerations in pharmaceutical reimbursement decision making). Enschede, The Netherlands: University of Twente. School of Management and Governance; 2010. Available from: http://www.utwente.nl/mb/htsr/education/completed%20assignments/Sandmann.pdf. Accessed July 23, 2011.
177. Petrikova A, Dolezal T, Lamka J, Klimes J. Description of the pricing and reimbursement system in the Czech Republic. Prague, Czechoslovakia: Institute of Health Economics and Technology Assessment; 2010. Available from: http://www.iheta.org/ext/files/27/Poster_ISPOR_PR_CZ.pdf. Accessed July 23, 2011.
178. Davidova J, Praznovcova L, Lundborg CS. Pricing and reimbursement of pharmaceuticals in the Czech Republic and Sweden. *Pharm World Sci*. 2008;30:57–64.
179. Davidova J, Ivanovic N, Praznovcova L. Participation in pharmaceutical costs and seniors' access to medicines in the Czech Republic. *Cent Eur J Public Health*. 2008;16:26–28. Available from: http://www1.szu.cz/svi/cejph/archiv/2008-1-06-full.pdf. Accessed July 23, 2011.
180. Spacilova L, Petrelli F, Grappasonni I, Scuri S. Health care system in the Czech Republic. *Ann Ig*. 2007;19:573–581.
181. Mossialos E, Srivastava D. Overview of the pharmaceutical system in Finland. In: Pharmaceutical policies in Finland: challenges and opportunities [Observatory Studies Series No. 10]. Copenhagen, Denmark: World Health Organization; European Observatory on Health Systems and Policies; Ministry of Social Affairs and Health Finland; 2008. Available from: http://www.euro.who.int/__data/assets/pdf_file/0020/80651/E91239.pdf. Accessed July 23, 2011.
182. Government decree on the Pharmaceuticals Pricing Board. Helsinki, Finland: Finland Ministry of Social Affairs and Health; 2008. Available from: http://www.stm.fi/c/document_library/get_file?folderId=71837&name=DLFE-10036.pdf. Accessed July 23, 2011.
183. Strandberg-Larsen M, Nielsen MB, Vallgarda S, Krasnik A, Vrangbaek K. Denmark: Health system review [Health Systems in Transition 2007;9]. Copenhagen, Denmark: World Health Organisation Regional Office for Europe. European Observatory on Health Care Systems; 2007. Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/80581/E91190.pdf. Accessed July 23, 2011.
184. Falissard B, Zylberman M, Cucherat M, et al. Real medical benefit assessed by indirect comparison. *Therapie*. 2009;64:225–232. French.
185. Haute Autorite de Sante. Cedex, France: Haute Autorite de Sante; 2010. Available from: http://www.has-sante.fr. Accessed July 23, 2011.
186. Yfantopoulos J. Pharmaceutical pricing and reimbursement reforms in Greece. *Eur J Health Econ*. 2008;9:87–97.
187. Rules of procedure of the social insurance inclusion of pharmaceuticals in Hungary. Budapest, Hungary: National Institute for Strategic Health Research. Office of Health Technology Assessment; 2011. Available from: http://www.eski.hu/new3/technologia_en/technologia_en_procedure.php. Accessed July 23, 2011.
188. ISPOR global health care systems road map: Italy – Pharmaceuticals. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research (ISPOR); 2011. Available from: http://www.ispor.org/HTARoadMaps/Italy.asp. Accessed July 23, 2011.
189. Godman B, Sakshaug S, Berg C, Wettermark B, Haycox A. Combination of prescribing restrictions and policies to engineer low prices to reduce reimbursement costs. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11:121–129.
190. Nizankowski R, Wilk N. From idealistic rookies to a regional leader: The history of health technology assessment in Poland. *Int J Technol Assess Health Care*. 2009;25 Suppl 1:156–162.
191. Ministerio da Saude: Decreto-Lei no. 48-A/2010. Oeiras, Portugal: Associacao Portuguese de Medicamentos Genencos; 2010. Available from: http://www.apogen.pt/conteudos/uploads/Files/apogen/PacoteMedicamento_13Maiode2010.pdf. Accessed July 23, 2011.
192. Jansson S. Implementing accountability for reasonableness – the case of pharmaceutical reimbursement in Sweden. *Health Econ Policy Law*. 2007;2(Pt 2):153–171.
193. Guidelines for pharmacoeconomic research, updated version. Diemen, The Netherlands: College voor Zorgverzekeringen; 2006. Available from: http://www.ispor.org/peguidelines/source/HTAGuidelinesNLupdated2006.pdf. Accessed July 23, 2011.
194. Healy P, Pugatch M. Theory versus practice: Discussing the governance of health technology assessment systems. Stockholm, Sweden: Stockholm Network; 2009. Available from: http://www.stockholm-network.org/downloads/publications/Theory_versus_Practice.pdf. Accessed July 23, 2011.
195. Sculpher M. Single technology appraisal at the UK National Institute for Health and clinical excellence: A source of evidence and analysis for decision making internationally. *Pharmacoeconomics*. 2010;28:347–349.
196. Kennedy I. Appraising the value of innovation and other benefits: A short study for NICE. London, UK: National Institute for Health and Clinical Excellence; 2009. Available from: http://www.nice.org.uk/media/98F/5C/KennedyStudyFinalReport.pdf. Accessed July 23, 2011.
197. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ*. 2004;329:224–227.
198. All Wales Medicines Strategy Group: Independent review process. Vale of Glamorgan, Wales: All Wales Medicines Strategy Group; 2007. Available from: http://www.wales.nhs.uk/sites3/Documents/371/Independent%20Review%20process%20_fina%20for%20website_.pdf. Accessed July 23, 2011.
199. General method for assessing health technologies. Paris, France: Haute Autorite de Sante, Department of Medical and Surgical Procedures Assessment; 2007. Available from: http://www.has-sante.fr/portail/upload/docs/application/pdf/general_method_eval_techno.pdf. Accessed July 23, 2011.
200. ISPOR global health care systems road map: Italy – Reimbursement process. Lawrenceville, NJ: International Society for Pharmacoeconomics and Outcomes Research; 2008. Available from: http://www.ispor.org/HTARoadMaps/Italy.asp. Accessed July 23, 2011.
201. Stolk EA, Rutten FF. The "health benefit basket" in the Netherlands. *Eur J Health Econ*. 2005;Suppl:53–57.
202. Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Econ*. 2004;13:437–452.
203. Pharmaceuticals Pricing Board: the Pharmaceuticals Pricing Board and the secretariat. Helsinki, Finland: Ministry of Social Affairs and Health/Social – Och Halsovardsministeriet; 2009. Available from: http://www.stm.fi/en/ministry/boards/pharmaboard/board. Accessed July 23, 2011.
204. Nasser M, Sawicki P. Institute for quality and efficiency in health care: Germany. *Issue Brief (Commonw Fund)*. 2009;57:1–12. Available from: http://www.commonwealthfund.org/~/media/Files/Publications/Issue%20Brief/2009/Jul/Chalkidou/1294_Nasser_CER_Germany_issue_brief_724.pdf. AccessedJuly 23, 2011.
205. Vandoros S, Kanavos P. Pricing, regulation, reimbursement and healthcare budgets. *European Cancer Patient Coalition*. 2009. Available from: http://www.ecpc-online.org/component/docman/doc_download/121-sotiri-vandoros-pricing-regulation-reimbursement-and-healthcare-budgets.html?ItemId=127. Accessed July 23, 2011.
206. Persson U, Willis M, Odegaard K. A case study of ex ante, value-based price and reimbursement decision-making: TLV and rimonabant in Sweden. *Eur J Health Econ*. 2010;11:195–203.

207. Moise P, Docteur E. Pharmaceutical pricing and reimbursement policies in Sweden [OECD Health Working Papers, No. 28]. Paris, France: Organisation for Economic Co-operation and Development (OECD); 2007. Available from: http://www.oecd.org/dataoecd/63/17/40699881.pdf. Accessed July 23, 2011.
208. Jansson S. Implementing accountability for reasonableness – the case of pharmaceutical reimbursement in Sweden. *Health Econ Policy Law*. 2007;2(Pt 2):153–171.
209. Willis M, Persson U, Zoellner Y, Gradl B. Reducing uncertainty in value-based pricing using evidence development agreements: The case of continuous intraduodenal infusion of levodopa/carbidopa (DuodopaR) in Sweden. *Appl Health Econ Health Policy*. 2010;8:377–386.
210. Stolk P, Schneeweiss S, Leufkens HGM, Heerdink ER. Impact analysis of the discontinuation of reimbursement: The case of oral contraceptives. *Contraception*. 2008;78:399–404.
211. Schafer W, Kroneman M, Boerma W, et al. The Netherlands: Health system review [Health Systems in Transition]. Copenhagen, Denmark: European Observatory on Health Care Systems, World Health Organization Regional Office for Europe; 2010. Available from: http://www.euro.who.int/en/home/projects/observatory/publications/health-system-profiles-hits/full-list-of-hits/netherlands-hit-2010. Accessed July 23, 2011.
212. Webb DJ. Value-based medicine pricing: NICE work? *Lancet*. 2011;377:1552–1553.
213. Kanavos P, Manning J, Taylor D, Schurer W, Checchi K. Implementing value-based pricing for pharmaceuticals in the UK. Final report. London, UK: 2020 Health; 2010. Available from: http://www.2020health.org/2020health/research/vbp-a.html. Accessed July 23, 2011.
214. A new value-based approach to the pricing of branded medicines: A consultation. London, UK: UK Department of Health. Medicines, Pharmacy and Industry Group; 2010. Available from: http://www.dh.gov.uk/en/Consultations/Liveconsultations/DH_122760. Accessed July 23, 2011.