A National Approach to Reimbursement Decision-Making on Drugs for Rare Diseases in Canada?
Insights from Across the Ponds

Démarche nationale quant aux décisions de remboursement des médicaments pour maladies rares au Canada?
Pistes provenant d'outremer

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Table B3. Elements of processes through which reimbursement recommendations or decisions on DRDs are formulated

Country	Advisory/ Decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Equity and efficiency assumptions/ethical considerations	Role of stakeholders
Australia *General Reimbursement* (PBAC 2008c, 2008c, 2008d, 2013c)	Pharmaceutical Benefits Advisory Committee (PBAC) is an independent expert body appointed by the Australian Government (Currently 17 members): • Pharmacists • General practitioners • Clinical specialists • Clinical pharmacologists • Health economists	DUSC: Assesses estimates on projected usage and financial cost of medicines and provides advice to PBAC ESC: Assess clinical and economic evaluations and advices PBAC on technical aspects of these evaluations PBAC: Advisory	1.Sponsors seek advice from the Pharmaceutical Evaluation Branch by notifying the PBAC Secretariat of your intention to receive general advice on how to best present information and confirm deadlines and other data cut off dates. Start discussions early about any usage and pricing issues with the DUSC and ESC	If product will cost the PBS more than $10 million a year, Department of Health makes a Cabinet Submission so cabinet can make funding decision • Quality and uncertainty in evidence • Equity • Extent of use • Total costs • Rule of Rescue criteria in exceptional	Equity: • Equity and rule of rescue used in decision-making criteria Efficiency: • Cost-utility analysis to determine value for money Ethical: • PBAC is aware of, and sympathetic to, the difficulties faced by sponsors	Provide comments on evaluation report and advice: • Applicant Present views during committee/ board meeting: • Applicant Participation in PBAC/sub-committees: • Providers • Patient representatives • Industry representatives

	• Patient representative 2 sub-committees to assist with analysis and advice: Drug Utilisation Sub Committee (DUSC) (14 members) Physicians Pharmacists Pharmaceutical researchers Patient representative Industry representative Economics Sub Committee (ESC) (13 members) Health economists Clinical pharmacologist Physicians (GPs and specialists) Industry representative	Minister of Health (or delegate): final decision	secretariats 2. Submit application that meets PBAC guidelines to the PBAC secretariat. The PBAC secretariat will confirm receipt. The ESC and DUSC secretariats evaluate and develop commentaries on major submissions 3.PBAC Secretariat prepares overview of the submission for PBAC 4.Pharmaceutical Pricing Section allocates provisional tier status to submissions 5.Sponsors advised of the tier status and inclusion of the submission on the PBAC agenda 6.Sponsor may provide written response to the evaluation report and overview to the PBAC Secretariat 7.ESC and DUSC meet to consider the submission, PBAC secretariat overview, the evaluation report and sponsor response and sub-committees prepare formal advice for the PBAC	circumstances: no alternative exists; disease is severe, progressive and expected to lead to premature death, small patient population, and worthwhile clinical improvement. • Clinical benefit and cost-effectiveness compared with other treatments/products • Financial implications for PBS and Australian government • Affordability in each year over 5 years (budget impact) • Value for money	of orphan drugs. Furthermore, the committee does not set a minimum standard for the type and level of evidence or other information that can be included in a submission to PBAC. However, it would be unlawful for PBAC not to consider comparative costs and effectiveness.	

			meetings 8.PBAC secretariat gives sponsors verbal advice of the PBAC decision 9.Pharmaceutical Benefits Pricing Authority secretariat will contact sponsor after the PBAC meeting to initiate formal pricing discussions 10. Risk sharing arrangements can be recommended by the PBAC, PBPA or Department of Health 11. Agreement on usage estimates 12. Minister of Health and Ageing authorizes the listing of items on the Schedule of Pharmaceutical Benefits			
Australia *Life Saving Drugs Program (LSDP)* (AGDH 2011; AGDH 2009; AGDH 2010a; AGDH 2013c)	Pharmaceutical Benefits Advisory Committee (PBAC) is an independent expert body appointed by the Australian Government (Currently 17 members): • Pharmacists • General	DAC (Advisory) PBAC (Recommendation) Department of Health and Ageing (final decision)	1. PBAC rejects the drug for listing on the PBS because it fails to meet cost effectiveness criteria 2. PBAC further consideration for listing the drug through the LSDP 3. Approval process commences for the	• Rare but clinically defined disease for which the drug is regarded as a proven therapeutic modality (i.e., Approved for that indication by the TGA) • Disease is identifiable with reasonable diagnostic precision	Equity: • Rarity, severity, and unmet clinical need considered to increase value for money (implicit) • "Drugs included on the LSDP have been shown to be effective in extending the lifespan of patients	Same as PBAC General Advise on clinical aspect of the management of the program: • DAC

	practitioners • Clinical specialists • Clinical pharmacologists • Health economists • Patient representative Disease Advisory Committee (DAC) members identified on the basis of their expert knowledge and potential contribution to the Committee. Role is to: 1) Determine patient eligibility for, and continuation of, therapy through the LSDP; 2) Review patient progress with treatment and provide advice on clinical aspects of the management of the program		drug to be listed to the LSDP—Minister and Government (During government consideration the department and the sponsor: negotiate terms of the Deed of Agreement including risk share arrangements, the Condition Guidelines; and the Disease Advisory Committee is formed) 4. Government approves funding of drug through the LSDP and announces the commencement date for listing—signature and execution of LSDP Deed of Agreement 5. Listing on the LSDP Patients and physicians then apply for and consent to receive funding for their treatment using standard forms	• Significant reduction in age-specific life expectancy for those suffering from the disease • The drug must be accepted as clinically effective, but rejected for PBS listing because it fails to meet the required cost effectiveness criteria • No suitable and cost-effectiveness alternative non-drug therapy modality (surgery/radiotherapy) • Cost of drug would constitute an unreasonable financial burden on the patient or his/her guardian • Proposed price of the drug compared with the effective price of the drug in comparable overseas market • Proposed cost of the drug compared with the cost of comparable drugs, if an, that are already funded through the LSDP Assessment of	suffering from life-threatening disease"—value for treatments that extend life • Value for life regardless of cost (implicit) Efficiency: • Drug must fail to meet cost-effectiveness thresholds through PBAC General procedure to be included in LSDP Ethical: • Although the LSDP does not meet the cost-effectiveness objective of the National Medicines Policy, it is noted that it performs a function that is not covered anywhere else in the health system	

				eligibility will be made with regard to the natural course and stage of the disease, as described in the relevant drug/condition LSDP Guidelines, and any exceptional circumstances that may apply		
Australia *Highly Specialised Drugs Program (HSDP)* (AGDH 2013b; Mabbott et al. 2010)	Highly Specialised Drugs Program: Highly Specialised Drugs Working Party PBAC Minister of Health	HSD Working Party: Advisory PBAC: Recommendation Minister of Health: Final decision	1. Same as PBAC General process 2. Hospital applies to supply highly specialized drugs require through Medicare Australia. Prescribing doctor certifies that the patient meets the PBAC criteria by writing the streamlined Authority code on the prescription if applicable (may also require written authority application) to the Department of Human Services	Evidence of: • Effectiveness • Cost-effectiveness • Clinical place of a product relative to other products Eligible patient must be insured under the Health Insurance Act and receive treatment at, or from, a hospital as: • A non-admitted patient • A day admitted patient • A patient on discharge To prescribe these drugs, medical practitioners are required to be affiliated with specialist hospital unit	Not found.	Same as PBAC General Apply to supply HSDs: • Hospitals Certify patient meets PBAC criteria: • Prescribing doctor
Austria *General*	Association of Austrian Social Security Institutions	Recommendation: HEK	1. Manufacturer submits electronic application for inclusion of	• Disease burden • Availability of alternative treatments	Equity: • Severity and unmet clinical need	*None specified*

reimbursement: Extramural drugs (Austrian Federation of Social Insurance Institutions 2007; Ayme and Rodwell 2013b; Bucholz 2009)	(HVB) *(decisions)* 20 members, including representatives from sickness funds, government, and healthcare professionals Pharmaceutical Evaluation Board (HEK) *(recommendations)*	Final decision: HVB	pharmaceutical on reimbursement list (EKO) to HVB 2. HVB reviews submission and prepares evaluation report 3. HEK reviews evaluation report and makes recommendation 4. HEK sends evaluation report and recommendations to HVB 5. HVB reviews recommendations and makes decision on inclusion in reimbursement code: - all newly submitted pharmaceuticals listed in "red box" for 24-36 months during HEK evaluation and price setting; reimbursement can be requested on case-by-case basis - subsequently, HVB can recommend pharmaceutical to be listed in "green box", (in general, no conditions), "yellow box" (approval must be obtained on case-by-case basis), or not listed	• Innovativeness • Comparative effectiveness • Budget impact • Cost-effectiveness	considered in decision-making criteria, which may increase value for money (implicit) Efficiency: • In practical terms, price comparisons with therapeutic alternatives are usually the determining factor in reimbursement decisions.	
Austria *General reimbursement: Intramural drugs*	Drug Commissions of Individual Regional Hospital Cooperations (decisions)	Final decision: Drug Commissions of the individual regional hospital cooperations	1. Clinician submits request for coverage of drug (either for individual or certain number of patients)	• Medical necessity • Pharmacological necessity • Value for money • Number of patients	No information found	Provide comments in decision-making process: • Clinicians of the respective medical discipline

(Austrian Federation of Social Insurance Institutions 2007; Ayme and Rodwell 2013b; Bucholz 2009; PHARMIG 2013)	The Horizon Scanning Program (on oncology drugs only) of LBI-HTA (advisory)		and inclusion in the hospitals drug list to head of drug commission 2. Head of drug commission brings the request into the monthly/ bi-monthly drug commission meeting 3. Decision is made for the respective hospital cooperation (there are 9 regions and 9 public hospital cooperations, including 4 medical university hospitals)	requiring the treatment • Budget impact		
Austria *Individual (case-by-case) reimbursement* (Ayme and Rodwell 2013b; Bucholz 2009; PHARMIG 2013)	Regional Sickness Fund *(decisions)* • head physician of sickness fund/chief medical officer	Final decision: Regional Sickness Fund	1. Prescribing physician submits electronic or written request for reimbursement to head physician of sickness fund 2. Final decision made by head physician within 30 minutes (No further information found)	• Medicinal necessity • Pharmacological necessity • Value for money	Equity: • Individual reimbursement allows access for some off-label and expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	
Belgium *General Reimbursement* (Denis et al. 2009; Bogaert and Klasa 2009; Denis et al. 2011)	The Drug Reimbursement Committee is composed of 28 members: • 22 voting members: · 7 academics · 8 representatives	College of Medical Doctors for Orphan Drugs (CMDOD): Advisory Drug Reimbursement Committee (DRC): recommendations	1. Manufacturers submit application to secretariat of DRC 2. Admissibility check by secretariat: form is sent over to Bureau of DRC 3. The DRC may decide to compose a group of	• Therapeutic value • Price and level of reimbursement • Proposed reimbursement tariff • Clinical value and budget impact	Equity: • Social and therapeutic needs considered in decision-making criteria; importance in clinical practice may be considered to increase value	Provide comments on evaluation report: • Experts • Applicant

	of the health insurance funds · 4 representatives of the physicians' association · 3 representatives of the pharmacists association • 6 non-voting members: · 3 ministry representatives (Ministry of Health, of Social Affairs and of Economical Affairs) · 1 representative of the NIHDI · 2 members of Pharma.be (which is the representative organization of the pharmaceutical industry in Belgium)	Minister of Social Affairs: final decision	experts to evaluate the justification of the reimbursement proposal. Even if not, a first temporary evaluation report will be elaborated by the DRC (together with the experts) and sent to the company within 30 days. 4. The final evaluation report is sent within 60 days of the dossier introduction. The company has 20 days to forward objections and remarks to the DRC, or to ask for more time to respond 5. After having received the company's answers, the DRC prepares a temporary proposal (containing the added value class (i.e. class 1), the reimbursement conditions, the reimbursement base, the reimbursement category and the revision criteria) for drug reimbursements if the proposal differs from the company's proposal. Otherwise the DRC will prepare a final proposal within a period of 150	(cost effectiveness is <u>not</u> considered) • Importance in clinical practice (i.e. social and therapeutic needs) • Other negotiable factors including price adjustments, employment incentives for manufacturers, diagnostic test funding by the company, and patient population restrictions	for money (implicit) Efficiency: • No pharmacoeconomic analyses considered; cost-effectiveness ratios should be presented to show what society is paying for: a Quality Adjusted Life Year (QALY) or life year gained.—value for life regardless of cost (implicit)	

			days following reception of the application. 6. The Minister of Social Affairs takes final decision and informs company. A final decision on the reimbursement is taken within 180 days following the submission of the request.			
Belgium *Special Solidarity Fund (SSF)* (Guillaume et al. 2010; Denis et al. 2009)	College of Medical Doctors for Orphan Drugs is composed out of the medical directors of each of the national sickness funds and some medical doctors from the NIHDI	Local sickness fund: recommendations College of Medical Doctors for Orphan Drugs: decision-maker DRC: advisory	1. The patient's MD (a specialist) submits the application for reimbursement of costs by the SSF to the health insurance institute through the local and national sickness fund 2. The administrative handling and the handling of the medical aspects of the request are taken care of by the social services of the local sickness funds and	• The applicant needs to have used all possible other rights to reimbursement by other (private of public) insurances he can benefit of • The treatment is expensive • Medical treatment is prescribed by a medical doctor specialized in the treatment of the related disorder and authorized to practice	Equity: • Unmet clinical need, severity and rarity considered to increase value for money (implicit)	Participation in CMDOD: • Physicians
Denmark *General Reimbursement* (Moller 2003; Danish Health and Medicines Authority 2012)	The reimbursement committee is composed of maximum of 7 people, 6 among them are physicians, 2 of the physicians are general practitioners, and one member	The Reimbursement Committee: Advisory Danish Medicines Agency (DMA): Final decision Decides on general	1. The manufacturer submits a request to the DMA 2. Submission reviewed by internal staff with support from external experts, if necessary, and evaluation report	• Therapeutic value on defined indication • Safety • Clinical efficacy and effectiveness • Benefits and harms compared to current standard treatment • Reasonableness of	No information found	Provide comments on evaluation report: • Applying manufacturer Participation on the Reimbursement Committee: • Physicians

	represents the regions (third party payer). The members are appointed for 4 years	reimbursement for pharmaceuticals, issues/ confirm individual reimbursement request	prepared with price survey prepared by DMA simultaneously 3. Economic analyses reviewed by expert in health economics 4. Clinical evaluation report, price survey, and review of economic analysis sent to the Reimbursement Committee 5. Report reviewed and recommendations formulated during committee meeting 6. If negative recommendation, manufacturer consulted by DMA before final decision is made 7. Decision finalized during Board meeting 8. The committee can only make decisions when the chairman and at least four members are present, however, the committee can still make the decisions with less number of attendants if postponing the	price relative to therapeutic value		

			decision will jeopardize important health considerations 9. The reimbursement committee (advisory committee) decides by simple majority. In the event of tie, the chairman has the casting vote.			
Denmark *Individual Reimbursement* (Moller 2003; Danish Health and Medicines Authority 2012)	The reimbursement committee is composed of maximum of 7 people, 6 among them are physicians, 2 of the physicians are general practitioners, and one member represents the regions (third party payer). The members are appointed for 4 years	The Reimbursement Committee: Advisory Danish Medicines Agency (DMA): Final decision	1. Physician applies for single reimbursement for drugs not entitled to general reimbursement 2. The Danish Medicines Agency evaluates the applications on a case by case basis (No further information found)	• The medicinal product plays a special role in the patient's treatment • The effect of the treatment on the patient has been seen • Other relevant methods of treatment have been found to be insufficient or inappropriate in the particular case • General reimbursement has been denied for the drug but is therapeutically valuable if used for narrowly and well defined indications	Equity: Individual reimbursement allows access for some unapproved and/or expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	Participation on the Reimbursement Committee: • Physicians
Finland *General Reimbursement* (Mossialos and	Pharmaceuticals Pricing Board consists of seven members and their deputies nominated	PPB Expert Group: Advisory PPB: Decisions	1. Holder of the marketing authorization submits application for reimbursement and	The PPB does not explicitly weight the criteria used in CE evaluation or the assessment for price	Efficiency: • No exact cost-effectiveness threshold in decision-making	Consult to PPB if negative recommendation: • Manufacturers

Srivastava 2008; Ministry of Social Affairs and Health 2013; Hallinen and Soini 2011)	by the Ministry for three years. Members must have at least a Master's degree, and they must include at least: • 1 medical representative • 1 pharmaceutical representative • 1 legal • 1 economic expert • 2 members of the PPB are from the Ministry of Social Affairs and Health • 1 from the Ministry of Finance • 2 from the Social Insurance Institution (Kela) • 1 from Fimea • 1 from the National Institute for Health and Welfare Expert group consisting of a maximum of 7 members operates as part of the PPB. This group represents medical, pharmacological, health economics and social insurance expertise. Members		reasonable wholesale price to the secretariat of the PPB 2. Submission reviewed by Secretariat staff with expertise in pharmacology, pharmacoepidemiology and pharmacoeconomics: evaluation report prepared; additional support from Expert Group 3. Report sent to Expert Group 4. Report and opinions of Expert Group sent to PPB 5. The chief pharmaceutical officers from the Secretariat present the applications to the PPB 6. PPB formulates recommendations 7. If negative recommendation, manufacturer consulted by PPB before decision is made (manufacturer may lower price) 8. Decision finalized during PPB meeting. Doctors required to issue a medical certificate to justify a patient's need	setting Value for money (no explicit threshold or willingness-to-pay level for the ICER that is considered to confirm the cost-effectiveness of treatments) Reasonable wholesale price To be eligible for special refunds, the following criteria are considered: • Nature of the illness/severity • Necessity and cost implications of the drug • Therapeutic value of the drug as shown in clinical practice and research No explicit criteria from Kela for eligibility of specific groups of patients for higher reimbursement categories	criteria (explicit)	Participate on PPB: • Providers • Manufacturer representative • Government • Insurer

	are appointed by the Ministry, and they do not make decisions.		for a drug in one of the higher reimbursement categories—submitted to Kela to qualify for higher reimbursement			
France *General Reimbursement* (Chicoye et al. 2009; Pelen 2000)	French National Authority for Health (HAS) Board has 8 appointed government representatives R Transparency Committee and specialist sub-committee comprising scientific and clinical experts	Recommendation: HAS Final decision: Ministry of Health and Social Services	1. Manufacturer submits application for reimbursement to HAS 2. Transparency Committee of HAS reviews submission and prepares evaluation report 3. Evaluation report sent to external experts, CEESP (if necessary) and finally, HAS specialist sub-committee for assessment of medical benefit and improvement in medical benefit (ASMR level assigned) 4. Recommendation sent to Ministry 5. Final decision made by Ministry	• Disease burden/severity • Clinical need • Risk-benefit ratio • Clinical effectiveness added value over existing treatments • Cost of treatment compared to existing treatment • Impact on public health	Equity: • Severity and unmet clinical need considered to increase value for money (implicit) Efficiency: • No cost-effectiveness analysis required	Provides comments on evaluation report and recommendations: • Patients • Healthcare providers • Payers • Industry • External experts (clinical and methodological experts)
France *Individual (case-by-case) or cohort reimbursement* (Natz and Campion 2012; Garau and Mestre-Ferrandiz 2009; Belorgy 2012; Ministere des Affaires Sociale et de la Sante 2014)	1) Temporary use authorization (ATU) (individual or cohort) Transparency Commission (under French National Authority for Health (HAS)) *(decisions)*	ATU authorization: AFSSAPS Reimbursement authorization: HAS	1. Prescribing doctor or manufacturer submits named patient application to AFSSAPS 2. AFSSAPS obtains dossier from manufacturer and performs assessment 3. ATU is rejected or granted by AFSSAPS 4. If ATU is granted, funding is granted by HAS	• pharmaceutical quality • safety • efficacy • availability of existing/alternative treatments • justification of use	Equity: • Unmet clinical need considered to increase value for money (implicit) • ATU allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include “rule of rescue” and	None specified

					solidarity).	
France *Individual (case-by-case) or cohort reimbursement* (Natz and Campion 2012; Garau and Mestre-Ferrandiz 2009; Belorgy 2012; Ministere des Affaires Sociale et de la Sante 2014)	2) Recommendation for therapeutic use (RTU) (cohort) Ministry of Health and Social Services *(decisions)* Transparency Commission (under French National Authority for Health (HAS)) *(recommendations)*	Recommendation: HAS, National Union of the Sickness Funds Final decision: Ministry of Health and Social Services	No information found	• Availability of existing/alternative treatments • Clinical need (pharmaceutical necessary to improve health or avoid deterioration)	Equity: • Unmet clinical need considered to increase value for money (implicit) • RTU allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	None specified
France *Individual (case-by-case) or cohort reimbursement* (Natz and Campion 2012; Garau and Mestre-Ferrandiz 2009; Belorgy 2012; Ministre des Affaires Sociale et de la Sante 2014)	3) Temporary protocol of treatment (PTT) Transparency Commission (under French National Authority for Health (HAS)) *(decisions)*	Final decision: HAS	No information found	• Availability of existing/alternative treatments • Clinical need (pharmaceutical necessary to improve health or avoid deterioration)	Equity: • Unmet clinical need considered to increase value for money (implicit) • PTT allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity)	None specified
Germany *General Reimbursement* (Fulda 2011; Holtorf	"G-BA" (Gemeinsamer Bundesausschuss) comprises 13 members including	G-BA: Final decision	1. Manufacturers file documentation to the G-BA on the benefits of a product since placed on the German	Considered during pricing negotiations: • Clinical effectiveness • Clinical need	Equity: • All EMA orphan drugs approved for reimbursement	Involvement in assessment: • Pharmaceutical company • Patients

2009; Heron et al. 2012)	representatives of doctors, dentists, hospitals, the SHI (Statutory Health Insurance) and patients		market 2. Within 6 months, the G-BA is required to assess the benefit of the drug and publish the assessment 3. For drugs designated as orphan drugs under the European regulation, the additional benefit is deemed to be demonstrated by the marketing authorization (all other pharmaceuticals require data on the additional medical benefit in relation to comparator therapies), but the G-BA has to provide an assessment on the extent of the added benefit. 4. The manufacturer must negotiate the reimbursement price within 6 months with the Federal Head Association of the Public Health Insurances 5. If the negotiations fail, an arbitration body has to determine the reimbursement price within a further three months	• Availability of alternative treatments • Medical and therapeutic value • Innovativeness (defined as different mechanism of action or less side effects • Efficiency	Efficiency: • Additional benefit of orphan drugs is assumed by EMA market authorization	• Healthcare providers • Insurance representatives • G-BA

Germany *Compassionate Use* (German Federal Ministry of Health 2010)	BfArM is an independent higher federal authority within the portfolio of the Federal Ministry of Health with roughly 1000 employees – including physicians, pharmacists, chemists, biologists, technical assistants and administrative staff	Federal Institute for Drugs and Medical Devices (BfArM): Final decision	1. A person who assumes responsibility for the commissioning, organization and financing of a compassionate use program (responsible person) shall be responsible for notifying the competent higher federal authority of the compassionate use program 2. The competent higher federal authority shall confirm to the responsible person that the notification is in accordance with regulations within a two-week period, following the receipt of subsequently submitted documents (confirmed notification) 3. The compassionate use program can be commenced as soon as the confirmed notification has been received and the competent higher federal authority has raised no objections 4. The competent higher federal authority shall confirm to the	No information found	Equity: • The compassionate use program allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity). Efficiency: • Program allows further information on a given drug to be gathered in deciding market authorization status	No information found

			responsible person that the notification is in accordance with regulations within a two-week period, following the receipt of subsequently submitted documents (confirmed notification) 5. The compassionate use program can be commenced as soon as the confirmed notification has been received and the competent higher federal authority has raised no objections			
Iceland *General Reimbursement* (Icelandic Medicine Pricing and Reimbursement Committee 2011a; Icelandic Medicine Pricing and Reimbursement Committee 2011b; Icelandic Medicine Pricing and Reimbursement Committee 2013; Ministry of Welfare 2011)	Icelandic Medicine Pricing and Reimbursement Committee consists of five members: • The Chairman is appointed by the Minister of Welfare • One member is appointed by the State Social Security Institute • One member is appointed by the Icelandic Medicines Control Agency • One member is appointed by the Directorate of	Icelandic Medicine Pricing and Reimbursement Committee: Final decision	Price and reimbursement can be applied for separately or joint. Timeframe for reimbursement decision is 90 days. Reimbursement decision is based on clinical and economical value of the drug to its comparator together with the forecasted budget impact. Timeframe for joint application for reimbursement and price are 180 days. Approved price is based on external price reference.	• Safety of the drug • Clinical effect- clear indication and place in therapy • Price is relative to efficacy and in comparisons to already reimbursed drugs • Budget impact – how many patients for how long	No information found	Consulted for evaluation: • External experts

	Health • One member is appointed by the Ministry of Finance		(No further information found)			
Ireland *General Reimbursement-Community Drug Schemes* (National Centre for Pharmacoeconomics 2013a; Office of the Attorney General 2004; National Centre for Pharmacoeconomics 2013b)	Health Services Executive Corporate Pharmaceutical Unit (HSE-CPU)	HSE-CPU: final decisions	1. Horizon scanning at the start of each year between manufacturers and HSE to identify upcoming technologies. 2. Formal request of Pharmacoeconomic assessment from HSE to NCPE (Minister of health and the DoH also has the right to request a pharmacoeconomic assessment) (ISPOR) 3. Scoping meeting between NCPE and company representatives 4. Formal submission of evidence on cost-effectiveness and budget impact 5. NCPE appraisal of company submission 6. NCPE appraisal sent to company for comment 7. NCPE appraisal submitted to the HSE	• Unmet need • Cost-effectiveness and value-for-money: use of QALY threshold of €45,000 (exceptional products which fail to satisfy the threshold for a variety of reasons may be processed as per normal subject to meaningful discussions between the HSE, DoH, relevant clinicians and the manufacturer) • Cost and budget impact • Quality and uncertainty of evidence • Price should be the average price of nominated EU States (Belgium, Denmark, France, Germany, the Netherlands, Spain, UK, Finland and Austria) New technologies and services must be:	Equity: • To meet the needs of the decision-makers, an attempt should be made to include equity considerations in the report, such as highlighting unmet needs of certain disadvantaged groups. Consideration should also be given to describing the potential impact of a drug in addressing this concern. (explicit) • Technologies that fail to meet the cost-effectiveness threshold may still be reimbursed based on other factors Efficiency: • Value for money based on cost-effectiveness threshold • No fixed ICER threshold, but a drug with an ICER	Consult with NCPE for submission requirements: • Manufacturers Consult to determine eligibility of drugs not considered cost-effective: • Government • Clinicians • Manufacturer

				• Beneficial • Effective • Efficient to improve, promote and protect health and welfare	of less than €45,000/QALY is more likely to be reimbursed	
Ireland *Named Patient Regime* (Health Service Executive 2006; Arthur Cox 2013)	Irish Medicines Board (regulatory) HSE: Primary Care Reimbursement Services (reimbursement)	No information found	1. No information found on how practitioners apply for IMB approval. 2. Product is supplied to a practitioner or pharmacist who will supervise the treatment 3. Applications for reimbursement of unauthorized products sent to HSE Primary Care Reimbursement Services	• Drug should be an allopathic medicinal product which has been industrially produced and which is appropriate for use in the community • No other authorized drug of essential similarity is available for prescription and supply • The prescribing physician is aware of the unauthorized status and has informed the patient • The drug is not being advertised or promoted in the state in any trade catalogue or price list • The application for reimbursement is accompanied by a copy of the invoice in relating to the supply of the drug to the pharmacist and is supported by an explanation of the	Equity: • The Named Patient Regime allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity)	No information found

				circumstances which require the supply of the unauthorized drug • Prescription is written • The cost should be reasonable in the context of medicinal products ordinarily supplied and used in the community and be of a category, if it were authorized, would be eligible for reimbursement in the CDS concerned		
Italy *General reimbursement* (Ayme and Rodwell 2013f; Bakowska et al. 2011; Garau and Mestre-Ferrandiz, 2009; Folino-Gallo et al. 2008)	Italian Medicines Agency (AIFA) – Scientific Technical Committee (CTS) 17 members, including healthcare professionals, pharmacists, and pharmacologists AIFA Pricing and Reimbursement Committee (CPR) Members include healthcare professionals, academics, and administrators in pharmaceutical management sector	Advice: CPR Final decision: CTS	1. Manufacturer submits application for inclusion of pharmaceutical on reimbursement list to AIFA 2. CTS reviews application and prepares evaluation report, which includes ranking and scoring of pharmaceuticals on basis of disease severity, innovativeness of treatment, availability of existing treatment, and potential benefit of treatment 3. CTS sends submission and evaluation to CPR 4. CPR reviews submission and evaluation and negotiates preliminary	• Disease burden/severity • Clinical need • Availability of alternative treatments • Benefit-harm ratio compared to existing treatments • Socio-economic benefit compared to existing treatments • Cost compared to existing treatments	Equity: • Severity and unmet clinical need considered to increase value for money (implicit) Efficiency: • No cost-effectiveness analysis required if no alternative treatment exists	Participation on AIFA: • Healthcare providers

			reimbursement status and price with CTS 5. CPR submits results to CTS 6. CTS makes final decision			
Italy *Individual or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009; Taruscio et al. 2011; Barham 2012)	**(Law 648/96)** AIFA – CTS	Final decision: CTS	Request or application submitted to CTS (No further information found)	• Safety • Clinical benefit	Equity: • Program allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	No information found
Italy *Temporary individual (case-by-case) reimbursement* (Barham 2012)	**(Law Decree 23/98)** Ministry of Health – Ethics Committee Members can include academics, healthcare professionals, pharmacists, pharmacologists, legal medicine specialists, bioethicists, and patient representatives	Final Decision: Ethics Committee	Physician submits request for individual (named patient) approval to Ethics Committee No further information found	• Safety • Clinical benefit	Equity: • Program allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	No information found
Italy *Individual (case-by-case) reimbursement*	**(AIFA 5% Fund)** AIFA – CTS	Final decision: CTS	No information found	No information found	Equity: • Program allows access for some expensive drugs that under the general procedure	No information found

					would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	
Japan *General Reimbursement* (Liu et al. 2009; Nagae 2011; Orphanet 2014)	Drug Pricing Organization (DPO) consists of 11 members including: • 6 physicians • 2 dentists • 2 pharmacists • 1 health economist Central social insurance medical council (Chuikyo) consists of 20 members including: • 7 representatives from health insurance • 7 healthcare providers • 7 members of the public	DPO: Recommendations Chuikyo: Final decision for listing	1. Submission from manufacturer received by the Ministry of Health, Labor and Welfare (MHLW) 2. Hearing held with Economic Affairs Division 3. Data submitted at hearing reviewed by Medical Economics Division and a pricing draft is prepared 4. Draft reviewed at DPO meeting; manufacturer and other experts consulted 5. DPO recommendations on pricing draft made 6. Recommendation sent to manufacturer to comment 7. Recommendations sent to Chuikyo for approval	• Availability of similar drugs • Suitability of similar drugs • "Necessity of applying premiums"	No information found	Provide comments on evaluation report: • Manufacturer • Experts Participation in DPO and/or Chuikyo: • Physicians • Insurance representatives • Public
Korea *General*	The Drug Benefit Coverage Assessment	Ministry of Health and Welfare: Final	1. Industry submission of application Industry submission	• Clinical benefit • Cost-effective (based on ICER	Equity: • Rule of rescue considered in	Participation on DBCAC: • Physicians and

Reimbursement (Ngorsuraches et al. 2012; Song et al. 2012)	Committee (DBCAC) is composed of several specialists, including representatives of the Korean FDA, consumers, medical experts, and HIRA. Under the DBCAC, as a subcommittee, HIRA has an economic subcommittee composed of five members, two medical, one statistical, and two health technology experts	decision Health Insurance Review Agency (HIRA): Recommendations	of application 2. Clinical benefit and safety assessment 3. Pharmacoeconomic evaluation and budget impact analysis 4. HIRA decides on listing 5. Price negotiation with the manufacturer by the National Health Insurance Corporation (NHIC) 6. Getting approval from ministry	threshold) • Reimbursement status and price in other countries • Impact on healthcare budget • Potential impact on other aspects of public health There are, however, some exceptions. These are collectively known as "rules of rescue," which include: • No alternative treatments • No alternative drugs for severe or life-threatening diseases • Drugs for rare diseases and necessary to treat these patients	decision-making • Unmet clinical need, severity, and rare considered to increase value for money (implicit) Efficiency: • "Flexible" application of ICERS for orphan drugs and end of life treatments (explicit)	medical experts • Public/patients (consumers)
Luxembourg *General Reimbursement* (Caisse National de Sante 2003; Caisse National de Sante 2011)	Commission of experts advise the Minister: • Four delegates from the Ministry with responsibility for health, including 2 doctors and 2 pharmacists • Two representatives of the medical profession • Two	Commission of Experts: advisory Minister of Health: final decision	1. Standard application filed by owner, including completed form and required documents—can be done before decision on the pricing has be obtained. 2. Where it is found that the information given in the application is inadequate, the information must be	• Legal, regulatory or statutory factors • Level of care and cost to the public	No information found	Participate on commission: • Government • Providers • Insurers

	representatives of the pharmaceutical profession, one of which is from the hospital sector and the other from extra-hospital sector • A representative of the Union of Health Insurance Funds • Two members of the Committee for Proprietary Medicinal Products		submitted. The receipt of this information is confirmed by the Union of Health Insurance Funds. 3. Decision on inclusion or not of the drug on the positive list is notified to the holder within 180 days after the receipt of all information.			
The Netherlands *General Reimbursement-Medicines Reimbursement System (GVS)* (Stolk et al. 2009; Niezen et al. 2007; International Society for Pharmacoeconomics and Outcomes Research 2007; Ministry of Health, Welfare, and Sport 2013)	Dutch Health Care Insurance Board (CVZ) Committee for Pharmaceutical Aid (CFH): • Pharmacists • Physicians • Economists • Psychologists • Epidemiologists • Ministry representatives	Dutch Health Care Insurance Board (CVZ): performs assessment and appraisal procedure (for both intramural and extramural drugs) and recommendations Ministry of Health, Welfare, and Sport: final decision	1. Manufacturer submits request for reimbursement to the Ministry of Health, Welfare, and Sport 2. CVZ reviews applications and perform an assessment and appraisal based on the submitted dossier 3. Consultation with external experts if needed; a full assessment may be commissioned to external independent academic group/agency 4. Evaluation report	<u>Extramural drugs:</u> • Severity and burden of illness • Clinical need • Quality and strength of evidence • "Therapeutic value" • Clinical efficacy and effectiveness • Benefits and harms compared to current treatment • Experience with the drug • Applicability • Value-for-money • Individual vs. collective responsibility • Affordability	Equity: • Economic evaluation is not required for pharmaceuticals used to treat rare conditions, life threatening conditions or conditions for which there are no other alternatives • Cost effectiveness may be adjusted based on need (e.g., severity or availability of alternative treatments) or equity considerations • All EMA approved	Participation on committees: • Physicians/healthcare providers • Government

			prepared and sent to appropriate committee 5. Report reviewed by CVZ 6. The director of CVZ sends recommendations to the Minister of Health, Welfare, and Sport regarding reimbursement of the drug in the reimbursement system and what list the drug should be placed <u>Intramural drugs:</u> 1. Due to limited hospital budgets, funding is provided through the following policy measures: • policy measure "expensive drugs" for hospitals: 80% reimbursement if purchase costs of a specific orphan drug account for more than 0.5% of the total drug cost of all hospitals on a macro level • policy measure "orphan drugs" for academic hospitals: if the orphan drug costs account for more than 5% of the hospital's	• "Other social, ethical, and legal considerations"	drugs are fully reimbursed (some must only be administered through a university hospital, some need to be ordered by a physician on a named-patient basis) Efficiency: • No cost-effectiveness thresholds, highly valid methodology for assessing cost-effectiveness given more favourability • Requires collection of more evidence on the clinical and cost effectiveness of drugs fitting in either group through outcomes research	

			drug budget, the surplus will be fully reimbursed to the hospital (No further information found)			
New Zealand *General Reimbursement-Pharmaceutical Schedule*	The PHARMAC Board consists of up to six members appointed by the Minister of Health Members of the PHARMAC Board: Stuart McLauchlan, Kura Denness, David Kerr, Jens Mueller, Jan White The following attend PHARMAC's Board meetings as observers: • Murray Georgel, CE MidCentral DHB • Kate Russell, Chair Consumer Advisory Committee • Sisira Jayathissa, Chair Pharmacology and Therapeutics Advisory Committee (PTAC)	Pharmaceutical Management Agency of New Zealand (PHARMAC) (decision-maker) Pharmacology and Therapeutics Advisory Committee (PTAC) (recommendation) Consumer Advisory Committee (CAC) (advisor)	1. Application received by PHARMAC 2. Application along with a summary of the application and the market dynamics for the medicine sent to PTAC for review. 3. Committee meeting to discuss applications with recommendations formed. Minutes of PTAC meeting published on PHARMAC website. PTAC may also refer an application to one of its Specialty Subcommittees for advice before making a final recommendation. 4. If a recommendation to fund is received from PTAC, PHARMAC carries out further economic assessment and the application (option for investment) is prioritized/ranked against all other funding options (i.e.	• Health needs of all eligible people within New Zealand • Particular health needs of Maori and Pacific peoples • Availability and suitability of existing medicines, therapeutic medical devices and related products • Clinical benefits and risks of pharmaceuticals • Cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services • Budgetary impact of any changes to the Pharmaceutical Schedule • Direct cost to health service users • Government's priorities for health funding • Other criteria as	Equity: • "Health needs of all eligible people within New Zealand" and the particular needs of Maori and Pacific peoples are taken into consideration • Unmet clinical need may be considered to increase value for money (implicit) Efficiency: • Cost-utility analysis uses QALYs to measure benefits • No cost-effectiveness thresholds	Provide additional comments on application: • Interested parties identified by the committees • Clinicians consulted via PTAC and its subcommittees • Consumers consulted via the CAC • Public members consulted via PHARMAC

			all other applications that also have a positive recommendation) based on PHARMAC's nine decision criteria. 5. If the "ranking" of the application is high enough, PHARMAC then carries out commercial negotiations with the supplier. 6. After a provisional listing agreement is reached with the supplier, PHARMAC consults with affected/interested parties on a proposal to fund the medicine by issuing a consultation letter which contains a summary of proposal and relevant background information. 7. A recommendation paper with details of the proposal (including PTAC recommendations and feedback received during consultation) is written and presented to the PHARMAC Board or its delegate.	PHARMAC sees fit; PHARMAC will carry out appropriate consultation when it intends to take any such "other criteria" into account		

			8. The paper is considered by the PHARMAC Board or its delegate and a final decision is made.			
New Zealand *Named Patient Pharmaceutical Assessment (Exceptional Circumstances) Policy (NPPA)* (PHARMAC 2012, 2011, 2013a)	The PHARMAC Board consists of up to six members appointed by the Minister of Health Members of the PHARMAC Board: Stuart McLauchlan, Kura Denness, David Kerr, Jens Mueller, Jan White The following attend PHARMAC's Board meetings as observers: • Murray Georgel, CE MidCentral DHB • Kate Russell, Chair Consumer Advisory Committee • Sisira Jayathissa, Chair Pharmacology and Therapeutics Advisory Committee (PTAC)	PHARMAC: Decision-maker NPPA Advisory Panel: Recommendations	There are two main pathways by which named patients can be considered for funding under the NPPA policy: 1. Unusual Clinical Circumstances (UCC) 2. Urgent Assessment (UA) In addition to the two pathways identified PHARMAC will also consider applications to fund drugs for named patients: 1. When the pharms are less expensive to health sector etc. 2. When the intent, but not the specific wording of a restriction for a drug listed on the Pharmaceutical Schedule is met PHARMAC also has general discretion to fund any patient in exceptional circumstances, beyond the situations outlined in the policy The steps in the NPPA	The same 9 decision criteria used for making Schedule funding decisions are also used for the NPPA Policy. Prior to considering the decision criteria	Equity: • Program allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity). Efficiency: • No cost-effectiveness threshold	Provide comments on evaluation: • Applicant

			decision-making process are as follows: 1. Upon receipt of a NPPA application, PHARMAC assesses the information provided to determine if the prerequisites are met. 2. Application may be forwarded to the NPPA Advisory Panel for its clinical advice. Additional specialist clinical advice may also be sought. 3. If the Advisory Panel recommends that PHARMAC decline the application, or if PHARMAC staff consider that any prerequisites are not met, the applicant is advised. The applicant has the opportunity to provide further information or contest any clinical error or clinical judgment that may have been made. 4. If more information is submitted the application is reconsidered. 5. If the prerequisites are met, the PHARMAC Board or			

			its delegate will then consider the application under PHARMAC's decision criteria and make a final decision.			
Norway *General Reimbursement* (Norwegian Medicines Agency 2013; Festoy et al. 2011)	NoMA is an organization of about 250 employees. • Director General • Assistant Director General • Department for Medicinal Product Assessment • Regulatory Department • Laboratory Department • Department for Inspection and Narcotic Drugs Control • Department of Pharmaco-economics • Department of Medical Information • Department of Administrative Affairs	Parliament (decision-maker) Ministry of Health (recommendations) NoMA (decision-maker) National Advisory Committee for Drug Reimbursement (advisor) National Advisory Committee for Health Care Priorities (advisor)	1. A manufacturer with a complete market authorization for its product can either send an application for maximum price and an application for reimbursement simultaneously or apply for maximum price first. A fixed initial maximum price is a prerequisite for reimbursement. The price is a decisive factor in cost-effectiveness for any product and therefore also the reimbursement process. 2. The time allocated to NoMA for dealing with both pricing and reimbursement is 180 days 3. If NoMA has questions about the application, the company has a maximum of three months to answer 4. If the application concerns a new	• Clinical need • Solidarity • Clinical efficacy and effectiveness • Value for money (cost-effectiveness) Reimbursement is provided only for "long-term" medication for chronic diseases, defined as more than three months of medication per year	Equity: • Solidarity principle applied in decision-making criteria Efficiency: • Rationality principle applied in decision-making criteria • Pharmacoeconomic analyses performed are to be evaluated on behalf of the society and should therefore be carried out both from a societal perspective and the perspective of the payer • Cost-effectiveness considered but no explicit cost-effectiveness threshold	None specified

			chemical entity, a new combination, a new indication or an extension of indication, NoMA is not authorized to grant reimbursement and will pass its appraisal on to the Ministry of Health and Care Services, provided that the applications fulfills to other conditions 5. In this process, NoMA may be advised by an external reimbursement committee (National Advisory Committee for Drug Reimbursement) on issues pertaining to the application such as verification of documentation, severity of the disease, and clinical criteria 6. The Ministry may in turn consult the National Council for Health Care Priorities to inquire whether the money would be well spent compared to other health challenges. (So far, the Ministry has not			

			consulted the Council in these matters) 7. Should the Ministry favour the approval, it will have to bring the case before Parliament in the form of a Budget Bill 8. The Budget Bill is voted on in the Parliament			
Norway *Individual Reimbursement* (Haga and Sverre 2002; Festoy et al. 2011)	**The Norwegian Health Economics Administration (HELFO)** (sub-ordinate institution directly linked to the Norwegian Directorate of Health)	Norwegian Health Economics Administration (HELFO): Final decision	No information found	No information found	No information found	None specified
Spain *General Reimbursement* (Bakowska et al. 2011; Ayme and Rodwell 2013b; Seoane-Vazquez 2009)	Ministry of Health, Social Services, and Equality (Directorate General of National Health Service and Pharmacy) Inter-Ministerial Pricing Commission (CIMP) Members include government representatives from Ministries of Health, Economy, and Industry	Final decision: Ministry	1. Ministry of Health identifies pharmaceutical for review 2. Ministry invites manufacturer to submit information 3. Ministry reviews submitted information and prepares evaluation report 4. CIMP reviews evaluation report 5. Ministry makes final decision	• Disease burden/severity • Clinical need • Availability of alternative treatments • Benefit-harm ratio compared to existing treatments • Drug expenditure limits • Social utility • Innovativeness • Price of comparable pharmaceuticals on the market • Contribution to the GDP	Equity: • Severity and unmet clinical need may be considered to increase value for money (implicit) Efficiency: • Cost-effectiveness not required (but preferred) Ethical: • Social utility considered in decision-making criteria	*None specified*

Spain *Individual (case-by-case) or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009; Whitfield et al. 2010)	**1) Temporary Use Authorization** Spanish Medicines Agency (AEMPS) *(decisions)*	Final decision: AEMPS	1. Physician/treating hospital (individual) or manufacturer (cohort) submits electronic application for reimbursement and dossier to AEMPS 2. Final decision and implementation protocol/conditions made by AEMPS	• Disease burden/severity • Clinical need • Availability of alternative treatments	Equity: • TUA allows access for some expensive drugs that under the general procedure would not be reimbursed. (implicit ethical principles applied include "rule of rescue" and solidarity) • Unmet clinical need and severity considered in decision-making criteria; these criterion may increase value for money (implicit)	*None specified*
Spain *Individual (case-by-case) or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009; Whitfield et al. 2010)	**2) Royal Decree 1015/2009** Spanish Medicines Agency (AEMPS) *(decisions)*	Final decision: AEMPS	1. Physician/treating hospital submits electronic application for reimbursement and dossier to AEMPS 2. Final decision made by AEMPS	• Disease burden/severity • Clinical need • Availability of alternative treatments	Equity: • Program allows access for some expensive drugs that under the general procedure would not be reimbursed. (implicit ethical principles applied include "rule of rescue" and solidarity) • Unmet clinical need and severity considered in decision-making criteria; these	*None specified*

					criterion may increase value for money (implicit)	
Spain *Individual (case-by-case) or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009; Whitfield et al. 2010)	**3) Act 29/2006** Spanish Medicines Agency (AEMPS) *(decisions)*	Final decision: AEMPS	Physician submits request for reimbursement approval to AEMPS No further information found	• Clinical need • Availability of alternative treatments	Equity: • Program allows access for some expensive drugs that under the general procedure would not be reimbursed. (implicit ethical principles applied include "rule of rescue" and solidarity) • Unmet clinical need and severity considered in decision-making criteria; these criterion may increase value for money (implicit)	*None specified*
Sweden *General Reimbursement* (International Society for Pharmacoeconomics and Outcomes Research 2011; TLV 2012b; Moise and Docteur 2007; Anell and Persson 2005; Davidova et al. 2008)	The Pharmaceutical Benefits Agency led by a Director-General and consists of six departments with approximately 80 employees. The departments include: • Department for New Medicines • Department for Review of Pharmaceutical Subsidies • Department for	Dental and Pharmaceutical Benefits Agency (TLV): final decision	1. An application is usually registered the same day it is received by the TLV 2. TLV selects a medical reviewer, a health economist, and a legal adviser who process the application. One of them is the responsible investigator for the application. 3. A copy of the application is sent to	TLV's position on reimbursement based on three principles: • Cost effectiveness of the product: costs for using a drug must be reasonable from a medical, humanitarian and socio-economic point of view • Human value principle: care shall be given with respect for the equal value of all human	Equity: • Decisions consider the human value principle- characteristics of patients must not influence decisions • Decisions consider the need and solidarity principle- patients with the greatest need (highest severity) are given priority • Cost effectiveness	Provide comments on report: • Manufacturer • External experts (if consulted)

	Dental Care Subsidies • Administration Department • Communication Department • Pharmacy Department Agency has two governing boards: • The Pharmaceutical Benefits Board The Dental Care Benefits Board		the county councils' pharmaceutical benefits group, who have at least four weeks to issue a report on the application 4. The investigator responsible for the review has the possibility to obtain information and input from other authorities, if necessary 5. TLV keeps contact with the applicant in order to clarify the circumstances concerning the application, to obtain clearer information, and to provide guidance concerning relevant questions. Sometimes a meeting of the reviewer group and the company will be arranged. 6. After the review phase, a proposal for a decision is compiled 7. TLV sends the proposal to the applying company and is given an opportunity to correct factual	beings and for the dignity of the individual • The need and solidarity principle: people with the greatest medical needs should be given priority Other criteria: • Budget impact • Different cost effectiveness thresholds for different characteristics of disease-linked severity (e.g., symptoms, patient autonomy)	threshold not fixed -may be adjusted based on severity of the given condition Efficiency: • Cost effectiveness principle—cost must be considered reasonable from a medical, humanitarian and socio-economic point of view	

			mistakes and to respond to the arguments on which the decision proposal is based 8. TLV may also send received clarify documents to the county councils' pharmaceutical benefits group in order to give the group the possibility to state their position on the complete documentation 9. Decisions on new original pharmaceuticals (orphan drugs fall under this category) are made at the Board meetings. These meetings are held monthly and a schedule for the upcoming meetings is prepared every six months 10. TLV sends the original decision to the company no later than ten working days after the decision was made unless there are specific reasons preventing this			
Switzerland	Federal Drug Commission (FDC)	FDC: Recommendation	1. Submissions are possible after a	• Clinical effectiveness	Equity: • Severity and unmet	Participate on advisory committee:

General Reimbursement- List of Specialties (International Society for Pharmacoeconomics and Outcomes Research 2011; Office Federal de la Sante Publique 2013)	made up of 16 members consisting of: • The President • 1 medical and pharmaceutical academy member • 3 physicians • 2 pharmacists • 1 hospital • 2 health insurers • 2 drug industry members • 1 Canton • 1 representative of the Swiss Agency for Therapeutic Products • 2 insured persons	Federal Office of Public Health: final decisions	positive opinion of the Swiss market authorization agency Swissmedic 2. Manufacturer submits reimbursement application to FOPH within 300 days of market authorization 3. FOPH mandates FDC to evaluate new drug against criteria for decision-making and classifies new drug in one of five categories: • Therapeutic breakthrough • Therapeutic progress • Saving compared to other drugs • No therapeutic progress and no saving • Not appropriate for social health insurance 4. FOPH makes final decision on reimbursement after recommendation from FDC If an innovative drug gets SATP authorization by the fast track approval process, an accelerated reimbursement process is in place)	• Appropriateness • Cost of drug in other countries and in similar indications • Severity of disease • Clinical need (unmet) • Availability of alternative treatments • Innovativeness (premium on innovation considered when evaluating drug cost: based on treatment comparison and therapeutic value/progress)	clinical need may be considered to increase value for money (implicit) • Principle of solidarity permits treatments to exceed 100,000 Swiss Francs per year per patient as long as they prove to be effective, adequate and economically justified Efficiency: • Cost effectiveness determined by value-for-money which is based on: - External price referencing (international benchmarking) - Therapeutic benchmarking	• Patient/public members • Universities • Cantons • Physicians & pharmacists • Providers • Insurers • Manufacturers

United Kingdom *General Reimbursement-Highly Specialised Technologies* (NICE 2013e, 2013b, 2014b, 2013c, 2014a, 2014c)	NICE recommendations on the use of highly specialised technologies are made by a NICE advisory committee called the Highly Specialised Technologies Evaluation Committee. Committee members are appointed for a three-year term, and are drawn from: • the NHS • patient and carer organizations • academia • pharmaceutical and medical devices industries.	Ministry of Health (final decision) NICE (recommendations) The Highly Specialised Technologies Evaluation Committee	A single HST evaluation can only cover a single drug for a single indication 1. The Department of Health (DH) produces a list of provisional evaluation topics. 2. **Consultees and commentators identified** 3. NICE works with the DH to develop a scope. The scope defines the disease, the patients and the drug covered by the evaluation and the questions it aims to answer 4. Consultees and commentators are requested to comment on the draft scope 5. The DH refers HST evaluation topics to NICE 6. The manufacturer or sponsor of the drug is invited to provide an evidence submission. NICE also invites all non-manufacturer consultees to submit a statement on the potential clinical effectiveness and value for money of a treatment. 7. NICE commissions	**Nature of the condition:** • Disease morbidity and patient clinical disability with current standard of care • Impact of the disease on carers' quality of life • Extent and nature of current treatment options **Impact of the new technology:** • Clinical effectiveness of the drug • Overall magnitude of health benefits to patients and, when relevant, carers • Heterogeneity of health benefits within the population • Robustness of the current evidence and the contribution the guidance might make to strengthen it • Treatment continuation rules **Cost to the NHS and Personal Social Services:** • Budget impact in the NHS and PSS • Robustness of	Efficiency: • Value-for-money determined by technical efficiency, productive efficiency, and allocative efficiency	Provide comments on evaluation report: • Health professionals • Carers • Manufacturers • Dept. of Health • External experts • Manufacturers of comparator technologies • Welsh government • National Collaborating Centre • Research groups working in the area • Scottish Medicines Consortium • British National Formulary • Medicines and Healthcare Products Regulatory Agency • Department of Health, Social Services and Public Safety for Northern Ireland • Professional or patient organizations covering Wales, Scotland, or Northern Ireland

			an independent academic centre to technically review the evidence submission and prepare an ERG report 8. Evaluation report prepared 9. An independent advisory committee considers the evaluation report and hears evidence from nominated clinical experts, patients and carers. Evaluation Committee discussions are held in public 10. The Evaluation Committee makes its provisional recommendations in the ECD. An ECD will be produced only if the recommendations from the Evaluation Committee are restrictive. A restrictive recommendation will be one that is more limited than the instructions for use that accompany the drug. Consultees and commentators have four weeks to comment on the ECD.	costing and budget impact information • Patient access agreements **Value for money:** • Technical efficiency (the incremental benefit of the new technology compared to current treatment) • Productive efficiency (the nature and extent of the other resources needed to enable the new technology to be used) • Allocative efficiency (the impact of the new drug on the budget available for specialised commissioning) **Impact of the technology beyond direct health benefits:** • Whether there are significant benefits other than health • Whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • The potential for		

			The ECD is also made available on our website so health professionals and members of the public can comment on it. 11. The Evaluation Committee considers the comments on the ECD if produced, then makes its final recommendations in the FED (Final evaluation determination) on how the drug should be used in the NHS in England. Consultees can appeal against the final recommendations in the FED. 12. If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.	long-term benefits to the NHS of research and innovation; **The impact of the technology on the delivery of the specialised service:** • staffing and infrastructure requirements, including training and planning for expertise		
Scotland *General Reimbursement* (Scottish Medicines Consortium, 2014b; Scottish Medicines Consortium 2014a; Scottish Medicines	SMC is a consortium of stakeholders from Area Drug and Therapeutic Committees and two representatives from the Association of British	Scottish Medicines Consortium: Recommendations NHS Boards: Final decision	SMC appraisal process: 1. Manufacturers submit application to SMC 2. Clinical and economic assessors conduct review 3. Advice from the assessment team gets reviewed by the New	The assessment process for orphan drug submissions is the same as for all other drug submissions. However, SMC will accept a greater level of uncertainty in the economic evaluation	Equity: • If economic uncertainty exists, SMC will consider additional criteria in its decision-making (severity, increases life expectancy/QoL,	Participate on SMC: • Physicians • Healthcare providers • Public members Participate in SMC meetings: • Public members

Consortium 2013b; Scottish Medicine Consortium 2007)	Pharmaceutical Industry. Doctors, primary and secondary care workers, pharmacists, healthcare managers, public partners and the pharmaceutical industry are all members of SMC and take a full part in its decision-making.		Drugs Committee (NDC) 4. NDC forwards its advice to SMC 5. SMC submits its recommendations to NHS boards	Additional factors considered: • Drug treats a life threatening disease • Drug substantially increases life expectancy and/or quality of life • Drug can reverse rather than stabilize the condition • Drug bridges a gap to a "definitive" therapy	reverses condition, or bridges gap to a definitive therapy) Efficiency: • Although Scotland does allow special considerations in its decision-making criteria, drugs often receive negative reimbursement if cost utility analyses are above £30,000/QALY	Patient and Clinician Engagement (PACE) is a stage in the SMC assessment for end of life treatments or for very rare conditions for patient representatives and healthcare professionals to provide information; information gathered will be presented at the main SMC meeting
Wales *General Reimbursement* (AWMSG 2014, 2013)	AWMSG brings together NHS clinicians, pharmacists, healthcare professionals, academics, health economists, industry representatives and patient advocates	The All Wales Medicine Strategy Group (AWMSG): Recommendations New Medicines Group (NMG): subgroup of AWMSG Ministry of Health: Final decision	NMG/AWMSG appraisal process: 1. Manufacturers apply to AWMSG for reimbursement 2. New Medicines Group (NMG) members consider the clinical and cost-effectiveness of the medicine and AWMSG members are asked to apply a broad strategic/social overview when considering a recommendation 3. Welsh Government officials consider the AWMSG recommendation and advise whether funding should be made available for the	NMG/AWMSG considers the same criteria for clinical and cost effectiveness of orphan medicines as those applied to other drugs: • Severity and burden of illness • Clinical need • Clinical effectiveness • Benefit-harm ratio • Quality and uncertainty in evidence • Value for money (based on cost-effectiveness threshold) (recognizes that the incremental cost-effectiveness ratios of many orphan	Equity: • Rarity of a disease is not in itself a reason to fund a drug • NMG/AWMSG recognizes that the incremental cost-effectiveness ratios of many orphan medicines will exceed the threshold cost-effectiveness range. In such cases, NMG/AWMSG will also consider evidence on: the degree of severity of the disease as presently managed, in terms of quality of life and survival Efficiency: Criteria	Participates on AWMSG: • Clinicians • Healthcare providers • Patient advocates • Industry representatives

			use of this medicine within NHS Wales 4. **If a medicine is recommended by AWMSG, there is a** <u>requirement</u> **on Health Boards to provide funding to enable implementation within three months of Ministerial ratification**	medicines will exceed the threshold cost-effectiveness range. In such cases, evidence on the degree of severity of the disease as presently managed, in terms of quality of life and survival, will also be considered Also considers: • Whether the drug can reverse, rather than stabilize the condition • Whether the medicine may bridge a gap to a "definitive" therapy • The innovative nature of the medicine (if it represents a significant improvement on existing therapy and whether it can plausibly generate substantial health gains over existing treatments)	considers both clinical and cost effectiveness Ethical: Recognizes that cost-effectiveness of many orphan drugs will exceed threshold range, therefore criteria considers other factors	
United Kingdom *Innovation Pass* (UK Department of Health 2009)	Innovation Pass Advisory Committee consists of: • 5 member who are active NHS	Innovation Pass Advisory Committee: Recommendations Department of	1. Application to NICE in parallel with market authorization submission 2. NICE performs application screening	• Significant medical innovation • Unmet clinical need • Substantial impact • Relative immaturity of data	Equity: Criteria includes unmet clinical need Efficiency: Application made in conjunction with market	Participates on Committee: • Clinicians • Public members

	clinicians • 3 members with expertise in healthcare industry research and development • 1 member with expertise in NHS research and development commissioning • 1 member with expertise in Primary Care Trust Commissioning • 1 member with a public health background • 2 lay members	Health: Final decision	to ensure bids are complete 3. NICE conducts fact check with manufacturers 4. Applications assessed by the Innovation Pass Review Panel against criteria 5. Recommendations to Department of Health DH decides whether to grant Innovation Pass	• Additional studies planned • Innovation Pass budget impact • Service impact • Other considerations	authorization application Ethical: Program development for individuals who require medical treatments that have not yet undergone an official NICE technology appraisal; Improvement of access	
England & Wales *Patient Access Scheme* (NICE 2013d, 2013e, 2009a)	Patient Access Scheme Liaison Unit (PASLU) is the part of the NICE Centre for Health Technology Evaluation that coordinates the review and evaluation of patient access schemes proposals and produces guidance to the Department of Health.	National Institute for Health and Care Excellence PASLU (recommendations) Department of Health (final decision)	1. A PAS is referred to NICE by the Department of Health to advise on whether its implementation is feasible. 2. On receipt of the manufacturer or sponsor's proposal, the PASLU checks the proposal for completeness. If incomplete, PASLU will request for clarification (normally within 10 working days of receiving the proposal) 3. For adequate proposals, the PASLU prepares draft advice on the	When advising whether a patient access scheme is feasible the PASLU considers the key principles for implementation of PASs in England and Wales: • Arrangements must respect the role of NICE in providing the NHS with an independent assessment and appraisal of the evidence on an intervention. • Schemes are to be discussed first and agreed in principle	Equity: • The PAS allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	Provide comments of evaluation report: • Specialists • Patient experts • Manufacturer • Sponsor

			feasibility of implementing the PAS in the NHS in England and Wales. If necessary, further discussion of the PAS with clinical and pharmaceutical specialists, and NHS and patient experts. The PASLU will seek legal advice if necessary. 4. The PASLU sends draft advice to the manufacturer or sponsor. The manufacturer or sponsor has 5 working days to check that the draft advice does not contain factual errors. The manufacturer or sponsor cannot submit additional evidence at this stage unless this has been agreed before the initial submission, or it is requested by PASLU. 5. Consideration by the Expert Panel informs the final advice developed by the PASLU project team and issued by NICE to the Department of Health. 6. After consideration of the feedback from the Expert Panel, the PASLU project team develops the final	by the Department and the company. NICE's principal role is to assess the impact of such proposals on cost-effectiveness taking into account the details of the proposed scheme. • The full costs to the NHS of any such arrangements should be included in the costs considered by the Appraisal Committee. • Schemes should be clinically robust, clinically plausible, appropriate and monitorable (e.g. if it is a responder scheme, there must be a relatively straightforward way to measure a patient's clinical response).		

			advice. The Director of the Centre for Health Technology Evaluation or, in their absence, the Technology Appraisals Programme Director reviews and approves the final advice. The final advice, together with the Expert Panel's conclusions, are sent to the manufacturer or sponsor of the drug for consideration of factual errors. The PASLU usually circulates the final advice to the manufacturer or sponsor of the drug within 5 working days of the Expert Panel meeting. In exceptional circumstances, this may take longer.			
Scotland *Patient Access Scheme* (Scottish Medicines Consortium 2013a)	Patient Access Scheme Assessment Group (PASAG) has a national focus, functioning under the auspices of NHS National Services Scotland (NSS). It is composed of members from across NHS Scotland, with different specialist backgrounds: • Director of Pharmacy (Co-	PASG (recommendations) SMC (recommendations) NHS Boards (decision-maker)	1. The company will submit application to the PASAG Secretariat via the SMC Secretariat. 2. PASAG Secretariat initiates rapid review. This may require dialogue with the submitting company and / or NHS Service providers in order to obtain clarification of key points of the proposed PAS. 3. SMC or HIS as	• Patients in NHS Scotland should benefit from any such scheme through improved access to new treatments on an equitable basis across Scotland. • Schemes must be clinically robust, plausible, practical and monitorable. • SMC / NICE, as appropriate will assess the impact of	Equity: • The PAS allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	Consulted: • External experts

	Chair) • Director of Finance (Co-Chair) • Senior Clinician Acute care (X2), Primary care (X1) • NHS Board Pharmacy operational representative • NHS Board Finance operational representative • NHS Board Business Manager representative • NSS National Procurement representative (X2) • Area Drug and Therapeutics Committee (ADTC) representative (X2) • Association of the British Pharmaceutical Industry (ABPI) representative • NHS Board Caldicott Guardian representative • NHS Board Public Health representative • NHS Board Medical Director representative • NSS Information Services Division (ISD) representative		appropriate will consult clinical experts and will forward the responses to the PASAG Secretariat. If the PASAG Secretariat has further additional questions, then the PASAG administrator will send the additional questions to clinical experts direct. 4. The PASAG Secretariat will send PAS questions to service providers in NHS Boards to obtain feedback on the operational feasibility of the PAS as appropriate. 5. A PAS Assessment Proforma will be completed by the PASAG Secretariat and submitted to PASAG for decision. 6. The company and SMC or HIS as appropriate will be notified of PASAG's decision. 7. If the PAS is not recommended, the company may resubmit a revised PAS. 8. When a product with a PAS is accepted for use in NHS Scotland,	any proposed scheme on the product's cost-effectiveness. • Any scheme should be operationally manageable for the NHS without unduly complex monitoring, disproportionate additional costs and bureaucracy. Any burden for the NHS should be proportionate to the benefits of the scheme for the NHS and patients. • There should be no risk of perverse incentives. • Compliance must be assured with NHS Scotland probity, governance and legislative requirements including formal agreements between the NHS and the pharmaceutical company regarding respective responsibilities including burden of costs and protection of commercial-in-confidence information.		

			SMC advice will be issued to NHS Boards. This will include brief, non confidential information relating to the PAS. 9. Where a product with an accepted PAS is accepted for use or restricted use in NHS Scotland, the PASAG Secretariat will prepare an Implementation Pack to support implementation of the PAS by NHS Boards.			
Wales *Patient Access Scheme* (AWMSG 2012a; AWMSG 2012b)	Members of the Patient Access Scheme Wales Group (PASWG): • Independent Chairman • Chief Pharmacist • Medical Director • Senior Finance Manager • Representative of the All Wales Therapeutics and Toxicology Centre • Representative of the All Wales Drug Contracting Group • Representative of ABPI Wales	All Wales Therapeutics and Toxicology Centre (AWTTC) (advisory) Patient Access Scheme Wales Group (PASWG) (recommendations) Welsh government (decision-maker)	1. The manufacturer must submit a WPAS proposal using the PASWG submission form, which is based on the PASLU template and PPRS criteria. 2. According to process timelines, all documentation should be received from the manufacturer eight weeks before the PASWG meeting. 3. AWTTC will review the WPAS proposal and provide a dossier including all relevant information (manufacturer's submission and clarification requests/responses) to	• Cost-effectiveness, taking into account the details of the proposed scheme. • The full costs to NHS Wales of any such arrangement should be included in the costs submitted for consideration. • Schemes should be clinically and financially robust and plausible, appropriate and monitorable. • Any scheme should be operationally manageable for NHS Wales without unduly complex monitoring, disproportionate	Equity: • The PAS allows access for some expensive drugs that under the general procedure would not be reimbursed. (Implicit ethical principles applied include "rule of rescue" and solidarity).	None specified

			Welsh Government who will forward to the PASWG Chairman. 4. A request for further clarification or evidence, if necessary, will be forwarded to the manufacturer within ten working days of receiving the proposal, and the manufacturer will have a maximum of 5 days to respond. 5. PASWG will not publicly comment on a WPAS proposal until final advice has been provided to the Welsh Government except in circumstances outlined in the PASLU process guidance document. After final advice has been received, the Welsh Government will convey its decision to AWTTC, who will then inform the manufacturer	additional costs and bureaucracy. • Any burden to NHS Wales should be proportionate to the benefits of the scheme for the NHS and patients. • It is important that any cumulative administrative burden of such schemes remains manageable for all parties involved in their operation, including front-line NHS staff. • Schemes should be consistent with existing financial flows in NHS Wales. • NHS Wales must be consulted on schemes by the applicant company, in particular where these involve additional data collection beyond that associated with the conventional purchase of medicines		