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 B1. Summary of reimbursement processes for accessing DRDs through public and social insurance

Country	**Advisor and/or decision-maker**	**Eligible drugs and definition of rare**	**Drug review requestor**	**Available option if drug fails to receive positive review through general process**	**Decision options**	**Role of stakeholders**	**Comments**
Australia *General Reimbursement- The Pharmaceutical Benefits Scheme (PBS)*(PBAC 2008b, 2008c, 2013c)	Department of Health (decisions) Pharmaceutical Benefit Advisory Committee (PBAC) (recommendations)	Eligible drugs; All new licensed outpatient drugs Definition of rare: Prevalence of 2,000 or fewer individuals in Australia	• Manufacturer • Sponsor • Medical bodies • Health professionals • Private individuals and their representatives	Life-Saving Drug Program if criteria are met	• Provide drug • Do not provide drug • Provide drug with conditions	Submit drugs for consideration: • Manufacturers • Medical bodies • Health professionals • Private individuals Public representatives	
Australia	Department of Health (decision-maker)	Eligible drugs: • Expensive life-	• Applicant who submitted drug	N/A	• Do not provide drug	Submit drugs for consideration:	

Life Saving Drugs Program (LSDP) (AGDH 2010a; AGDH 2011; Australian Government Solicitor 2013a; PBAC 2008a)	PBAC (recommendations) Disease Advisory Committee (advisory)	saving drugs for very rare life-threatening conditions • Must be accepted by PBAC as clinically effective, but not recommended for inclusion on the PBS due to unacceptable cost-effectiveness Includes drugs for rare diseases (no distinct process for rare diseases)	for PBS listing through PBAC		• Provide drug with conditions- Patient must: 1) Satisfy relevant criteria for treatment with a drug as detailed in the relevant drug/condition LSDP Guidelines 2) Participate in evaluation of effectiveness of drug by periodic assessment 3) Not be suffering from any other medical condition that might compromise the effectiveness of the drug treatment 4) Be a permanent resident who qualifies for Medicare	• Manufacturers • Medical bodies • Health professionals • Private individuals • Public representatives	
Australia *Highly Specialised Drugs Program (HSDP)*(AGDH 2010b; Mabbott et al. 2010; State Government of Victoria 2013)	Minister of Health (final decision) Pharmaceutical Benefits Advisory Committee (recommendation) Highly Specialised Drugs Program: Highly Specialised Drugs Working Party (advisory)	<u>Eligible drugs:</u> • Drugs used to treat chronic conditions that are restricted to supply through public and private hospitals having access to appropriate specialist facilities • Drugs that meet	• Highly Specialised Drugs Working Party • Manufacturer	Drugs administered in hospital typically not considered for PBS funding	• Provide drug with conditions (when PBAC recommends a drug for inclusion in the HSDP it also defines the clinical indications that the Commonwealth will subsidize) • Do not provide drug	Submit drugs for consideration: • HSDWP • Manufacturer	

		the following criteria: 1) Ongoing specialized medical supervision required 2) Treatment of longer term medical conditions, not episodes of in-patient treatment or treatment of acute conditions 3) Drug highly specialized and an identifiable patient group 4) Subject to regulatory approval and its specific therapeutic indications 5) High unit cost Includes drugs for rare diseases (no distinct process for rare diseases)					
Austria *General reimbursement: Extramural drugs* (Ayme and Rodwell 2013b; Bucholz 2009; PHARMIG	Ministry of Health (oversees HVB and HEK; can veto decisions) Association of Austrian Social Security Institutions	<u>Eligible drugs:</u> All new, licensed outpatient drugs <u>Definition of rare:</u> Follows European Regulation on	• Manufacturer	Case-by-case	• Provide drug • Provide drug with conditions • Provide drug with special authorization (approval must be sought from the head physician of the	Submit drugs for consideration: • Manufacturers	

2013)	(HVB) (decisions) Pharmaceutical Evaluation Board (HEK) (recommendations)	Orphan Medicinal Products definition of rare diseases (prevalence ≤5/10,000 in European Community)			sickness fund) • Do not provide drug		
Austria *General reimbursement: Intramural drugs* (Ayme and Rodwell 2013b; Bucholz 2009; PHARMIG 2013)	Drug Commissions of Individual Regional Hospital Cooperations (decisions) The Horizon Scanning Program (on oncology drugs only) of LBI-HTA (advisory)	<u>Eligible drugs:</u> Intramural (hospital-based only) drugs Includes drugs for rare diseases (no distinct process for rare diseases)	• Prescribing physician	Case-by-case	No information found	Submit drugs for consideration: • Physicians	
Austria *Individual (case-by-case) reimbursement* (Aymes and Rodwell 2013b; Bucholz 2009)	Regional Sickness Fund (decision-maker) • Head physician of sickness fund/chief medical officer	<u>Eligible drugs:</u> All non-reimbursable (e.g., inpatient) and off-label drugs if: 1) There is no adequate alternative drug listed, and 2) The drug is a therapeutic necessity • Use must be outside clinical trial Includes drugs for rare diseases (no distinct process for rare diseases)	• Prescribing physician	N/A	• Provide drug temporarily • Do not provide drug	Submit drugs for consideration: • Physicians	
Belgium *General Reimbursement* (Denis et al. 2009;	Minister of Social Affairs (decision-maker) Drug Reimbursement	<u>Eligible drugs:</u> All new licensed drugs Includes drugs for	• Manufacturer • Marketing Authorization Holder (MAH)	Special Solidarity Fund	• Provide drug • Provide drug with conditions (specific patients, prescribers or centres)	Submit drug for consideration: • Manufacturers • MAH	

Bogaert and Klasa 2009)	Committee (DRC) of the National Institute for Health and Disability Insurance (NIHDI) (recommendations)	rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Life-threatening and/or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them As a guide, "low prevalence" is less than 5 per 10,000 individuals in the European Community			• Do not provide drug		
Belgium *Special Solidarity Fund (SSF)* (Guillaume 2010; Denis et al. 2009)	National Institute for Health and Disability Insurance (NIHDI) College of Medical Doctors for Orphan Drugs (CMDOD) (decision-maker)	<u>Eligible drugs:</u> Orphan drugs not (yet) reimbursed by the compulsory health insurance Main reimbursable categories: • Rare indications • Rare diseases requiring a specific physiopathological treatment • Rare diseases requiring a continuous and complex treatment	• Prescribing physician	N/A	• Provide drug temporarily • Do not provide drug	Submit drugs for consideration: • Physicians	Reimbursement will only be granted if the patient has been through all other reimbursement options, including all applicable legislation at national, European or international level as well as private insurances and reimbursement systems

		• Innovative treatment techniques • Chronically ill children • Medical treatment abroad					
Denmark *General reimbursement* (Moller 2003; Danish Health and Medicines Authority 2012)	Danish Medicines Agency (DMA)-pharmacoeconomic division (decision-maker) The Reimbursement Committee (recommendations)	<u>Eligible drugs:</u> All newly licensed drugs Includes drugs for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> No official definition of rarity in Denmark • The Danish Health and Medicines authority defines a rare disease as one that affects 500 to 1000 patients in the Danish population • Other general criteria are: severe, genetic or congenital	• Manufacturer	Case-by-case	• Provide drug • Provide drug with conditions (specific patients, prescribers or centres) • Do not provide drug • Provide drug with data collection (i.e., access with evidence development)	Submit drugs for consideration: • Manufacturers	
Denmark *Individual reimbursement (case-by-case basis)* (Moller 2003; Danish	Danish Medicines Agency (DMA)-pharmacoeconomic division (decision-maker)	<u>Eligible drugs:</u> Drugs not reimbursed through the general reimbursement process	• Prescribing physician	N/A	• Provide drug temporarily • Do not provide drug	Submit drugs for consideration: • Physicians	

Health and Medicines Authority 2012)	The Reimbursement Committee (recommendations)						
Finland *General Reimbursement* (Finland Ministry of Social Affairs and Health 2013; Ayme and Rodwell 2013b; Mossialos and Srivastava 2008; Pharmaceuticals Pricing Board, 2013, 2011)	Pharmaceutical Pricing Board (PPB) decides on wholesale prices and reimbursement (Decisions)	<u>Eligible drugs:</u> • Drugs with a wholesale price approved by the Pharmaceuticals Pricing Board refund category <u>Definition of rare:</u> No official definition Generally follows European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000 in European Community)	• Manufacturers • Patient • Pharmacy on behalf of the patient	No information found	• Provide drug • Provide drug with conditions (restrict to certain providers/patient) • Do not provide drug	Submit drugs for consideration: • Manufacturers • Patients • Pharmacy	
France *General Reimbursement* (Ayme and Rodwell 2013d; Chicoye et al. 2009; Pelen 2000)	Ministry of Health and Social Services (decisions) Transparency Commission (under French National Authority for Health (HAS)) (recommendations)	<u>Eligible drugs:</u> All licensed outpatient and inpatient drugs Includes drugs for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Follows European Regulation on Orphan Medicinal	• Manufacturer	Case-by-case	• Provide drug • Provide drug with conditions (specific patients, prescribers or centres) • Do not provide drug • Provide drug with data collection (i.e., access with evidence development)	Submit drugs for consideration: • Manufacturers	

		Products definition of rare diseases (prevalence ≤5/10,000)					
France *Individual (case-by-case) or cohort reimbursement* (Natz and Compion 2012; Garau and Mestre-Ferrandiz 2009; Belorgy 2012; Ministre des Affaires et de la Santé 2014)	*Temporary use authorization (ATU) (individual or cohort)* Transparency Commission (under French National Authority for Health (HAS)) (decisions) *Note: Involves assessment and regulatory approval by the French Agency for the Safety of Health Products (AFSSAPS) and simultaneously reimbursement approval by HAS	<u>Eligible drugs:</u> Must meet all of the following criteria: 1) Non-licensed drugs for rare or severe diseases with no satisfactory alternative treatment 2) Where treatment cannot be postponed 3) The safety and efficacy of the drug are presumed 4) The patient cannot be treated within a clinical trial Includes those for rare diseases (no distinct process for rare diseases)	• Prescribing physician • Centre of Excellence Request for cohort coverage can be submitted by: • Manufacturer	N/A	• Provide drug temporarily(individual-duration of treatment; cohort - up to one year) according to therapeutic protocol with data collection/follow-up • Do not provide drug	Submit drugs for consideration for an individual patient: • Physician • Centre of Excellence Submits drugs for consideration for cohort of patients: • Manufacturers	
France *Individual (case-by-case) or cohort reimbursement* (Natz and Compion, 2012; Garau 2009; Belorgy 2012; Ministre des Affaires et de la Santé 2014)	*Recommendation for therapeutic use (RTU) (cohort)* Ministry of Health and Social Services (decisions) Transparency Commission (under French National Authority for Health (HAS))	<u>Eligible drugs:</u> Off-label drugs for diseases with no alternative treatment Includes those for rare diseases (no distinct process for rare diseases)	• Prescribing physician • Centre of Excellence	N/A	• Provide drug temporarily according to therapeutic protocol with data collection/follow-up • Do not provide drug	Submit drugs for consideration: • Physician Centre of Excellence	

	(recommendations) *Note: Involves assessment and regulatory approval by the French Agency for the Safety of Health Products (AFSSAPS) and simultaneously reimbursement approval by HAS						
France *Individual (case-by-case) or cohort reimbursement* (Natz 2012; Garau 8 Mestre-Ferrandiz 2009; Belorgy 2012; Ministre des Affaires et de la Santé 2014)	*Temporary protocol of treatment (PTT)* Transparency Commission (under French National Authority for Health [HAS]) (decisions) *Note: Involves assessment and regulatory approval by the French Agency for the Safety of Health Products (AFSSAPS) and simultaneously reimbursement approval by HAS	<u>Eligible drugs:</u> Off-label high-cost inpatient drugs Includes those for rare diseases (no distinct process for rare diseases)	• Prescribing physician	N/A	• Provide drug temporarily according to therapeutic protocol • Do not provide drug	Submit drugs for consideration: • Physician Centre of Excellence	
Germany *General Reimbursement* (Ayme and Rodwell 2013e, Holtorf 2009; Fulda 2011)	Joint Federal Committee (G-BA) (decision-maker) Note: All drugs with market approval are automatically reimbursed. The review process is used to determine	<u>Eligible drug:</u> All EMA (European Medicines Agency)-authorized drugs <u>Definition of rare:</u> Follows European Regulation on	• G-BA • Ministry of Health • Institute for Quality and Efficiency in Health Care (IQWiG)	Case-by-case	• Provide drug at negotiated price • Provide drug with conditions (specific patients, prescribers or centres) at negotiated price • Provide drug with data collection (i.e., access with evidence	Submit drugs for consideration: • G-BA • Ministry of Health • Institute for Quality and Efficiency in Health Care (IQWiG)	

	reimbursement price	Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)			development) at negotiated price		
Germany *Compassionate Use* (Federal Ministry of Health 2010)	Federal Institute for Drugs and Medical Devices (BfArM) (decision-maker) Note: Drugs approved for compassionate use by the regulatory authority must be provided at no cost to the patient	<u>Eligible drugs:</u> Off-label drug • Patients with a disease which leads to severe disability or which is life-threatening and who cannot be satisfactorily treated with an approved medicinal product • cohort programs which are intended for a group of patients	Request for program approval can be made by: • Manufacturers Request for patient access can be made by: • Physicians	N/A	• Provide drug with conditions • Do not provide drug	Submit drugs for consideration: • Manufacturers • Physicians	
Ireland *General Reimbursement-Community Drug Schemes* (Health Service Executive 2006; National Centre for Pharmacoeconomics 2013a)	*Relevant Community Drug Schemes for Orphan Drugs:* • **Long-term illness** (entitles patient suffering from any 1 of the 15 specified chronic conditions to full drug reimbursement irrespective of	<u>Eligible drugs:</u> All new licensed drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Follows European Regulation on	Technologies can be submitted by: Manufacturers	N/A	• Provide drug • Do not provide drug • Provide drug with conditions (restrict to certain patients/providers)	Submit technologies: • Manufacturers • Government	No specific orphan drug policy

	income) • **High-tech drugs** (facilitates the supply by community pharmacies of certain high-cost medicines) Health Information and Quality Authority (HIQA)/National Centre for Pharmacoeconomics (NCPE) Health Services Executive Corporate Pharmaceutical Unit (HSE-CPU) (decisions)	Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)					
Italy *General Reimbursement* Ayme and Rodwell 2013f; Bakowska et al. 2011; Folino-Gallo et al. 2008; Taruscio et al. 2011)	Italian Medicines Agency (AIFA) – Scientific Technical Committee (CTS) and Board of Directors (decisions) AIFA Pricing and Reimbursement Committee (CPR) (advice) Note: All drugs with market approval are automatically reimbursed. The review process is used to determine	<u>Eligible drug:</u> All new licensed outpatient drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Follows European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)	• Manufacturers	N/A	• Provide drug at negotiated price • Provide drug with conditions (specific patients, prescribers or centres) at negotiated price • Provide drug with data collection (i.e., access with evidence development) at negotiated price	Submits drugs for consideration: • Manufacturer	

	reimbursement price and eligible patient populations						
Italy *Individual or cohort reimbursement* (Natz and Campion 2012; Taruscio et al. 2011)	**(Law 648/96)** AIFA – CTS (decisions)	Eligible drugs: • Off-label pharmaceuticals for conditions with no alternative/existing treatment • Non-licensed pharmaceuticals that have undergone clinical trials • Innovative pharmaceuticals licensed abroad, but not in Italy	• Prescribing physician • University • Centre of Reference • Patients/patient organizations	N/A	• Provide (case-by-case) • Do not provide (case-by-case)	Submits drugs for consideration: • Physician • University • Centre of Reference • Patient organizations	
Italy *Temporary individual (case-by-case) reimbursement* (Natz and Campion 2012; Taruscio et al. 2011)	**(Law Decree 23/98)** Ministry of Health – Ethics Committee (decisions)	Eligible drugs: Off-label drugs for conditions with no alternative/existing treatment Includes those for rare diseases (no distinct process for rare diseases)	• Prescribing physician	N/A	• Provide (case-by-case) • Do not provide (case-by-case)	Submits drugs for consideration: • Physician	
Italy *Individual (case-by-case) reimbursement* (Natz and Campion 2012; Taruscio et al. 2011)	**(AIFA 5% Fund – Law 323/2003)** AIFA – CTS (decisions)	Eligible drugs: All off-label or non-licensed orphan drugs for conditions with no alternative/existing treatment	• Prescribing physician	N/A	• Provide drug temporarily • Do not provide drug	Submits drugs for consideration: • Physician	
Japan	Ministry of Health, Labour, and Welfare	Eligible technologies:	• Manufacturers	No information	• Provide drug • Do not provide drug	Submits drugs for consideration:	

General Reimbursement (Liu et al. 2009; Nagae 2012; Orphanet 2014)	(decision-maker) Drug Pricing Organization (DPO) (recommendations) Central social insurance medical council (Chuikyo) (recommendations)	All new licensed drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Formally defined as fewer than 50,000 patients in the whole population or less than 4 in 10,000 Also part of a bigger term "Nanbyo" or intractable diseases: • Resulting from an unidentifiable cause, without clearly established treatment, and having a considerable high risk of disability • Chronically developed and require a significant amount of labour for patient's care • Causing a heavy		found		• Manufacturer	

		burden on other family members, both mentally and financially					
Korea *General Reimbursement* (Ngorsuraches et al. 2012)	Ministry of Health and Welfare. Drug Pricing & Reimbursement Committee (DPRC) / also called the Drug Reimbursement Evaluation Committee (DREC) (decision-maker) Health Insurance Review & Assessment service (HIRA) (recommendations)	<u>Eligible drugs:</u> All new licensed drugs <u>Definition of Rare:</u> Formally defined as affecting fewer than 20,000 Includes those for rare diseases (no distinct process for rare diseases)	• Manufacturer	No information found	• Provide drug • Do not provide drug	Submits drugs for consideration: • Manufacturer	
Luxembourg *General Reimbursement* (Ayme and Rodwell, 2013g, Caisse nationale de santé 2003; Dispositions legislatives et satutaires 2011)	Ministry of Health (decision-maker) Commission of Experts (advisor)	<u>Eligible drugs:</u> All new licensed drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of Rare:</u> Follows European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)	• Manufacturer	No information found	• Provide drug • Do not provide drug • Provide drug with conditions (subject to treatment protocol, subject to prior authorization, limitation of care)	Submits drugs for consideration: • Manufacturer	

		Note: Vital and expensive drugs used in chronic illnesses considered for 100% reimbursement					
The Netherlands *General Reimbursement-Medicines Reimbursement System (GVS)* (Stolk et al. 2009; Ayme and Rodwell 2012; Niezen et al. 2007; Ministry of Health, Welfare and Sport 2013; International Society for Pharmacoeconomics and Outcomes Research 2007)	Minister of Health, Welfare, and Sport (decision-maker) Dutch Health Care Insurance Board (CVZ) (advisor) Central Indicatieorgaan Zorg, (CIZ) (advisor)	<u>Eligible drug:</u> • All new licensed outpatient drugs • Inpatient orphan drugs (paid by the hospital budgets, where hospitals can apply for additional funding) <u>Definition of rare:</u> Follows European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)	• Manufacturers • CVZ • Ministry of Health, Welfare, and Sport • Health Council • Insurance funds • Patients & carers • Healthcare providers	No information found	<u>Outpatient drugs:</u> • Provide drug • Provide drug with conditions (specific indications, according to practice or professional guidelines, specific prescribers) • Do not provide drug <u>Inpatient drugs:</u> • Provide drug with conditions (additional information must be collected on the efficiency of the drug) • Do not provide the drug	Submits drugs for consideration: • Manufacturers • CVZ • Ministry of Health, Welfare, and Sport • Health Council • Insurance funds • Patients & carers • Healthcare providers	
New Zealand *General Reimbursement-Pharmaceutical Schedule* (PHARMAC 2013b; BPAC 2013; NZORD 2013).	Pharmaceutical Management Agency of New Zealand (PHARMAC) (decision-maker) Pharmacology and Therapeutics Advisory Committee (PTAC) (recommendation)	<u>Eligible drugs:</u> New licensed drugs • All drugs used in the community setting and all cancer treatments used in the hospital setting Includes those for	• Anyone	Named Patient Pharmaceutical Assessment (Exceptional Circumstances) Policy (NPPA)	• Provide drug • Provide drug with conditions (specific patients, prescribers or centres) • Do not provide drug	Submits drugs for consideration: • Anyone	

	Consumer Advisory Committee (CAC) (advisor)	rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> No official definition					
New Zealand *Named Patient Pharmaceutical Assessment (Exceptional Circumstances) Policy (NPPA)* (PHARMAC 2013a, 2012)	PHARMAC (decision-maker) NPPA Advisory Panel (recommendations)	<u>Eligible drugs:</u> Drugs not otherwise funded in the community or in District Health Board hospitals Three schemes: 1) Community EC – for patients with rare or unusual clinical situations (i.e. less than ten nationally) 2) Hospital EC – enables District Health Board hospitals to dispense medicines for people being discharged from hospital 3) Cancer EC – allows District Health Boards to fund cancer drugs not otherwise funded	• District Health Board (DHB) prescribing physicians • Any prescribing physician (for a community treatment)	N/A	• Provide drug temporarily • Provide temporarily with conditions • Do not provide drug	Submit request for access: • Physician	
Norway	The Norwegian Medicines Agency	<u>Eligible drugs:</u> All newly licensed	• Manufacturers	Case-by-case	• Provide drug • Provide drug with	Submits drugs for consideration:	

General Reimbursement (Haga and Sverre 2002; Festoy et al. 2011; OrphaNews Europe 2009; Haga 2007)	(NoMA) (decision-maker)	pharmaceuticals <u>Definition of rare:</u> Formally defined as affecting < 1 in 10,000 individuals			conditions (specific patients, prescribers or centres) • Do not provide drug (but NoMA can forward a recommendation to the Ministry for priority decision on the next level)	• Manufacturers	
Norway *Individual/case-by-case* (Haga and Sverre 2002; Festoy et al. 2011)	The Norwegian Health Economic Administration (HELFO) (decision-maker)	<u>Eligible drugs:</u> Drugs without market approval in Norway, but with market approval in another EU country and: • Treat a serious disease or condition which requires long-term treatment, and the accepted products available for general reimbursement do not provide sufficient effect or cause unacceptable adverse reactions OR • Are used in the long-term treatment of conditions which are considered to	Request for access can be made by: • Prescribing physician	N/A	• Provide drug • Do not provide drug	Submits request for access: • Physician	

		be serious and rare, but for which no medicines are included in the list for general reimbursement					
Spain *General Reimbursement* (Ayme and Rodwell 2013b; Bakowska et al. 2011; Seoane-Vazquez et al. 2009)	Ministry of Health, Social Services, and Equality (Directorate General of National Health Service and Pharmacy) (decisions)	<u>Eligible drugs:</u> All new licensed drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Accept Community Action Programme on Rare Diseases definition of rare diseases (prevalence ≤ 5/10,000 or a maximum of 250,000 citizens in the European Union or a maximum of 250,000 citizens in the European Union)	• The Ministry of Health, Social Services, and Equality	Case-by-case	• Provide drug • Provide drug with conditions (specific providers or patients) • Do not provide drug	Submits drugs for consideration: • Ministry of Health	
Spain *Individual (case-by-case) or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009, Whitfield et al. 2010)	*Temporary Use Authorization* Spanish Medicines Agency (AEMPS) (decisions)	<u>Eligible drugs:</u> Non-licensed drugs for: • Chronic or life-threatening disease with no satisfactory alternative treatment (case-by-case use)	Request for individual reimbursement can be submitted by: • Prescribing physician • Treating	N/A	• Provide drug temporarily with data collection according to specified therapeutic protocol/conditions • Do not provide drug	Submits drugs for consideration (under individual reimbursement): • Physician • Treating hospital	

		OR • A significant group of patients (cohort use) Use must be outside clinical trial Includes those for rare diseases (no distinct process for rare diseases)	hospital Request for cohort reimbursement can be submitted by: • Manufacturer • Regional Health Authorities			Submits drugs for consideration (under cohort reimbursement): • Manufacturer • Regional Health Authorities	
Spain *Individual (case-by-case) or cohort reimbursement* (Garau and Mestre-Ferrandiz 2009; Whitfield et al. 2010)	*Royal Decree 1015/2009* Spanish Medicines Agency (AEMPS) (decisions)	<u>Eligible drugs:</u> Drugs without market approval in Spain but with market approval in authorized in countries other than Spain Must meet the following criteria: • No existing authorized drug with the same composition or available dosage offers an appropriate treatment OR • No existing authorized alternative treatment available Includes those for rare diseases (no distinct process for	• Prescribing physician • Treating hospital	N/A	• Provide drug • Do not provide drug	Submits drugs for consideration: • Physician • Treating hospital	

		rare diseases)					
Spain *Individual (case-by-case) or cohort reimbursement* (Garau et al. 2009)	**Act 29/2006** Spanish Medicines Agency (AEMPS) (decisions)	<u>Eligible drugs:</u> Off-label drugs where there are: • Exceptional circumstances AND • Lack of therapeutic alternatives Includes those for rare diseases (no distinct process for rare diseases)	• Prescribing physician	N/A	• Provide drug • Do not provide drug	Submits drugs for consideration: • Physician	
Sweden *General Reimbursement* (Ayme and Rodwell 2013h; Moise and Docteur 2007; TLV 2012a)	Dental and Pharmaceutical Benefits Agency (TLV) (decision-maker)	<u>Eligible drugs:</u> All outpatient drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Formal definition: "Disorders resulting in substantial disability and affecting no more than one hundred individuals per million population."	• Manufacturers	Not applicable	• Provide drug • Provide drug with conditions (specific providers or patients) • Do not provide drug	Submits drugs for consideration: • Manufacturers	
Switzerland *General Reimbursement- List of Specialties*	Federal Office of Public Health (FOPH) (decision-maker) Federal Drug	<u>Eligible drugs:</u> All new, licensed drugs Includes those for	• Manufacturer • Department of Interior	Case-by-case	• Provide drug • Do not provide drug (usually based on cost of drug) • Provide drug with	Submit technologies: • Manufacturers • Government	

(Blankart et al. 2011; International Society for Pharmacoeconomics and Outcomes Research 2011; Paris and Docteur 2007; Office Federal de la Sante 2013; Von Stokar et al. 2013; Ayme and Rodwell 2013i; Federal Office of Public Health 2013)	Commission (FDC) (recommendations)	rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> No official definition for rare but normally uses European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)			conditions (referred to as limitations related to amount or medical indications)		
Switzerland *Individual/Case-by-case* (Blankart et al. 2011; International Society for Pharmacoeconomics and Outcomes Research 2011; Paris and Docteur 2007; Office Federal de la Sante 2013; Von Stokar et al. 2013; Ayme and Rodwell 2013i; Federal Office of Public Health 2013)	Federal Office of Public Health (FOPH) (decision-maker) Federal Drug Commission (FDC) (recommendations)	<u>Eligible drugs:</u> Off-label drugs or drugs without market approval in Switzerland but with market approval in another country recognized as equivalent Must meet the following criteria: 1) Treats a life-threatening disease and the drug offers important therapeutic benefit 2) There is no reimbursed alternative Needs prior approval by health	• Prescribing physician	N/A	• Provide drug • Do not provide drug	Submits drugs for consideration: • Physician	

		insurer and price will be negotiated and set by the health insurer Includes those for rare diseases (no distinct process for rare diseases)					
United Kingdom *General Reimbursement-Highly Specialised Technologies* (Ayme and Rodwell 2013j; NICE 2014c, 2013c)	Department of Health (final decision) National Institute for Health and Care Excellence (NICE) (recommendations) (211) Local Clinical Commissioning Groups (final decision) (for products not selected for appraisal by NICE)	<u>Eligible drugs:</u> "Highly specialised technologies" Drugs must meet all of the following criteria: • The target patient group for the drug in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS • The target patient group is distinct for clinical reasons • The condition is chronic and severely disabling • The drug is expected to be used exclusively in the context of a highly specialised service • The drug is likely to have a very high acquisition cost • The drug has the	• The Secretary of State for Health formally	N/A	• Provide the drugs ("recommended") • Provide with conditions ("optimized" - the recommendations have a material effect on the use of a drug and it is recommended for a smaller subset of patients than originally stated by the marketing authorization) • Provide drug with data collection ("only in research" (treatment is recommended for use only in the context of a research study) • Do not provide ("not recommended")	Refers technologies for consideration: • The Secretary of State for Health	

		potential for life-long use • The need for national commissioning of the drug is significant <u>Definition of rare:</u> Ultra-orphan diseases: affect less than 500 people in England					
Scotland *General Reimbursement* (Scottish Medicines Consortium 2013b)	NHS boards (final decision) Scottish Medicines Consortium (SMC) (recommendations)	<u>Eligible drugs:</u> All new licensed drugs Includes those for rare diseases (no distinct process for rare diseases) <u>Definition of rare:</u> Follows European Regulation on Orphan Medicinal Products definition of rare diseases (prevalence ≤ 5/10,000)	• Manufacturers	N/A	• Provide drug • Provide drug with conditions (specific providers or patients) • Do not provide drug	Submits drugs for consideration: • Manufacturers	
Wales *General Reimbursement* (AWMSG 2014)	All Wales Medicines Strategy Group (AWMSG)(decisions)	<u>Eligible technologies:</u> All new, licensed drugs Includes those for rare diseases (no	• Manufacturers	N/A	• Provide drug • Provide drug with conditions (specific providers or patients) • Provide drug with data collection (i.e., access with evidence	Submits drugs for consideration: • Manufacturers	

		distinct process for rare diseases) <u>Definition of rare:</u> Formal definition for ultra-orphan diseases: prevalence of < 1 in 50,000 individuals in the European Union at the time of submission of the ultra-orphan drug designation application to the European Medicines Agency			development) • Do not provide drug		
United Kingdom *Innovation Pass* (UK Department of Health 2015)	Department of Health (final decision) Innovation Pass advisory committee (recommendations) National Institute for Health and Care Excellence (NICE) (advisory)	<u>Eligible drugs:</u> Unlicensed drugs • NICE "Innovation Pass": A scheme that permits patients with rare or uncommon disorders to access select innovative treatments that have not yet been subject to appraisal by NICE Includes those for rare diseases (no distinct process for	• Manufacturers • Sponsor companies (Usually in conjunction of application for regulatory approval)	N/A	• Provide drug temporarily • Do not provide drug	Submits drugs for consideration: • Manufacturers • Sponsors	

		rare diseases)					
England & Wales *Patient Access Scheme* (NICE 2009)	Department of Health (decision-maker) National Institute for Health and Care Excellence(NICE) (appraisal and recommendations) The Patient Access Scheme Liaison Unit (PASLU) (subcommittee of NICE)	<u>Eligible drugs:</u> High cost drugs Includes those for rare diseases (no distinct process for rare diseases)	• Manufacturers • Sponsor companies	N/A	• Provide drug through PAS • Do not provide drug through PAS	Submits drugs for consideration: • Manufacturers • Sponsors	
Scotland *Patient Access Scheme* (Scottish Medicine Consortium 2013a)	Patient Access Scheme Assessment Group (PASAG) Scottish Medicines Consortium (SMC)	<u>Eligible drugs:</u> High cost drugs Includes those for rare diseases (no distinct process for rare diseases)	• Manufacturers	N/A	If the PAS was proposed as part of a SMC submission, then the drug may be: • Provide the drug • Provide the drug with or without the PAS • Do not provide the drug	Submits drugs for consideration: • Manufacturers	
Wales *Patient Access Scheme* (AWMSG 2012b)	All Wales Therapeutics and Toxicology Centre (AWTTC) (advisory) Patient Access Scheme Wales Group (PASWG) (recommendations) Welsh government (decision-maker)	<u>Eligible drugs:</u> High cost drugs Includes those for rare diseases (no distinct process for rare diseases)	• Manufacturers	N/A	No information found	Submits drugs for consideration: • Manufacturers	