RESEARCH PAPER

Reimbursement of Drugs for Rare Diseases through the Public Healthcare System in Canada: Where Are We Now?

Remboursement, par le système de santé public au Canada, des médicaments pour maladies rares : où en sommes-nous?

DEVIDAS MENON, DEREK CLARK AND TANIA STAFINSKI

Table 1. Mechanisms through which DRDs may be considered for reimbursement through the publicly funded healthcare system in Canada

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Alberta (2011a, 2012b, 2012c, 2014m) *General reimbursement process*	Expert Committee on Drug Evaluation and Therapeutics (Recommendations) Minister of Health (Decisions)	Received final recommendation from the CDR OR Under regulatory review by Health Canada, but submission will not be considered until market authorization has been granted	Manufacturers Working groups	Provide drug Provide drug with conditions (when there are concerns about safety or appropriate use) Do not provide drug	
Alberta (2011d, Bennett, 2013) *Case-by-case review*	*Short Term Exceptional Drug Therapy Program* Medical Director, Pharmacy Services, Alberta Health Services (Recommendations) Alberta Health (Decisions for drugs >$100,000)	May or may not have market authorization but must be used to treat a debilitating disease where no other treatments are available (includes when a patient could not tolerate or did not respond to standard therapy)	Physicians	Provide drug with conditions (continued monitoring and reporting) Do not provide drug	Provides coverage for drugs not listed on the formulary

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Alberta (2008b, 2012e) *DRD-specific program*	*Rare Diseases Drug Coverage Program* Alberta Rare Diseases Clinical Review Panel (Recommendations) Minister of Health (Final decisions)	Indicated for genetic, lysosomal storage disorder affecting less than 1 in 50,000 Must have received final recommendation from the CDR Eligible patients must not have another significant illness that is likely to substantially reduce life expectancy	Physicians (rare disease specialists)	Provide drug with conditions (ongoing monitoring and reporting; continued coverage contingent upon outcomes – discontinued if patient deteriorates) Do not provide drug	Drugs have been provided for the following conditions: Gaucher's disease, Fabry disease, MPS-I, Hunter syndrome and Pompe disease
British Columbia (2004, 2010a, 2012f, 2014g, 2014o, 2014p, 2014q) *General reimbursement process*	Drug Benefit Council (Recommendations) Ministry (Decisions)	All outpatient drugs	Manufacturers	Provide drug Provide drug with conditions Do not provide drug	
British Columbia [personal communication, D. Wong-Rieger] *DRD-specific program*	Expensive Drugs for Rare Diseases Advisory Committee (Recommendations) Ministry of Health (Decisions)	Treats a condition (not cancer) with a prevalence <1.7 per 100,000 Canadians	Physicians (rare disease specialists)	Provide drug with conditions (ongoing monitoring and reporting; continued coverage contingent upon clinical criteria) Do not provide drug	
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l)	Manitoba Drug Standards and Therapeutics Committee (MDSTC) (Recommendations) Minister of Health (Decisions)	All outpatient drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l) *Case-by-case*	*Exception Status Drugs Program* Provincial Drug Programs Review Committee (Recommendations) Minister of Health (Decisions)	Not ordinarily administered to in-patients, but is being administered outside of hospital because of unusual circumstance Not ordinarily prescribed or administered in Manitoba, but is required to diagnose or treat a condition rarely found in Manitoba Therapeutic and economic evidence support a specific treatment regimen including the use of the drug	Physicians	Provide drug with conditions clinical criteria) Do not provide drug	
New Brunswick (2014f, 2014l) *General reimbursement process*	New Brunswick Prescription Drug Program (Recommendations) Minister of Health (Decisions)	All outpatient drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions (clinical and maximum daily supply) Do not provide drug	
New Brunswick (2014f, 2014u) *Case-by-case review*	New Brunswick Prescription Drug Program (Recommendations) Minister of Health (Decisions)	No specific criteria	Physicians	Provide drug with conditions Do not provide drug	
New Brunswick (2014s, 2014u) *DRD-specific program*	*Drugs for Rare Diseases Plan* No information found	Must be one of the five drugs specified in the plan: 1. Laronidase for Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) 2. Idurulfase for Hunter Syndrome 3. Canakinumab for Cryopyrin-Associated Periodic Syndrome (CAPS) 4. Alglucosidase alfa for infantile/early and adult/late onset Pompe disease 5. Miglustat) for Niemann Pick Type C (NPC)	Physicians	Provide drug with conditions Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Newfoundland and Labrador (2009, 2013d, 2013n, 2014a) *General reimbursement process*	Department of Health and Community Services (Decisions)	Outpatient drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions (clinical criteria) Do not provide drug	
Newfoundland and Labrador (2009, 2013d, 2013n, 2014a,) *Case-by-case review*	*Non-Funded Process* Department of Health and Community Services (Decisions)	Not specified	Physicians	Provide drug with conditions Do not provide drug	
Northwest Territories (1998, 2008c, 2011f, 2014v,) *Case-by-case review* Note: Uses NIHB process for general reimbursement	Independent professional pharmacist (Recommendations) Deputy Minister (Decisions)	Not specified	Physicians	Provide drug with conditions (not exceeding 12 months) Do not provide drug	
Nova Scotia (2012j, 2013j, 2013k) General reimbursement process	Minister of Health (Decisions)	Outpatient drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions (clinical criteria) Do not provide drug	
Nova Scotia (2012j, 2013j, 2013k) *Case-by-case review*	*Exception Status Drugs Program* Minister of Health (Decisions)	Not specified	Physicians	Provide drug with conditions Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Nunavut (2007b) *Case-by-case review* Note: Uses NIHB process for general reimbursement	Independent pharmacist from outside Nunavut (Recommendations) Deputy Minister (Decisions)	Not specified	Physicians	Provide drug with conditions (not exceeding 12 months) Do not provide drug	
Ontario (2000 Gershon 2011; Winquist et al. 2012, 2012m, 2013a, 2013e, 2013p, McArthur, 2013, 2013l, 2014z, 2014w) *General reimbursement process*	Committee to Evaluate Drugs (CED) (Recommendations) Executive Officer – Ontario Public Drugs Program (Decisions)	Outpatient drugs	Manufacturers Working groups	Provide drug Provide drug with conditions (e.g., fixed time period, clinical criteria) Do not provide drug	
Ontario (2011a, 2011c) *Case-by-case review*	*Compassionate Review Policy and Exceptional Access* Executive Officer – Ontario Public Drugs Program (Decisions)	Manufacturer has not made a submission to the Ministry and the CED has not reviewed it Used in rare clinical circumstances or in immediately life-, limb- or organ-threatening conditions where drugs on the benefit list have been tried and do not work Without an NOC and DIN issued by Health Canada if a physician indicates in the request that approval has been obtained through the Health Canada Special Access Program	Physicians	Provide drug with conditions (for a maximum of 6 months following discharge from a hospital) Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Ontario (2011b, 2011e, 2013a, 2013h; Winquist et al., 2012, Fraser, 2013) *DRD-specific program*	*DRD Evaluation Framework* Drugs for Rare Diseases Working Group (Recommendations) Executive Officer – Ontario Public Drugs Program (Decisions)	Treats a condition/disease with an annual incidence <1 in 150,000 individuals in Canada Where no clinical studies measuring clinically important outcomes have been conducted	Manufacturers Physicians/physician groups	Provide drug with conditions Do not provide drug	
Prince Edward Island (2013f) *General reimbursement process*	PEI Pharmacare (Decisions)	Outpatient drugs Special Authorization drug status for circumstances when: • Therapeutic alternatives listed in the Formulary are contraindicated or ineffective • There is no alternative listed in the Formulary	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions Do not provide drug	
Prince Edward Island (2013f) *Case-by-case review*	PEI Pharmacare (Decisions)	New drugs not yet approved for sale in Canada or not yet reviewed by the CDR	Physicians	Provide drug with conditions (fixed time period) Do not provide drug	
Quebec (2007a, 2010b, Singh, 2012, 2013i, 2014b, 2014i, 2014t, 2014x) *General reimbursement process*	Institut national d'excellence en santé et en services sociaux (INESSS) (Advisory) Minister of Health and Social Services (Decisions)	Drugs (including those not appearing on the List of Medications) Market-authorized products only	Manufacturers Physicians/physician groups	Provide drug Provide drug with conditions Do not provide drug Do not make a decision until more data are available	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Quebec (2007a, 2010b, Singh, 2012, 2013i, 2014b, 2014i, 2014t, 2014x) *Case-by-case review*	Institut national d'excellence en santé et en services sociaux (INESSS) (Advisory) Régie de l'assurance maladie du Québec (RAMQ) (Decisions)	Where there are no other pharmacological treatments already reimbursed or where those treatments are contraindicated or there is significant intolerance to the treatment or it is ineffective Treats a severe condition (i.e., serious health threat and high probability that the patient will require use of a number of services in the health network) and chronic, acute or palliative	Physicians	Provide drug with conditions (fixed time period) Do not provide drug	
Saskatchewan (2003, 2014bb, 2010d, 2012g, 2013g, 2013o, 2014c, 2014k, 2014n, 2014r) *General reimbursement process*	Drug Advisory Committee of Saskatchewan (DACS) (Recommendations) Minister of Health (Decisions)	Outpatient drugs	Manufacturers	Provide drug Provide drug with conditions Do not provide drug	
Saskatchewan (2003, 2010d, 2012g, 2013g, 2013o, 2014bb, 2014cc, 2014k, 2014n, 2014r) *Case-by-case review*	*Exception Status Drugs Program* Drug Advisory Committee of Saskatchewan (DACS) (Recommendations) Minister of Health (Decisions)	Non-approved indication "Not ordinarily prescribed or administered in Saskatchewan, but being prescribed because it is required in the diagnosis or treatment of an illness, disability, or condition rarely found in Saskatchewan"	Physicians	Provide drug with conditions Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Saskatchewan [personal communication, K. Wilson] *DRD-specific program*	EDRD Process Saskatchewan Drug Plan (Recommendations) Minister of Health (Decisions)	Treats condition that occurs in less than 1 in 150,000 individuals in Canada (may be an off-label indication)	Physicians	Provide drug Provide drug with conditions (fixed timeframe with a progress report outlining various aspects of the patient's response to treatment) Do not provide drug	
Yukon (2005, 2013r, 2013s, 2014y) *General reimbursement process*	Formulary Working Group – Health Services Branch (Recommendations) Director, Health Care Insurance (Decisions)	Drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions Do not provide drug	
Yukon (2005, 2013r, 2013s, 2014y) *Case-by-case review*	*Exception Drug Status Program*	Not specified	Physicians	Provide drug with conditions (for 30 days, for preapproved drugs with specific clinical coverage criteria) Do not provide drug	

Table 1. Continued

Jurisdiction	Advisor and/or decision-maker	Eligible drugs	Individuals able to submit reimbursement requests	Decision options	Comments
Federal (2012h, 2012i, 2013q, 2013t) For First Nations and Inuit	*Non-insured Health Benefits (NIHB) Program* NIHB Drugs and Therapeutics Advisory Committee (DTAC) (Recommendations) NIHB Director General (Decisions)	Drugs	Manufacturers (through CDR submission)	Provide drug Provide drug with conditions Do not provide drug	
Federal (2012h, 2012i, 2013q, 2013t) For First Nations and Inuit	*NIHB Exception Drug Status Program* NIHB Drugs and Therapeutics Advisory Committee (DTAC) (Recommendations) NIHB Director General (Decisions)	For recognized clinical indication and dose which is supported by published evidence or authoritative opinion Where there is significant evidence that it is superior to drugs already listed as benefits Where patient has experienced an adverse reaction to alternatives Where there is supporting evidence that available alternatives are ineffective, toxic or contraindicated	Physicians Patients	Provide drug with conditions Do not provide drug	

Table 2. Summary of information requirements across different reimbursement processes

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Alberta (2014m 2011a, 2012b, 2012c) *General reimbursement process*	Expert Committee on Drug Evaluation and Therapeutics (Recommendations) Minister of Health (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information Letter from manufacturer confirming ability to supply the drug based on anticipated demand Evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis	Manufacturer submission to CDR CDR recommendations Opinions from external scientific experts	Same as CDR Comparative studies with other listed drug products are most relevant	Same as CDR - Comprehensive pharmacoeconomic analysis in accordance with CADTH guidelines for economic evaluation – cost-effectiveness and cost-utility data and impact on direct healthcare costs are most useful Budget Impact Assessment for the Alberta Health Drug Benefit List form – considers 3-year timeframe and from a payer perspective	Submit information for consideration: • Manufacturer • External scientific experts (invitation only)
Alberta (Bennett 2013) *Case-by-case review*	*Short Term Exceptional Drug Therapy Program* Medical Director, Pharmacy Services, Alberta Health Services (Recommendations) Alberta Health (Decisions for drugs >$100,000)	Patient information (diagnosis and clinical condition) Prescriber information Reason for apply for the drug Previous treatments tried and response Evidence of clinical effectiveness of requested drug Cost information	Completed form from physician Expert scientific opinion	List of peer-reviewed, controlled studies or case series	Estimates of utilization Budget impact assessment	Submit information for consideration: • Requesting physician • Scientific experts (invitation only)
Alberta (2008b, 2012e) *DRD-specific program*	*Rare Diseases Drug Coverage Program* Alberta Rare Diseases Clinical Review Panel (Recommendations) Minister of Health (Final decisions)	Patient information (diagnosis, clinical condition and co-morbidities)	Completed form from physician Advice from Alberta Rare Diseases Clinical Review Panel	Not specified	Not specified	Submit information for consideration: • Requesting physician • Alberta rare diseases clinical review panel

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
British Columbia (2004, 2010a, 2012f, 2014g, 2014o, 2014p, 2014q) *General reimbursement process*	Drug Benefit Council (Recommendations) Ministry (Decisions)	Evidence of safety, efficacy and effectiveness Economic evaluation (pharmacoeconomic evidence) Budget impact analysis Patient preferences and ethical considerations	Manufacturer submission to CDR CDR recommendations Opinions from BC clinicians and scientific experts Patients, caregivers or patient groups through "Your Voice" using standard questionnaire. Input includes information on how disease affects patients, experience with the drug and alternative treatments and additional factors they would like considered in the review	Same as CDR Table of ongoing trials for indications other than the one being requested	Same as CDR Budget impact assessment Required Pharmacare resources to cover the cost of the drug	Submit information for consideration: • Manufacturers • Patients and families • Clinical and scientific experts (invitation only)
British Columbia [personal communication, D. Wong-Reiger] *DRD-specific program*	Expensive Drugs for Rare Diseases Advisory Committee (Recommendations) Ministry of Health (Decisions)	Patient information (diagnosis, clinical condition, prognosis and co-morbidities) Prescriber information Natural disease history Evidence of clinical efficacy and effectiveness Expected treatment outcomes Consequences if treatment is withdrawn or not provided Pharmacoeconomic evidence Budget impact analysis	Completed form from physician	Clinical guidelines and clinical evidence	Pharmacoeconomic evidence Budget impact assessment	Submit information for consideration: • Requesting physician • Expensive drugs for rare diseases advisory committee

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l)	Manitoba Drug Standards and Therapeutics Committee (MDSTC) (Recommendations) Minister of Health (Decisions)	Indications for drug, including recommended dosage and duration Disease prevalence Alternative drug and non-drug treatments Evidence of clinical efficacy and effectiveness Impact on health care services Drug cost per patient per month Budget impact analysis Direct drug costs Incremental drug costs and savings Sensitivity analyses Projected market	Manufacturer submission to CDR CDR recommendations Opinions from external scientific experts	Same as CDR	Same as CDR (comparator for economic analysis specified as lowest cost relevant drug comparator) Budget impact assessment	Submit information for consideration: • Manufacturers
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l) *Case-by-case*	*Exception Status Drugs Program* Provincial Drug Programs Review Committee (Recommendations) Minister of Health (Decisions)	Patient and prescriber information Drug name, dosage and duration Diagnosis and indication for use Proposed therapy results or outcome measurement Previous therapies tried and response to those therapies Additional information such as supporting literature to support the review	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
New Brunswick (2014u, 2014f) *General reimbursement process*	New Brunswick Prescription Drug Program (Recommendations) Minister of Health (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Letter from manufacturer confirming ability to supply the drug based on anticipated demand Clinical evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers
New Brunswick (2014u, 2014f) *Case-by-case review*	New Brunswick Prescription Drug Program (Recommendations) Minister of Health (Decisions)	Patient and prescriber information Drug name, dosage and duration Reason for the request (including diagnosis and previous treatments)	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician
New Brunswick (2014l, 2014s) *DRD-specific program*	*Drugs for Rare Diseases Plan* No information found	No information found	Request from physician	No information found	No information found	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Newfoundland and Labrador (2013d, 2014a, 2009, 2013n) *General reimbursement process*	Department of Health and Community Services (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Letter from manufacturer confirming ability to supply the drug based on anticipated demand Clinical evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers
Newfoundland and Labrador (2013d, 2014a, 2009, 2013n) *Case-by-case review*	*Non Funded Process* Department of Health and Community Services (Decisions)	Patient and prescriber information Drug name, dosage and duration Reason for the request (including diagnosis and previous treatments)	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician
Northwest Territories (2014v, 2011f, 2008c, 1998) *Case-by-case review* Note: Uses NIHB process for general reimbursement	Independent professional pharmacist (Recommendations) Deputy Minister (Decisions)	Patient and prescriber information Drug name, dosage and duration Reason for the request (including diagnosis and previous treatments)	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Nova Scotia (2013k, 2013j, 2012j) *General reimbursement process*	Minister of Health (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Letter from manufacturer confirming ability to supply the drug based on anticipated demand Clinical evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers • CDR
Nova Scotia (2013k, 2013j, 2012j) *Case-by-case review*	*Exception Status Drugs Program* Minister of Health (Decisions)	Patient and prescriber information Drug name, dosage and duration Reason for the request (including diagnosis and previous treatments)	Request from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician
Nunavut (2007b) *Case-by-case review* Note: Uses NIHB process for general reimbursement	Independent pharmacist from outside Nunavut (Recommendations) Deputy Minister (Decisions)	Not specified	Request from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Ontario (Winquist et al., 2012, 2014z; 2013p, 2013e, 2014w; Gershon, 2011; McArthur, 2013, 2013l, 2000, 2013a, 2013a) *General reimbursement process*	Committee to Evaluate Drugs (CED) (Recommendations) Executive Officer – Ontario Public Drugs Program (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Letter from manufacturer confirming ability to supply the drug based on anticipated demand Evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis Patient preferences and experiences	Manufacturer submission to CDR (CED review if off-label) Opinions from specialist group CDR recommendations Patient advocacy group submissions. These submissions include information on impact of the disease/condition; treatment outcomes that matter most to patients; and specific patient evidence on drug under review (i.e., positive and negative impacts, treatment of symptoms, difference to long-term health and wellbeing, side-effects and how it compares to other treatments)	Preference for well-designed, comparative RCTs Published and unpublished studies considered Post-marketing studies Supporting documents considered (i.e., abstracts, consensus statements, review articles and opinion papers) Multiple comparators should be evaluated where appropriate (i.e., least expensive and most widely used alternative) Information on adverse drug reactions	Utilization in other jurisdictions and projected number of patients in Ontario Economic evaluation (Cost-utility if quality of life is improved, cost-minimization analysis, cost-consequence, cost-effectiveness or cost- benefit analysis) Cost impact outside of drug expenditures Comparators: lowest cost alternative, most commonly used products or products recommended in published studies Budget impact analysis Financial impact analysis including summary of potential market size, rate of growth and extrinsic factors	Submit information for consideration: • Manufacturers • Patients and families • Clinical and Scientific experts

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Ontario (2011c, 2011a) *Case-by-case review*	*Compassionate Review Policy and Exceptional Access* Executive Officer – Ontario Public Drugs Program (Decisions)	Patient information (diagnosis and clinical condition) Prescriber information Reason for apply for the drug Previous treatments tried and response Evidence of clinical effectiveness of requested drug Cost information	Completed form from physician Literature search conducted by the drug program	Minimum requirement is case-series or multiple case reports with n ≥ 25 (preferably published) RCT preferred Individual case reports and expert opinion may be considered insufficient to support compassionate requests	If cost impact is significant, a more detailed analysis of cost and benefits may be conducted	Submit information for consideration: • Requesting physician
Ontario (2013c, 2013h; Winquist et al., 2012, 2011b, 2011e; Fraser, 2013) *DRD-specific program*	*DRD Evaluation Framework* Drugs for Rare Diseases Working Group (Recommendations) Executive Officer – Ontario Public Drugs Program (Decisions)	Proposed drug benefit price Letter confirming ability to supply anticipated demand for product Relevant clinical trial data Budget impact analysis Disease information – incidence, natural history, description of disease variants, treatment options, QOL information Patient preferences and experiences	Manufacturer submission to CDR Opinions from specialist group CDR recommendations Patient advocacy group submissions. These submissions include information on impact of the disease/condition; treatment outcomes that matter most to patients; and specific patient evidence on drug under review (i.e., positive and negative impacts, treatment of symptoms, difference to long-term health and wellbeing, side-effects and how it compares to other treatments)	Available RCTs with clinically relevant outcomes and validated/non-validated surrogate outcomes	Cost-effectiveness analysis Cost information for drug – major determinants of cost Economic or burden of illness studies	Submit information for consideration: • Manufacturers • Patients and families • Clinical and Scientific experts

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Prince Edward Island (2013f) *General reimbursement process*	PEI Pharmacare (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Letter from manufacturer confirming ability to supply the drug based on anticipated demand Clinical evidence of safety, efficacy and effectiveness Economic evaluation Budget impact analysis	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers
Prince Edward Island (2013f) *Case-by-case review*	PEI Pharmacare (Decisions)	Patient and prescriber information Drug name, dosage and duration Reason for the request (including diagnosis and previous treatments)	Request from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Quebec (Singh, 2012, 2014t, 2014b, 2007a, 2013i, 2010b, 2014i, 2014x) *General reimbursement process*	Institut national d'excellence en santé et en services sociaux (INESSS) (Advisory) Minister of Health and Social Services (Decisions)	Health Canada Notice of Compliance, product monograph and DIN Price information (proposed listing price) Disease information: burden of illness, duration and evolution of the disease or targeted health condition, duration of therapy, clinical development following use of the drug, actions required for monitoring the conditions, adverse effects Effect of service based on a timeline Net impact analysis Can submit 5 clinical studies Sensitivity analysis Estimated market share Cost-effectiveness analysis	Manufacturer submission Opinions from experts Patient advocacy group submissions	Comparative studies (based on the most commonly used alternative or most cost-effective alternative) At least one clinical study required. Double- blinded RCTs preferred, but recommendations based on consensus with clinical experts possible Note: Drugs for a rare disease for which clinical studies are available, but not of the level typically required, may still be recommended	Pharmacoeconomic studies that meet CDR standards (from societal perspective preferably), including cost-consequences, cost-minimization, cost-effectiveness and cost-utility Budget impact assessment	Submit information for consideration: • Manufacturers • Patients and families
Quebec (Singh, 2012, 2014t, 2014b, 2007a, 2013i, 2010b, 2014i, 2014x) *Case-by-case review*	Institut national d'excellence en santé et en services sociaux (INESSS) (Advisory) Régie de l'assurance maladie du Québec (RAMQ) (Decisions)	No information found	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Saskatchewan (2012g 2013g, 2014bb, 2014c, 2014r, 2014k, 2014n, 2003, 2010d, 2013o) *General reimbursement process*	Drug Advisory Committee of Saskatchewan (DACS) (Recommendations) Minister of Health (Decisions)	NOC Product monograph Clinical evaluation data Evidence on cost-effectiveness and budget impact Letter confirming ability to supply product	Manufacturer submission to CDR CDR recommendations	Same as CDR Information on impact on patterns of practice	Same as CDR Additional information on anticipated costs Cost-utility analysis is encouraged Budget impact assessment	Submit information for consideration: • Manufacturers
Saskatchewan (2012g, 2013g, 2014bb, 2014cc, 2014r, 2014k, 2014n, 2003, 2010d, 2013o) *Case-by-case review*	*Exception Status Drugs Program* Drug Advisory Committee of Saskatchewan (DACS) (Recommendations) Minister of Health (Decisions)	Patient information (diagnosis and clinical condition) Prescriber information Reason for apply for the drug Previous treatments tried and response Other options available and why they are not appropriate Evidence of clinical effectiveness of requested drug Outcome measure that will be followed to assess the effect of the drug	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician
Saskatchewan [personal communication, K. Wilson] DRD-specific program	Expensive Drugs for Rare Diseases Program Saskatchewan Drug Plan (Recommendations) Minister of Health (Decisions)	Clinical evidence	Request from physician CDR recommendations EDRD programs in other provinces Opinions of clinical experts	Journal articles, including RCTs, meta-analyses, review articles, case series and case reports	No information found	Submit information for consideration: • Requesting physician • Clinical experts

Table 2. Continued

Jurisdiction	Advisors and/or decision-makers	Information inputs	Information sources	Evidence requirements		Role of stakeholders
				Clinical	Economic	
Yukon (2005, 2013s, 2013r, 2014y) *General reimbursement process*	Formulary Working Group – Health Services Branch (Recommendations) Director, Health Care Insurance (Decisions)	Clinical evidence Economic evaluation	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers
Yukon (2005, 2013s, 2013r, 2014y) *Case-by-case review*	*Exception Drug Status Program* Director, Health Care Insurance (Decisions)	"Comprehensive supporting information"	Completed form from physician		Not specified	Submit information for consideration: • Requesting physician
Federal (2012h, 2013q, 2013t, 2012i) For First Nations and Inuit	*Non-insured Health Benefits (NIHB) Program* NIHB Drugs and Therapeutics Advisory Committee (DTAC) (Recommendations) NIHB Director General (Decisions)	Same as CDR	Manufacturer submission to CDR CDR recommendations	Same as CDR	Same as CDR Budget impact assessment	Submit information for consideration: • Manufacturers
Federal (2012h, 2013q, 2013t, 2012i) For First Nations and Inuit	NIHB Exception Drug Status Program NIHB Drugs and Therapeutics Advisory Committee (DTAC) (Recommendations) NIHB Director General (Decisions)	Varies according to specifics of the case, but usually requires clinical information	Completed form from physician	Not specified	Not specified	Submit information for consideration: • Requesting physician

Table 2. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Alberta (2011a, 2012b, 2012c, 2014m) *General reimbursement process*	Expert Committee on Drug Evaluation and Therapeutics (Recommendations) • Physicians • Pharmacists • Academic researchers • AH staff (liaisons) • Representatives from Alberta Blue Cross (provide administrative and scientific support) Minister of Health (Decisions)	Expert Committee on Drug Evaluation and Therapeutics: Recommendations Executive Director, Pharmaceutical Funding and Guidance: Recommendations Minister of Health: Decisions	1. Alberta Health receives CDR submission and recommendations (for drugs not eligible for review under the CDR procedure, manufacturers send submission to Alberta Blue Cross, where it is preliminarily screened for completeness) 2. The Expert Committee and/or Alberta Health may request the Drug Product file from Health Canada's Therapeutic Products Directorate, as well as additional information 3. The Expert Committee evaluates the submission and makes a recommendation to the Executive Director 4. The Executive Director makes recommendation to the Minister of Health 5. Minister makes a final decision	Therapeutic advantage (includes: benefit/harm ratio, toxicity, compliance, clinical outcomes, Health Canada warnings and advisories, population health issues and any other factor which affects the therapeutic value) Clinical safety, efficacy and effectiveness Available alternatives Value-for-money CDR recommendations Confirmed price and supply Affordability Utilization patterns Status in other programs and jurisdictions Issues, concerns, objectives, goals and or mandates related to any government policies, plans or programs Patient impact	Membership on Expert Committee: • Physicians • Academics • Administrators
Alberta (2011d; Bennett, 2013) *Case-by-case review*	*Short Term Exceptional Drug Therapy Program* Medical Director, Pharmacy Services, Alberta Health Services (Recommendations) Alberta Health (Decisions for drugs >$100,000)	STEDT Independent Clinical Expert Reviewers: Advisory Medical Director, Pharmacy Services: Recommendations Alberta Health (final decisions for drugs >$100,000)	1. Physician submits request to Medical Director, Pharmacy Services 2. STEDT Independent Clinical Expert Reviewers engaged as necessary for advice 3. Medical Director provides recommendation to Alberta Health 4. Alberta Health makes final decision	Disease severity Available alternatives No further information found other than "qualification for funding based on set criteria"	Review requests and give advice: • Physicians

Table 3. Steps involved in reimbursement decision-making across reimbursement processes

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Alberta (2012e, 2008b) *DRD-specific program*	*Rare Diseases Drug Coverage Program* Alberta Rare Diseases Clinical Review Panel (Recommendations) Minister of Health (Final decisions)	Review Panel: Advisory Expert Committee on Drug Evaluation and Therapy: Recommendations Minister of Health: Decisions	1. Physician submits an application to Alberta Blue Cross 2. It screens the application for completeness 3. The application is forwarded to Alberta Health to confirm the patient meets the insurance plan registration requirement 4. Review panel assesses the application and provides advice to Alberta Health 5. Expert committee makes a recommendation to the Minister of Health 6. Minister of Health makes a decision 7. Alberta Blue Cross notifies the individual's Rare Disease specialist and the individual on the decision	CDR recommendation Eligibility for coverage (including residency, clinical criteria and lack of severe comorbidities)	Membership on Review Panel: • Physicians
British Columbia (2004, 2010a, 2012f, 2014g, 2014o, 2014p, 2014q) *General reimbursement process*	Drug Benefit Council (DBC) (12 members total) made up of 9 professionals, including those with expertise in: • Critical appraisal • Medicine • Ethics • Pharmacy • Health economics • 3 members of the public	DBC: Recommendations Ministry of Health: final Decision	1. Once Health Canada and CDR reviews are complete, Ministry sends drug submission to DRRC 2. DRRC establishes review requirements, including requesting reports and other inputs 3. DRRC assigns expert review teams (DRRTs) to complete required review reports 4. DRRT forwards written reports to drug sponsor for review 5. Patient input is received through "Your Voice" patient submission site 6. Staff review documents and forward them to the DBC for review 7. DBC makes a recommendation to the Ministry 8. Ministry makes a decision on drug listing	Clinical effectiveness Value-for-money Available alternatives Current clinical practice Ethical considerations Patient impact CDR recommendations	Membership on committee: • Physicians • Public Review DRRT reports: • Manufacturers

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
British Columbia [personal communication, D. Wong-Rieger] *DRD-specific program*	EDRD Advisory Committee includes: • Pediatric and adult rare disease specialist physicians • Experts in medical genetics and biochemical disease • Pharmacists • Health administrators • Health economist • Ethicist	EDRD Advisory Committee: Recommendations Ministry of Health: Decision	No information found	Annual cost of drug must be $50,000 or greater Rarity (i.e., prevalence less than 1.7 in 100,000 Canadians) Severity Clinical effectiveness and efficacy Available alternatives	Membership on committee: • Physicians
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l)	Manitoba Drug Standards and Therapeutics Committee appointed by the MoH with recommendations from College of Physicians and Surgeons of Manitoba, Doctors Manitoba, the Manitoba Pharmaceutical Association and the University of Manitoba, and includes: • Three physicians • Three pharmacists	MDSTC: recommendations Minister of Health: final decisions	1. Submission received through manufacturer or CDR recommendation 2. MDSTC completes provincial review of drug 3. MDSTC makes a recommendation the Minister of Health 4. Manufacturer must sign a utilization management agreement 5. Minister of Health makes final decision	Clinical effectiveness Therapeutic advantage Available alternatives Affordability CDR recommendations Impact on health care services Uncertainty in evidence	Membership on committee: • Physicians
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l) *Case-by-case*	*Exception Status Drugs Program* Provincial Drug Programs Review Committee Minister of Health	Provincial Drug Programs Review Committee: Recommendations Minister of Health: Decisions	Physician applies in writing to the Provincial Drug Programs Review Committee No further information found	No information found	No information found
New Brunswick (2014u, 2014f) *General reimbursement process*	Decisions made by the New Brunswick Prescription Drug Program (NBPDP)	NBPDP: Decisions	1. Manufacturer sends submission to NB Prescription Drug Program and CDR 2. NBPDP receives recommendation from CDR 3. NBPDP makes listing decision based on recommendation	Clinical effectiveness Value-for-money CDR recommendation Affordability Program's mandate, priorities and resources	No information found

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
New Brunswick (2014u, 2014f) *Case-by-case review*	Decisions made by the New Brunswick Prescription Drug Program (NBPDP)	NBPDP: Decisions	1. Physician submits application to the NBPDP 2. NBPDP reviews application and makes a decision No further information found	No information found	No information found
New Brunswick (2014l, 2014s) *DRD-specific program*	No information found	NBPDP: Decisions	No information found	No information found, except that it will partner with Ontario DRD Evaluation to deliver the plan	No information found
Newfoundland and Labrador(2013d, 2014a, 2009, 2013n) *General reimbursement process*	Ministry of Health and Community Services Executive Committee	Executive Committee: Decisions (low budget impact drugs) Cabinet: Decisions (high budget impact drugs)	1. Manufacturers makes submission to CDR and Pharmaceutical Services Division 2. CDR makes recommendations and sends them to Pharmaceutical Services Division 3. A summary of the recommendations is prepared and forwarded to the Executive Committee of the Department of Health and Community Services 4. Once a decision is made, manufacturers are informed of the listing decision, including established approval criteria	Clinical effectiveness Value-for-money CDR recommendation Affordability Program's mandate, priorities and resources	No information found
Newfoundland and Labrador (2013d, 2014a, 2009, 2013n) *Case-by-case review*	Ministry of Health and Community Services Executive Committee	Pharmaceutical Services Division staff: Recommendations	1. Physician submits application to Pharmaceutical Services Division staff 2. Staff review application No further information found	No information found	No information found

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Northwest Territories (2014v, 2011f, 2008c, 1998) *Case-by-case review* Note: Uses NIHB process for general reimbursement	Minister and Deputy Minister of Health and Social Services Independent pharmacist reviews exemption applications	Minister of Health: Formulary decisions Independent pharmacist: Recommendations in case-by-case review Deputy Minister of Health: Decisions for case-by-case reviews	Manufacturer makes submission to NIHB (NWT uses NIHB formulary) 1. Physician submits request for coverage 2. Minister appoints independent pharmacist to review application 3. Deputy Minister makes a decision	No information found	Provides advice to decision-maker: • Pharmacist
Nova Scotia (2013k, 2013j, 2012j) *General reimbursement process*	Pharmaceutical Services Branch (Department of Health and Wellness)	Pharmaceutical Services Branch: final recommendations Provincial cabinet: final decisions	1. Manufacturers makes submission to CDR and Nova Scotia Pharmacare office 2. CDR makes recommendations and sends them to Nova Scotia Pharmacare office 3. Pharmacare office makes funding recommendation 4. Provincial cabinet makes final listing decision	Clinical effectiveness Value-for-money CDR recommendation Affordability Program's mandate, priorities and resources	No information found
Nova Scotia (2013k, 2013j, 2012j) *Case-by-case review*	Pharmaceutical Services Branch (Department of Health and Wellness)	No information found	1. Physician submits application to Nova Scotia Pharmacare staff 2. Staff review application (pharmacist consultant or drug exception analyst) No further information found	No information found	Ho information found

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Nunavut (2007b) *Case-by-case review* Note: Uses NIHB process for general reimbursement	An independent pharmacist reviews exception drug applications	Minister of Health: Formulary decisions Independent pharmacist: Recommendations in case-by-case review Deputy Minister of Health: Decisions for case-by-case reviews	Manufacturer makes submission to NIHB (NWT uses NIHB formulary) 1. Physician submits request for coverage 2. Minister appoints independent pharmacist to review application 3. Deputy Minister makes a decision	No information found	Provides advice to decision-maker: • Pharmacist

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Ontario (Winquist et al., 2012, 2014z, 2013p, 2013e, 2014w; Gershon, 2011; McArthur, 2013, 2013l, 2000, 2013a, 2012m) *General reimbursement process*	Committee to Evaluate Drugs (CED) advises Ministry on operations of programs (i.e., establishing criteria for Exceptional Access Program coverage): • Not more than 16 members plus the chair of which 2 members are lay persons • Director of Drug Programs Branch (acts as Executive Secretary) and Associate Director of the DPB (acts as Senior Consultant) • Members must have professional degree in medicine, pharmacy, pharmacology or health economics, should be active in practice and/or research in either the community hospital or academic setting	Committee to Evaluate Drugs (CED) (Recommendations) Executive Officer – Ontario Public Drugs Program (Decisions)	1. Submission received by Ontario Public Drug Programs. Executive Officer may also request that the CED perform a review and provide a recommendation for a drug or indication in the absence of a manufacturer submission. 2. CED reviews submission and consults with appropriate specialist groups (i.e., the Inherited Metabolic Disorder subcommittee) It also considers any patient evidence submissions received. These submissions are collated by the Ministry and reviewed and presented by a patient representative on the CED. 3. CED makes a recommendation to the Executive Officer 4. The Executive Officer makes a decision	Clinical effectiveness, efficacy and safety Therapeutic advantage Value-for-money (ICERs) threshold ($40-60,000) (Winquist et al., 2012) Affordability Quality and uncertainty in evidence Appropriateness Rewarding innovations Patient impact and access Impact on health services Social and ethical values (i.e., evidence-based decision-making, equity, compassion, public good, quality of life and efficiency) CDR recommendations Advice from other advisory bodies (e.g., Citizens' Council) Patient and societal impact Public interest Organizational factors (e.g., government priorities)	Membership on committee: • Physicians • Patients Present information at meetings: • Patients Consult with committee to formulate recommendation: • Appropriate specialist groups

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Ontario (2011c, 2011a) *Case-by-case review*	External reviewers (at least 3). For some specialties, only one or two reviewers are available. At least one reviewer must be a specialist with an understanding of the disease condition	External reviewers: recommendations Executive Officer: final decisions	1. Physician submits request, preferably with supporting literature evidence to Ontario Public Drug Programs 2. If no evidence is submitted, literature search is performed 3. Requests are sent to three reviewers (external medical experts) for their opinion 4. At least two of the three reviewers must recommend the drug in order for the request to be considered further 5. The request is then reviewed internally 6. Executive Officer makes a decision	Rare clinical circumstances (i.e., the disease itself is not rare, but the patients symptoms and co-morbidities make the clinical situation rare (less than 25 similar requests/ year anticipated) Severity – either directly or indirectly life, limb or organ threatening Clinical efficacy and safety Available alternatives Clinical need Affordability	Review requests: • Physicians

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Ontario (2013c, 2013h; Winquist et al., 2012, 2011b, 2011e; Fraser, 2013) *DRD-specific program*	Drugs for Rare Diseases Working Group conducts reviews. The group consists of: • Physicians • Health economist • Pharmacist	DRD Working Group: Recommendations Executive Officer: Decisions	1. Submission received from manufacturer or physician/physician group 2. DRD Working Group reviews submission: • Confirms the disease is truly rare and adequately powered clinical studies to assess important outcomes are not feasible • Understands the basic pathophysiology, natural history and health effects of the disease • Understands the mechanism of action of the candidate drug and its actual or potential treatment effects • Evaluates the potential value of the drug using all relevant and accessible clinical data. Where clinical data are sparse or questionable, the criteria described by Bradford Hill for assessing causation are applied • Models the potential clinical effectiveness of the drug. Clinical effectiveness can be estimated using modeling techniques that include estimates of the magnitude and the variability of treatment effects, with explicit acknowledgment of the limitations of the data and techniques used • Evaluates budget impact (cost-effectiveness is not a deciding factor but affordability remains a consideration) 3. Evidence submissions from patient groups are reviewed 4. DRD Working Group makes a recommendation. For positive funding recommendations, it develops clinical eligibility criteria, including start, renewal and stop criteria 5. Executive officer makes a final funding decision	Affordability Confirmed supply Clinical effectiveness Incidence of disease less than 1 in 150,000/year (i.e., rarity) DRD working group recommendations Advice from other advisory bodies (e.g., Citizens' Council) Patient and societal impact Public interest Product listing agreements with manufacturers and drug program budgets Organizational factors (e.g., government priorities)	Membership on working group: • Physicians • Health economist • Pharmacist Input taken into account in recommendations and decisions: • Public • Physicians • Patients and families

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Prince Edward Island (2013f) General reimbursement process	Minister of Health and Wellness	Minister of Health: Decisions	1. Manufacturer makes submission to CDR review 2. Manufacturer makes submission to Department of Health and Wellness, authorizing communication between PEI Pharmacare and other bodies 3. CDR provides recommendation to Minister 4. Minister makes final funding decision	CDR recommendations No further information found	No information found
Prince Edward Island (2013f) *Case-by-case review*	Minister of Health and Wellness	Minister of Health: Decisions	1. Physician submits application to PEI Pharmacare 2. Minister makes final decision No further information found	No information found	No information found
Quebec (Singh, 2012, 2014t, 2014b, 2007a, 2013i, 2010b, 2014i, 2014x) *General reimbursement process*	Scientific Listing Committee includes (19 members): • Clinicians • Pharmacoeconomist • Statistician • Ethics specialists • Pharmacists • Citizen members • Observers from INESSS and the Régie	INESSS (Scientific Listing Committee): Recommendations Board of Directors: Ratify recommendations Minister: Decisions	1. Drug manufacturer submits application to INESSS 2. If the application is complete, INESSS adds the drug product to its work plan, and plan is posted on the INESSS website 3. During 30-day period, that work plan is posted, and professional and consumer associations/groups can submit feedback or observations on the drug (which is shared with the Scientific Listing Committee) 4. Application is evaluated by the Scientific Listing Committee and associated experts 5. An evaluation report outlining the recommendations is prepared 6. Evaluation report and recommendations are sent to the INESSS Board of Directors to be ratified 7. Minister makes decision	Severity Available alternatives Reasonableness and fairness Value-for-money (cost-effectiveness ratio) Impact on the health of the population Impact on healthcare services	Membership on committee: • Public • Pharmacists • Physicians

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Quebec (Singh, 2012, 2014t, 2014b, 2007a, 2013i, 2010b, 2014i, 2014x) *Case-by-case review*	Institut national d'excellence en santé et en services sociaux (INESSS) (Advisory) Régie de l'assurance maladie du Québec (RAMQ) (Decisions)	No information found	No information found	No information found	No information found
Saskatchewan (2012g, 2013g, 2014bb, 2014c, 2014r, 2014k, 2014n, 2003, 2010d, 2013o) *General reimbursement process*	Drug Advisory Committee of Saskatchewan (DACS) appointed by Ministry of Health and composed of: • 2 public representatives • Clinical specialists in the areas of medicine, pharmacology and pharmacy	DACS: Recommendations Minister of Health: Decisions	1. Manufacturer submits drug to CDR or DACS 2. DACS completes provincial review of drug and makes a recommendation to Minister of Health, including inclusion in Inherited Metabolic Disease List. Patient letters may be included in DACS meeting materials 3. Minister of Health makes final decision	Clinical effectiveness Affordability Available alternatives Patient impact (including undesirable effects and improved dosing schedule) Organizational factors (i.e., plan mandates, priorities and resources)	Membership on committee: • Public • Physicians
Saskatchewan (2012g, 2013g, 2014bb, 2014cc, 2014r, 2014k, 2014n, 2003, 2010d, 2013o) *Case-by-case review*	Saskatchewan Drug Plan (no further information found)	Saskatchewan Drug Plan: Recommendations Minister of Health: Decisions	1. Physician submits an application to the Saskatchewan Drug Plan No further information found	No further information found	No further information found
Saskatchewan [personal communication, K. Wilson] *DRD-specific program*	Saskatchewan Drug Plan (no further information found)	Saskatchewan Drug Plan: Recommendations Minister of Health: Decisions	1. Physician submits an application to the Saskatchewan Drug Plan 2. The Plan makes a recommendation based on criteria from Ontario's EDRDEF to the Minister of Health 3. Minister of Health makes a decision	CDR recommendations Criteria from Ontario EDRD Evaluation Process: affordability, confirmed supply, clinical effectiveness incidence of disease less than 1 in 150,000/year (i.e., rarity) and status in other jurisdictions	No information found

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Yukon (2005, 2013s, 2013r, 2014y) *General reimbursement process*	Director, Health Care Insurance Yukon Formulary Working Group (appointed by Director): • Pharmacist • Pharmaceutical program manager • Program officers • Other consultants as needed for drug review and recommendation	YFWG: Recommendations Director: Decisions	1. Manufacturer makes submission to CDR 2. CDR recommendation is forwarded to YFWG 3. YFWG makes a recommendation to the Director 4. Director makes funding decision	CDR recommendations No further information found	Membership on committee: • Pharmacists • Other consultants (physicians)
Yukon (2005, 2013s, 2013r, 2014y) *Case-by-case review*	Director, Health Care Insurance Yukon Formulary Working Group (appointed by Director): • Pharmacist • Pharmaceutical program manager • Program officers • Other consultants as needed for drug review and recommendation	YFWG: Recommendations Director: Decisions	1. Physician submits an application to the YFWG 2. YFWG makes a recommendation 3. Director makes a decision	No information found	Membership on committee: • Pharmacists • Other consultants (physicians)

Table 3. Continued

Jurisdiction	Advisory/decision-making committee membership	Committee authority	Steps in decision-making process	Pre-defined decision-making criteria/factors	Role of stakeholders
Federal (2012h, 2013q, 2013t, 2012i) For First Nations and Inuit	NIHB Drugs and Therapeutics Advisory Committee (DTAC) includes medical and pharmaceutical experts	DTAC: Recommendations (if necessary) NIHB Director General: Decisions	1. Manufacturer makes submission to CDR (sent to NIHB Program for information purposes) 2. CDR recommendations are forwarded to the NIHB 3. The NIHB reviews recommendation internally and the Director makes listing decision based on these recommendations. If additional clarification or changes are needed, NIHB may bring it to DTAC for additional review	Needs of First Nations and Inuit clients Clinical effectiveness, efficacy and safety Therapeutic advantage Value for money Available alternatives Current clinical practice Coverage in other jurisdictions CDR/DTAC recommendations Organizational factors (e.g., mandate, priorities and resources)	Membership on committee: • Physicians • Pharmacists
Federal (2012h, 2013q, 2013t, 2012i) For First Nations and Inuit	NIHB Drugs and Therapeutics Advisory Committee (DTAC) includes medical and pharmaceutical experts	DTAC: Recommendations (if necessary) NIHB Director General: Decisions	1. Physician submits an application to the NIHB No further information found	No information found	No information found

Table 4. Transparency of decisions and implementation considerations across reimbursement processes for DRDs

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Alberta (2011a, 2012b, 2012c, 2014m) *General reimbursement process*	Publicly accessible, transparent reporting system that provides information about drugs being reviewed and the reasons for listing or not listing is being implemented	No information found	The Expert Committee and/or Alberta Health may review the benefit status of a product at any time if one or more of the following criteria are met: • Significant change to the product • Product no long demonstrates therapeutic advantage • Product is not long cost-effective • To enable broader coverage of higher priority products • Product is discontinued by manufacturer • Product changed from prescription to non-prescription • Any factors they consider appropriate	Guidelines for coverage decisions include 120 days after completion of Common Drug Review and 150 days for products that require societal and ethical input Drugs available through the Drug Benefit List or Specialized High Cost Drug Program may be subject to a product listing agreement (PLA)	Coverage under Alberta Blue Cross for eligible Albertans	Initiate reassessment: • Expert committee • Government
Alberta (2011d; Bennett, 2013) *Case-by-case review*	No information found	No information found	Decisions reviewed after six months. Reviews may be conducted on an individual or drug product basis.	Coverage dependent on ongoing data collection and monitoring	Limited budget grant program requiring annual renewal Joint program between Alberta Health and Alberta Health Services	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Alberta (2012e; 2008b) *DRD-specific program*	No information found	No information found	No information found	Eligibility effective the date coverage is approved by the Review Panel Drugs may be subject to a PLA Approval granted for a specific period (max. 12 months) Prescription quantities limited to one month supply (to avoid wastage)	Technology covered under Alberta Blue Cross (government-sponsored drug plan)	No information found
British Columbia (2004, 2010a, 2012f, 2014g, 2014o, 2014p, 2014q) *General reimbursement process*	For non-CDR drug submission, the Ministry has the discretion to determine whether the drug review reports will be made publically available Prior to posting publically, sponsor has 15 days to request the non-disclosure of any specific portions that it deems confidential/proprietary	Manufacturer may file a Request for Reconsideration based on grounds: 1. Ministry/DBC did not follow proper process 2. DBC recommendation not supported by evidence or input reviewed Manufacturer may file resubmission if new information becomes available	No information found	Standard drug reviews should be completed in nine months, and complex reviews should take 12 months. Priority reviews should be completed in six months	Drugs receiving a positive funding decision are funded through one of the programs administered by British Columbia Pharmacare.	Initiate appeals and reassessment: • Manufacturers

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
British Columbia [personal communication, D. Wong-Rieger] *DRD-specific program*	Decisions and rationale are not made public	No information found	No information found	Manufacturer participates in negotiations around pricing and managed access terms	Drugs receiving a positive funding decision are funded through one of the programs administered by British Columbia Pharmacare.	Participates in pricing and access negotiations: • Manufacturers
Manitoba (2008a, 2012k, 2012n, 2014e, 2014j, 2014h, 2012l)	Benefit listing decisions made public through Bulletin	Resubmission can be made to the MDSTC if there is new clinical information or a better value proposition identified	No information found	Coverage valid from date of application to date of expiration Manufacturers for all drugs under consideration for listing must sign a PLA	Cost will be covered through the appropriate Provincial Drug Program (e.g. Pharmacare, Home Cancer Drug Program, etc.)	
Manitoba (2008a, 2012c, 2012k, 2012n, 2014e 2014h, 2014j) *Case-by-case*	Decisions are rationale are not made public	An individual or provider can appeal a negative decision through the MDSTC in writing	No information found	No information found		Initiate appeal of decision: • Patients • Physician
New Brunswick (2014f, 2014l) *General reimbursement process*	No information found	No information found	Atlantic Common Drug Review (ACDR) used for line extensions and reviews of benefit status Benefit status review occurs if: • New evidence about clinical safety/effectiveness published • Change in regulatory status of drug • Change in drug cost • New development of comparable product	No information found	New Brunswick Prescription Drug Program offers 11 different "Plans" with various fees, benefits, beneficiaries and governing legislation	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
New Brunswick (2014f, 2014u) *Case-by-case review*	No information found	No information found	No information found	No information found	No information found	No information found
New Brunswick (2014s, 2014u) *DRD-specific program*	No information found	No information found	No information found	No information found	No information found	No information found
Newfoundland and Labrador (2009, 2013d, 2013n, 2014a) *General reimbursement process*	Decisions are also communicated to pharmacists, physicians and the public via bulletin, Nexxus newsletter and posting on the NLPDP website	No information found	Atlantic Common Drug Review (ACDR) used for line extensions and reviews of benefit status Benefit status review occurs if: • New evidence about clinical safety/effectiveness published • Change in regulatory status of drug • Change in drug cost • New development of comparable product	No information found	Newfoundland and Labrador Prescription Drug Program has 5 main "Plans": Foundation, 65Plus, Access, Assurance and Special Needs	No information found
Newfoundland and Labrador (2009, 2013d, 2013n, 2014a) *Case-by-case review*	No information found	No information found	No information found	No information found	No information found	No information found
Northwest Territories (1998, 2008c, 2011f, 2014v) *Case-by-case review* Note: Uses NIHB process for general reimbursement	No information found	Same as NIHB	NWT Pharmacy and Therapeutics (P&T) Committee reviews formulary on an annual basis	Same as NIHB	Drugs funded by: • Northwest Territories Health Care Plan • NIHB	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Nova Scotia (2012j, 2013j, 2013k) *General reimbursement process*	Formulary updates (decisions) made public through program website	No information found	Atlantic Common Drug Review (ACDR) used for line extensions and reviews of benefit status Benefit status review occurs if: • New evidence about clinical safety/effectiveness published • Change in regulatory status of drug • Change in drug cost • New development of comparable product	No information found	Funding provided by Nova Scotia Pharmacare program	No information found
Nova Scotia (2012j, 2013j, 2013k) *Case-by-case review*	No information found	No information found	No information found	No information found	No information found	No information found
Nunavut (2007b) *Case-by-case review* Note: Uses NIHB process for general reimbursement	No information found	Same as NIHB	NWT Pharmacy and Therapeutics (P&T) Committee reviews formulary on an annual basis	Same as NIHB	Drugs funded by: • Northwest Territories Health Care Plan • NIHB	No information found
Ontario (2000, Gershon, 2011; Winquist et al., 2012, 2013p, 2013m, 2014w, 2014z, McArthur, 2013, 2013a, 2013l) *General reimbursement process*	Status of submissions and the rationale supporting CED and Ministry decisions are made public through website	Manufacturers have the opportunity to respond to CED negative recommendations and Limited Use recommendations Manufacturers have six months to respond to second negative recommendation	No information found	Listing may require PLA between Ministry and manufacturer to obtain better value for money	Drugs funded by Ontario Drug Benefit Program	Opportunity to respond to concerns related to negative recommendations: • Manufacturers

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Ontario (2011a, 2011c) *Case-by-case review*	No information found	No information found	For continued coverage, there must be an objective measure of response provided	If approval granted, a short-term trial period will be provided	No information found	No information found
Ontario (2011b, 2011e; Fraser, 2013; Winquist et al., 2012, 2013c, 2013h) *DRD-specific program*	Status of submissions and decisions are publicly available through the program's website	Feedback on funding decisions from manufacturers, patient groups and physicians are considered. The Ministry and DRD Working Group considers the clinical merits of the feedback to determine whether re-evaluation is warranted No time limit on when additional information can be provided	Drugs are periodically re-evaluated. Re-evaluations can be triggered by stakeholder feedback or emergence of new clinical data. These reviews are conducted by the DRD Working Group and entail literature searches and reviews to update the disease model and reassessment of reimbursement guidelines.	Listing may require a PLA between the Ministry and manufacturer to improve affordability Funding requires monitoring of patient outcomes Approval for specific time period	Funding available through the Exceptional Access Program for beneficiaries of the ODB program	Respond to concerns related to negative recommendations: • Manufacturers • Physicians • Patient groups
Prince Edward Island (2013f) *General reimbursement process*	No information found	No information found	Atlantic Common Drug Review (ACDR) used for line extensions and reviews of benefit status Benefit status review occurs if: • New evidence about clinical safety/effectiveness published • Change in regulatory status of drug • Change in drug cost • New development of comparable product	No information found	Funding available through a number of reimbursement programs administered by PEI Pharmacare	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Prince Edward Island (2013f) *Case-by-case review*	No information found	No information found	No information found	No information found	No information found	No information found
Quebec (Singh, 2012, 2007a, 2010b, 2013i, 2014b, 2014i, 2014t, 2014x) *General reimbursement process*	Notice to the Minister, which explains recommendations and rationale, is publicly available on the website	If patient is dissatisfied with decision following review, he/she can write to the secretariat of the Tribunal administratif du Québec within 60 days of the date of the review decision	When drug is listed, the criteria of reimbursement of other already listed drugs are reviewed and modified to ensure coherence	No information found	No information found	Initiate appeals: • Patients • Physicians
Quebec (Singh, 2012, 2007a, 2013i, 2014b, 2014t, 2010b, 2014i, 2014x) *Case-by-case review*	No information found	No information found	No information found	No information found	No information found	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Saskatchewan (2003, 2010d, 2012g, 2013g, 2013o, 2014bb, 2014c, 2014k, 2014n, 2014r) *General reimbursement process*	Listing decisions for the Saskatchewan Formulary are communicated to physicians and pharmacists through regular Saskatchewan Formulary Bulletins	No information found	The Minister of Health may remove a product from the Formulary upon recommendation from the DACS Listing decisions may be reconsidered by DACS. This reconsideration may be after a manufacturer resubmission, prescriber criteria change request or an internal Drug Plan request for advice/ clarification. The review process for reconsideration requests involves documentation to explain the reason for the request, clinical evidence in support of the request and cost information associated with potential listing changes.	Drugs used to treat Inherited Metabolic Diseases (IMD) may be placed on the IMD Drug Benefit List (e.g., Kuvan). The Ministry of Health will consider confidential product listing agreements to assist in managing financial risk if cost has been identified as a key barrier to obtain a Saskatchewan Formulary listing	Drugs funded by the Saskatchewan Drug Plan Patients with high eligible medication costs may wish to apply for the Special Support program	Initiate reassessments: • Minister of Health • DACS Provide more information for reassessment: • Patients • Providers
Saskatchewan (2003, 2010d, 2012g, 2013g, 2013o, 2014bb, 2014c, 2014r, 2014k, 2014n) *Case-by-case review*	No information found	In most cases, if request is denied, the Drug Plan will ask for more information and reconsider coverage. If after consideration of the new information, the patient still does not meet the criteria, the request is denied	Listing decisions and/or EDS criteria may be reconsidered by DACS	No information found	No information found	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Saskatchewan [personal communication, K. Wilson] *DRD-specific program*	Decisions not made public	Physicians may contact the Drug Plan with additional clinical information. Depending on the request, there may be sufficient information for approval, or alternatively, the request may be taken to the committee for review.	No information found		If positive funding decision, costs covered by the Drug Plan	Initiate appeals: • Physicians
Yukon (2005, 2013s, 2013r, 2014y) *General reimbursement process*	No information found	Any decision of the Yukon Formulary Working Group can be appealed by sending a letter of appeal to the Chronic Disease Program or Pharmacare Program Letters of appeal sent to programs are "reviewed by Director when required." See "Federal" section for information on NIHB	No information found	Same as NIHB	Funding provided by: • Yukon Pharmacare program • NIHB	Appeals reviewed by: • Yukon Formulary Working Group • Director
Yukon (2005, 2013s, 2013r, 2014y) *Case-by-case review*	No information found	No information found	No information found	Coverage is provided until a physician requests a change in the status or until reassessment is required	No information found	No information found

Table 4. Continued

Jurisdiction	Transparency	Appeals mechanisms	Reassessment or review of decisions	Conditions of implementation	Funding mechanism	Role of stakeholders
Federal (2012h, 2012i, 2013q, 2013t,) For First Nations and Inuit	Listing decisions are made public through the website (NIHB Drug Benefit List (DBL and the DBL Updates are available online)	Three levels of appeal are available for NIHB clients	Modifications to current NIHB DBL listing criteria and/or delisting of a drug from the NIHB DBL is at the discretion of the NIHB Program. A drug may be delisted when: • Drug is discontinued from Canadian market • The drug no longer possesses therapeutic or safety advantages compared to listed alternatives or placebo • New toxicity or safety data shift the risk/benefit ratio • New information demonstrates the product does not have the anticipated therapeutic benefit • Purchase cost is disproportionate to the benefits • Drug has high potential for misuse or abuse		Drugs funded through NIHB Program	Initiate appeals: • Patients • Physicians
Federal (2012h, 2012i, 2013q, 2013t) For First Nations and Inuit	No information found	No information found	No information found	Approval time period may be specified in order to ensure the medication is providing a clinical benefit before further coverage is provided (e.g., 6 months initial approval)	No information found	No information found

Table 5. Publicly funded access to DRDs by jurisdiction (disease specified where multiple indications exist)

Drug name (and indication if greater than one rare disease indication)	AB	BC	MB	NB	NL	NS	ON	PEI	PQ	SK	NVT*	NWT*	YK	Total n (%)
Alimentary tract and metabolism products														
Agalsidase alfa														0 (0)
Agalsidase beta														0 (0)
Alglucosidase alfa						X	X		X	X				4 (30.77)
Idursulfase				X			X							2 (15.38)
Laronidase														0 (0)
Miglustat							X							1 (7.69)
Sapropterin dihydrochloride							X		X	X				3 (23.08)
Velaglucerase alfa							X							1 (7.69)
Antineoplastic and immunomodulating agents														
Abatacept	X	X	X	X	X	X	X	X	X	X	X	X	X	13 (100)
Adalimumab	X	X	X	X	X	X	X	X	X	X	X	X	X	13 (100)
Belimumab														0 (0)
Pirfenidone											X	X	X	3 (23.08)
Rituximab	X	X	X	X	X	X	X	X	X	X	X	X	X	13 (100)
Tocilizumab	X	X	X	X	X	X	X		X	X	X	X	X	12 (92.31)
Plerixafor				X										1 (7.69)
Eculizumab (PNH)	X		X	X			X							4 (30.77)
Eculizumab (Atypical HUS)	X						X							2 (15.38)

Table 5. Continued

Drug name (and indication if greater than one rare disease indication)	AB	BC	MB	NB	NL	NS	ON	PEI	PQ	SK	NVT*	NWT*	YK	Total n (%)
Blood/Blood-forming organ agents														
Eltrombopag olamine							X		X	X				3 (23.08)
Romiplostim							X							1 (7.69)
Treprostinil sodium		X		X	X	X	X		X	X				7 (53.85)
Cardiovascular system agents														
Ambrisentan		X	X	X	X	X	X	X	X	X	X	X		11 (84.62)
Sildenafil citrate		X		X	X	X	X	X	X	X	X	X	X	11 (84.62)
Sitaxsentan sodium														0 (0)
Tadalafil		X					X		X	X	X	X		6 (46.15)
Musculo-skeletal system agents														
Collagenase Clostridium histolyticum														0 (0)
Clostridium botulinum neurotoxin type A (blepharospasm)	X	X	X	X		X	X		X	X	X	X		10 (76.92)
Clostridium botulinum neurotoxin type A (cervical dystonia)	X	X	X	X		X	X		X	X	X	X		10 (76.92)
Nervous system agents														
Rufinamide		X	X	X	X	X	X	X	X	X	X	X		11 (84.62)
Sodium oxybate														0 (0)
Respiratory system agents														
Ivacaftor	X		X			X	X		X	X			X	7 (53.85)
Systemic anti-infective agents														

Table 5. Continued

Drug name (and indication if greater than one rare disease indication)	AB	BC	MB	NB	NL	NS	ON	PEI	PQ	SK	NVT*	NWT*	YK	Total n (%)
Aztreonam	X	X			X		X		X	X				6 (46.15)
Voriconazole (invasive aspergillosis)	X	X		X	X	X	X	X	X	X	X	X	X	12 (92.31)
Voriconazole (candidemia)	X	X		X	X	X	X	X	X		X	X	X	11 (84.62)
Systemic hormonal preparations														
Lanreotide acetate	X		X	X	X	X	X		X	X				8 (61.54)
Pegvisomant						X								1 (7.69)
Potentially accessible drugs per province	12 (36.36)	14 (42.42)	11 (33.33)	16 (48.48)	12 (36.36)	16 (48.48)	24 (72.73)	8 (24.24)	19 (57.58)	18 (54.55)	13 (39.39)	13 (39.39)	9 (27.27)	

Notes: X = drug is accessible and reimbursed through at least one of the three categories (general reimbursement, case-by-case or DRD-specific program)

N/A = drug not submitted to jurisdiction for reimbursement decision

"No Access" = "Do Not Reimburse" decision or "Under Review"

Uses the Non-Insured Health Benefits of First Nations and Inuit reimbursement decision-making process

Table 6. Degree of agreement between publicly funded provincial and territorial drug plans on the reimbursement status of DRDs (kappa scores)

	AB	BC	MB	NB	NL	NS	ON	PEI	PQ	SK	NVT	NWT	YK
AB													
BC	0.4046												
SMB	0.5982	0.4556											
NB	0.4211	0.6842	0.5789										
NL	0.3214	0.7293	0.3686	0.6316									
NS	0.4211	0.6842	0.5789	0.6842	0.6316								
ON	0.2893	0.3592	0.2567	0.3684	0.3840	0.3684							
PEI	0.1582	0.6122	0.3192	0.5263	0.7595	0.5263	0.2540						
PQ	0.3770	0.6336	0.3270	0.4211	0.5847	0.6316	0.6232	0.3838					
SK	0.4211	0.5789	0.4737	0.3684	0.4211	0.5789	0.4737	0.2105	0.8421				
NVT	0.3214	0.7293	0.3686	0.5263	0.5476	0.5263	0.2893	0.6392	0.5847	0.4211			
NWT	0.3214	0.7293	0.3686	0.5263	0.5476	0.5263	0.2893	0.6392	0.5847	0.4211	1.0000		
YK	0.4673	0.4493	0.2716	0.3684	0.4673	0.4737	0.1059	0.5398	0.3306	0.2632	0.5857	0.5857	

Table 7. Degree of agreement on reimbursement status of DRDs across jurisdictions by ATC group

ATC	Kappa	95% confidence interval
Alimentary tract and metabolism products	0.0512	0.020 to 0.115
Antineoplastic and immunomodulating agents	0.5675	0.345 to 0.602
Blood and blood-forming organ agents	0.1136	-0.045 to 0.206
Cardiovascular system agents	0.4454	0.094 to 0.544
Musculoskeletal system agents	0.4868	0.487 to 0.664
Nervous system agents	0.7111	N/A*
Respiratory system agents	-0.0833	N/A*
Systemic anti-infective agents	0.1483	-0.083 to 0.206
Systemic hormonal preparations	0.1698	-0.078 to 0.283
All DRDs	0.4760	-0.406 to 0.541

*Not calculable, as there was a only one drug with a kappa value in the ATC group