

VALUE IN PHARMACEUTICAL PRICING

COUNTRY PROFILE: CANADA

Valérie Paris, Annalisa Belloni



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List of acronyms

ATP	Average Transaction Price
CADTH	Canadian Agency for Drugs and Technology in Health
CDR	Common Drug Review
CEDAC	Canadian Expert Drug Advisory Committee
CPI	Consumer Price Index
HDAP	Human Drug Advisory Panel
INESSS	National Institute for Excellence in Health and Social Services (Institut national d'excellence en santé et en services sociaux)
NCE	New Chemical Entities
OPMS	Office of Pharmaceutical Management Strategies
OTC	Over-the-counter
pERC	Pan-Canadian Expert Review Committee
pCODR	Pan-Canadian Oncology Drug Review
PMPRB	Patented Medicine Prices Review Board
SPB	Strategic Policy Branch
VCU	Voluntary Compliance Undertaking

VALUE IN PHARMACEUTICAL PRICING COUNTRY PROFILE: CANADA

This country profile was prepared to inform the OECD report Value in pharmaceutical pricing (Health Working Paper No. 63) and was last updated in July 2013. It does not include policy changes that occurred since then. This country profile benefited from input and comments from the Patented Medicines Pricing Review Bureau (PMPRB), the Common Drug Review (CDR) housed within The Canadian Agency for Drugs and Technologies in Health (CADTH) and the Office of Pharmaceutical Management Strategies (OPMS) within Strategic Policy Branch (SPB) Health Canada. Authors remain responsible for any errors or omissions.

Contextual information on pharmaceutical coverage and pricing

1. Canadian residents are covered through a tax-funded universal system for a wide range of health care services. Drugs administered in hospitals are fully covered through the universal, publicly financed Medicare programme, but out-patient prescription drugs are not included among the insured benefits guaranteed by the *Health Canadian Act*.
2. Provinces and territories (P/Ts) and the federal government provide coverage to about one third of Canadian residents through publicly financed programmes targeting some populations (seniors, social assistance beneficiaries, indigenous persons, veterans, etc.). P/Ts and the federal government make coverage decisions and establish formularies for each of the public plan they manage. About two-third of Canada's residents are covered for prescription drugs by private insurance (employer-based or individual contracts). Private plans establish their own formularies and tend to be more inclusive than public plans though some of them mirror public plans coverage. In Québec, all plans are required to offer coverage at least equal to the public formulary (Paris and Docteur, 2006).
3. Canada regulates the prices of *all* patented medicines (whether covered or not) at the federal level to ensure that the price of patented drugs are not “excessive”. A maximum ex-factory price is determined at the federal level by reference to prices in other countries for the most innovative products, and by reference to prices of existing drugs in Canada for the less innovative ones.
4. Many provincial governments have been using economic evaluation to make decisions on drug listing for their public programmes. They decided to join their efforts and created in 2003 the Common Drug Review. The intergovernmental Common Drug Review (hereafter CDR), part of the Canadian Agency for Drugs and Technologies in Health (CADTH), systematically assesses the comparative clinical effectiveness and the cost-effectiveness of products with new active substances to inform coverage decisions of public drug schemes managed at federal or provincial level –except for Québec (Paris and Docteur, 2006). P/T governments and federal programmes participating to the CDR make their own decisions about inclusion of new products in their formularies and are not obliged to follow CDR's recommendations. Public plans currently negotiate prices and British Columbia set reference prices for some clusters of products (e.g. proton-pomp inhibitors). In the province of Québec, the *Institut national d'excellence en santé et en services sociaux* (INESSS) conducts assessment and makes recommendations to the Ministry of Health and Social Services.

Price regulation of patented drugs at federal level

5. Since 1987, the prices of patented medicines have been regulated at the federal level to ensure that they are not “excessive”.

General objectives and scope of pricing regulation

6. The Patented Medicine Prices Review Board (PMPRB) was created in 1987 through amendments to the *Patent Act*. At that time, price regulation of patented pharmaceuticals was accepted by the brand-name pharmaceutical industry in exchange for enhanced patent protection.

7. The PMPRB mandate is limited to the regulation of manufacturers’ prices of all patented drugs for the duration of their patent life, whatever their status (available OTC or only with a prescription, for human or veterinary use). The Board does not regulate off-patent drugs, and does not consider distributors’ margins. The PMPRB must report annually to the parliament on its activities, on R&D spending by drug patentees and on drug pricing trends.

8. The PMPRB has the mandate to protect Canadian consumers by ensuring that the prices of patented drugs sold in Canada are not “excessive”. In making this judgement the Board compares the proposed Canadian price either to prices of existing drugs in Canada, or to prices in seven markets designated in the regulations: France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States. These countries were selected in 1987 as ones that had or aspired to have a strong national presence of the pharmaceutical industry.

9. Price increases are limited to changes in the Consumer Price Index (CPI).¹ In addition, the price of a patented drug may, at no time, exceed the highest price of the same drug in the seven foreign countries.

Institutions, experts and stakeholders involved

10. The PMPRB operates as an independent, quasi-judicial body, empowered to enforce sanctions and impose price reductions for patented pharmaceutical products. The Board consists of no more than five members, appointed by the governor-in-council, including a chairperson and a vice-chairperson. The chairperson is designated under the Patent Act as the Chief Executive Officer of the PMPRB with the authority and responsibility to supervise and direct its work. At present, there are four appointed Board members, who operate on a part time basis.

11. Within the PMPRB, the Human Drug Advisory Panel (HDAP) is responsible for the scientific review of new products. HDAP is composed of members with expertise in drug therapy, clinical research and statistical analysis. HDAP currently has five members. They meet four times per year (PMPRB, 2011).

12. The PMPRB assesses the added therapeutic value of new marketed patented drugs in order to categorise them (scientific review) and then check that the price set in Canada by the manufacturer is not excessive (price review).

1. To assess the compliance with this rule regarding price increases, the price of a product in year t is compared to its price three years before, adjusted by three-year cumulative CPI. In addition, the price cannot increase by more than 1.5 times the CPI increase for a given year.

Criteria for assessment

13. The *scientific review process* is an evidence-based process that assesses the level of therapeutic improvement of a patent drug product and recommends, where appropriate, the drug products to be used for comparison purposes and the comparable dosage regimens. The review is based on information from a variety of sources (patentee submission, research by a Drug Information Centre, research by Board staff and research by HDAP members). In its submission, the manufacturer suggests the category that it believes is appropriate for considering the drug's price. The manufacturer also indicates the drug's primary use, its comparators and their dosage regimens and, if relevant, the comparative therapeutic class.

14. Before 2010, the HDAP used to classify drugs in three categories according to their degree of innovation.² According to various stakeholders, this classification failed to recognise adequately the benefits of incremental innovation (Paris and Docteur, 2006). The system changed from January 2010 and the HDAP currently classifies new drugs in four categories according to their level of therapeutic improvement (PMPRB, 2009):

- A *breakthrough* drug product is the first one to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.
- A drug product offering *substantial improvement* is one that, relative to other drug products sold in Canada, provides substantial improvement in therapeutic effects.
- A drug product offering *moderate improvement* is one that, relative to other drug products sold in Canada, provides moderate improvement in therapeutic effects.
- A drug product offering *slight or no improvement* is one that, relative to other drug products sold in Canada, provides slight or no improvement in therapeutic effects.

15. According to new guidelines for assessment published in 2009, factors to be considered in order to assess the level of therapeutic improvement of a drug are the following (PMPRB, 2009):

- Primary factors: increased efficacy; reduction in incidence or grade of important adverse reactions;
- Secondary factors: route of administration, patient convenience, compliance improvements leading to improved therapeutic efficacy, caregiver convenience, time required to achieve the optimal therapeutic effect, duration of usual treatment course, success rate, percentage of affected population treated effectively, and disability avoidance/saving.

16. The primary factors should be given the greatest weight, followed by an assessment of any additional improvement as a result of the secondary factors. In recommending the level of therapeutic improvement of new patented drug products, factors such as the following will generally not be taken into consideration, unless the impact of these factors results in either increased efficacy and/or a reduction in

2. The three categories were defined as follows. Category 1 comprised drug products that were a new strength (e.g., 50 mg v. 100 mg) or a new dosage form (e.g., tablet v. capsule) of an existing medicine. Category 2 comprised drug products that represented a therapeutic breakthrough or provide substantial improvement (including cost savings) over comparable existing medicines. Category 3 comprised drug products that provided moderate, little or no therapeutic advantage over comparable medicines (Paris and Docteur, 2007).

the incidence or grade of important adverse reactions: the mechanism of action, a new chemical entity, a different pharmacokinetic profile (PMPRB, 2009).

17. Primary factors are considered in order to assess if the new patented drug product is a breakthrough, or represents substantial, moderate or slight/no improvement relative to other drug products available in Canada. Secondary factors are then considered. These factors will be weighed by the HDAP based on sound evidence and reasonable clinical judgement. These secondary factors could result in the level of therapeutic improvement being assessed at up to the level of moderate therapeutic improvement.

18. The level of therapeutic improvement for new patented drug products with multiple approved indications or multiple uses will be based on the approved indication or use for which the drug product offers the greatest therapeutic advantage in relation to alternative therapies for the same indication/use in a significant patient population. This would exclude rare medical conditions or diseases.

19. In 2010, the PMPRB received submissions for 68 new medicines (PMPRB, 2010). The degree of innovation was assessed for 50 medicines (other drugs being still under review at the time of the publication of the annual report). Two medicines were considered as “breakthrough” and eight were assessed as having a moderate improvement.

The price review process

20. The ***price review process*** is conducted in order to “establish the maximum average potential price at introduction for the new patented drug product; and assess whether or not the price of an existing patented drug product appears to be excessive” (PMPRB, 2011).

21. The price review uses the level of therapeutic improvement to determine the maximum average potential price at introduction. Following the categorisation of the medicine, a corresponding price test is then applied to determine if the price may be considered excessive (see Table 1).

22. The price review is based on price levels furnished by the manufacturer to the PMPRB for four classes of customers (hospitals, pharmacies, wholesalers and other) in all provinces of Canada, as well as prices in the seven comparator countries, when relevant. Although the PMPRB considers the national average transaction price (ATP) and market-specific average transaction prices, it retains authority to act on the basis of any manufacturer’s price found to be excessive for any class of customers in any market in Canada. The PMBRP checked the validity of data provided by manufacturers on foreign prices in 2000 and concluded they were reliable (Paris and Docteur, 2006).

Table 1. Prices tests according to level of therapeutic improvement of new drugs (updated July 2013)

Level of therapeutic improvement	Definition of excessive introductory price
Breakthrough	National average transaction price or any market-specific average transaction price exceeds the maximum average potential price at introduction determined by the median international price comparison test (MIPC test).
Substantial improvement	National average transaction price or any market-specific average transaction price exceeds the maximum average potential price at introduction determined by the higher of: <ul style="list-style-type: none"> - The highest non excessive price of comparator products, based on a therapeutic class comparator test (TCC test); - The median international price as determined by the median international price comparison test (MIPC test).
Moderate Improvement	National average transaction price or any market-specific average transaction price exceeds the maximum average potential price at introduction determined by the higher of: <ul style="list-style-type: none"> - The highest non-excessive price of comparator products (TCC test); - The mid-point between the price just mentioned and the median international price (MIPC test). <p>If the HDAP is unable to find suitable comparators, the median international price will be used.</p>
Slight Improvement	National average transaction price or any market-specific average transaction price exceeds the highest non-excessive price of comparator products based on TCC test. <p>If the HDAP has not found any suitable comparator product, the average transaction price will be excessive if it exceeds the lower of: the lowest non-excessive price of superior drugs identified by the HDAP and the median international price.</p> <p>Introductory prices of new products which are a new presentation of an existing drug are excessive if the national average transaction price or any market-specific average transaction price exceeds the result of the reasonable relationship test.</p>
All levels of therapeutic improvement	The average transaction price of a new patented drug at the national level, for pharmacy and hospital customer classes, and for each province and territory shall not exceed the highest international price.

Source: Adapted from Patented Medicine Prices Review Board, 2009.

Frequency and consequences of excessive prices

23. In 2010, the PMPRB reviewed the prices of 68 new patented drugs, of which: 48 had non-excessive prices; two had prices that appeared to be excessive that did not trigger an investigation; seven had prices that appeared to be excessive and investigations were commenced; and eleven were still under review at the time of publication of the 2010 Annual Report. That same year, the PMPRB reviewed the

price of 1 128 existing drugs, of which: 1039 were within the guidelines or did not trigger an investigation; 78 were under investigation; nine were under review; and two were pending a price hearing (PMPRB, 2011). The executive director of the PMPRB estimated in 2011 the degree of compliance with the guidelines at 93-95% (Boudreau, 2011).

24. The Board launches an investigation into the price of a patented medicine when any of the following criteria are met (Boudreau, 2011):

- For new products: the “average transaction price”³ is 5% above the maximum average potential price; or cumulative excess revenues generated by the excessive price are greater than CAD 50 000; or a complaint was filed.
- For existing products: cumulative excess revenues generated by the excessive price are greater than CAD 50 000 or more over the life of the patent; or a complaint was filed.

When an investigation is launched, the patent holder is given the opportunity to make further written submissions to PMPRB to justify its price.

25. When the PMPRB considers a price to be excessive, there are two alternatives:

- The patentee may submit a Voluntary compliance undertaking (VCU) to reduce its price and to offset any excess revenues by making a payment to the Government of Canada; or
- The Board may hold a public hearing to determine whether there is an excessive price and if so, issue an Order for the reduction of the price of the medicine and the offset of any excess revenues by making a payment to the Government of Canada. The patentee may appeal the Board’s decision to the federal court of Canada.

26. In 2010, the Board approved 12 VCUs and an amendment to a VCU concluded in 2009. Patent holders must ensure that the prices of their patented drug products remain within the Board’s guidelines in all periods in which the drug products remain under the PMPRB’s jurisdiction.

Pricing and reimbursement in public drug schemes

27. If a manufacturer wants a new product to be reimbursed by public plans – except Québec and a few exceptions – it has to send a submission to the Common Drug Review (CDR). If the new drug is a cancer medicine, the application must be filed to the pan-Canadian Oncology Drug Review (pCODR), created in 2010 as a separate body to assess oncology drugs. In Québec, health technology assessment is undertaken by the National institute for excellence in health and social services (INESS).

28. After CDR or pCODR recommendations, each participating public drug plan may pursue evaluations to make its own decisions. Each provincial plan reviews cost-effectiveness and budget impact, makes reimbursement decisions and has the possibility to further negotiate prices with manufacturers. In Québec, the minister of health makes decisions on coverage.

3. I.e. the national average transaction price or any market-specific average transaction price.

Scientific assessment for reimbursement status

Institutions, experts and stakeholders

Common drug review

29. The Common Drug Review (CDR) was launched in 2003. The CDR is an intergovernmental⁴ collaborative body which aims at evaluating new chemical entities (NCEs) and new combinations of existing drugs to inform an official recommendation as to whether a drug should be included in the formularies of participating publicly financed drug plans.

30. The CDR is part of the Canadian Agency for Drugs and Technology in Health (CADTH), created in 1989 to assess medical services and to inform decision-makers' health technology choices. The CADTH is funded by Canadian federal, provincial and territorial governments.

31. Recommendations regarding formulary inclusion are made by the Canadian drug expert committee (CDEC),⁵ an independent advisory body composed of individuals with expertise in drug therapy and drug evaluation. CDEC is appointed by and accountable to the CADTH Chief Executive Officer. The CDEC may recommend a drug be listed, a drug be listed with criteria, a drug not be listed, or that a recommendation be deferred pending clarification of information.

Pan-Canadian Oncology Drug Review

32. The pan-Canadian Oncology Drug Review (known as pCODR)⁶ was established in 2010 by provincial and territorial Ministries of health "to bring consistency and clarity to the assessment of new cancer drugs, by looking at both clinical evidence and cost-effectiveness" (pCODR website). Assessments conducted by experts in oncology provide evidence-based recommendations to P&T for their funding decisions.

33. The pCODR has a steering committee and an expert review committee. The steering committee is composed of ten P/T representatives and two observers as follows: six senior level P/T Ministry of Health representatives (as per the funding blocks; one from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, and one from Atlantic Canada); four senior level cancer agency representatives (one from British Columbia, one from the Prairie Provinces, one from Ontario, and one from Atlantic Canada); one senior representative from the Canadian Partnership Against Cancer (as an observer); and one senior representative from the Canadian Agency for Drugs and Technologies in Health (as an observer). The co-chairs of the pCODR steering committee are chosen by the voting members from amongst the ten provincial/territorial representatives. P/T and cancer agency members are appointed to the Committee by their P/T jurisdiction/regional group, and observers will be appointed by their organization. There are no specific limits set on term of membership for pCODR Steering Committee members.

34. The pCODR Expert Review Committee (pERC) is composed of 13-16 members, including the chair as follows: five to seven cancer specialists (oncologists); one "non-oncology" physician; two pharmacologists; two health economists; one to two pharmacists; two patient representatives and a patient representative alternate. At least one of these members should also have expertise in health ethics. If

4. All Canadian jurisdictions (provinces and territories) participate in the CDR, with the exception of Québec.

5. Previously known as CEDAC, for Canadian Expert Drug Advisory Committee.

6. From April 2014, the pan-Canadian Oncology Drug Review is being transferred to the CADTH. pCODR's practices will be progressively aligned with those of the Common Drug Review.

vacancies exist due to lack of available expertise, the overall composition of the pERC will be discussed by the steering committee to determine appropriate action, which may include but is not limited, to a temporary or permanent revision in the composition of the pERC.

Québec

35. In Québec, the *Institut National d'Excellence en Santé et Services Sociaux* (INESSS) evaluates medicines and makes recommendations to the Ministry of Health. The INESSS is composed of physicians (GPs and specialists), pharmacists, a pharmaco-economist and an expert in ethics.

Assessment criteria

Common Drug Review

36. In formulating recommendations, the CDEC considers clinical studies demonstrating safety and/or efficacy of the drug in appropriate patient populations; therapeutic advantages and disadvantages of the drug relative to accepted therapy, and cost-effectiveness of the drug relative to accepted therapy.

37. Outcomes used in cost-effectiveness analysis include life years, QALYs, and important events (such as fracture, stroke, and myocardial infarction). Products that demonstrate benefits in other outcome areas (patient-reported, non-clinical outcomes) only require “cost-consequence analyses”. Surrogate markers (such as reduced cholesterol level) are considered only if evidence on final end-points (such as reductions in morbidity or mortality) is not available.

38. The Canadian Agency for Drugs and Technologies in Health publishes guidelines for submissions to the CDR (CADTH, 2013),⁷ which define submission requirements in terms of health outcomes, level of evidence and economic analysis. Figure 1 and Table 2 below summarise this information.

39. The CADTH provides guidelines for the choice of the comparator. The new therapy should be compared with the accepted therapy (existing practice), where accepted treatment would be the single most prevalent clinical practice (if there is one that is dominant). Where generic versions of the accepted therapies exist, the price of the generic drug should be used. All other reasonable alternative therapies should be at least discussed in the report (CADTH, 2013).

40. In terms of economic evaluation, several perspectives are accepted but they should be presented separately. The preferred perspective is the perspective of the publicly funded health care system, which includes direct costs for publicly funded health care system and publicly funded services outside the health system (such as home help or income transfer payments such as disability benefits). Direct costs to patients and their relatives (e.g. OOP payments, travel costs, net from income transfer payments received) might be considered. A wider social perspective may be accepted including lost productivity or costs for the employer but these costs must be reported separately (CADTH, 2006 and 2013).

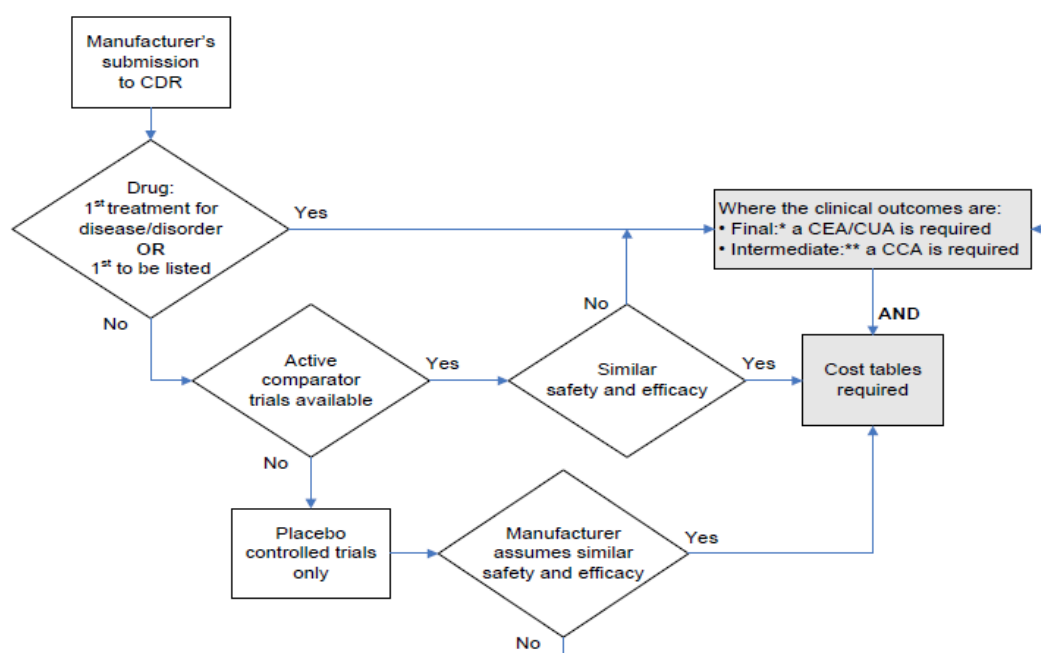
41. Analytic methods to be used depend on the measurement of outcomes (CADTH, 2013). Where clinical outcomes are final (i.e. an event that is relevant and noticeable to patients), the analytical method should be cost-effectiveness analysis (CEA) or cost-utility analysis (CUA). Where clinical outcomes are intermediate (i.e. subjective clinical measures where extrapolation of health benefits to life-years or QALY is more difficult, non-clinical endpoints, or surrogate endpoints), CEA and CUA can be used when data are

7. New guidelines have been published, see www.cadth.ca/media/cdr/process/CDR_Submission_Guidelines.pdf for 2014 guidelines (consulted on October 2014).

available to support the relationship between surrogate and final clinical outcomes, otherwise cost-consequences analysis (CCA) is required (CADTH, 2013). The preferred clinical outcomes for the CDR are final clinical outcomes. If both final and intermediate outcomes are available, the former should be used in the submitted analysis.

42. Depending on the perspective adopted, the following costs can be considered (CADTH, 2013):
- Direct health care costs: costs of treatment (administration of drug, monitoring, other costs induced through use of the drug like treatment of adverse events or complications; costs that may be impacted by treatment like specify surgery or in-hospital stay) and costs incurred beyond treatment (medical costs like cost of treating disease, complications with treatment).
 - Non-health care resources and costs, where relevant. These include patient's time (treatment time and loss of productivity), caregiver time and out-of-pocket costs (including travel expenses, child care etc.). Patient and caregiver time must be converted to costs.
43. There are no explicit weightings for severity.

Figure 1. Summary of the guidelines for the type of economic analysis to submit to the Common Drug Review, as of 2013



CEA = cost-effectiveness analysis; CCA = cost-consequence analysis; CUA = cost-utility analysis;

* Final Clinical Outcome = an event that is relevant and noticeable to patients;

**Intermediate Clinical Outcome = includes subjective clinical measures where extrapolation of health benefits to life-years or quality-adjusted life-years (QALYs) is more difficult (migraine pain score, urinary symptom scale), non-clinical endpoints, or surrogate endpoints.

Source: Canadian Agency for Drugs and Technology in Health (2013).

Table 2. Guidelines for economic analyses to be submitted to the CDEC if the drug is the first available treatment, in 2013

Clinical Outcomes	Final	Intermediate
Primary analysis	CEA/CUA	CEA/CUA CCA
Acceptable pharmacoeconomic outcomes	- Cost per LYG - Cost per QALY - Cost per event avoided	CCA: - Cost analysis - Cost per event avoided - Cost per additional response <i>Only</i> if surrogate has been shown to be a valid surrogate for a final outcome: - Cost per QALY or LYG
Comparator	Standard or current care	
Details of cost estimates	Price comparison table and health care cost tables	

CEA = cost-effectiveness analysis; CCA = cost-consequence analysis; CUA = cost-utility analysis; LYG = life-year gained; QALY = quality-adjusted life-year.

1. Guidelines published in 2014 no longer provide guidance for economic evaluation in case of intermediate outcomes. See www.cadth.ca/media/cdr/process/CDR_Submission_Guidelines.pdf.

Source: Canadian Agency for Drugs and Technology in Health (2013)

Pan-Canadian Oncology Drug Review

44. Within the pCODR, the Expert Review Committee (pERC) is responsible for providing recommendations on public funding of cancer drugs. The first mandate of pERC was to establish the methodology to evaluate the therapeutic value and cost-effectiveness of cancer drug products. The terms of reference published for pERC includes a detailed list of criteria taken into account in its deliberations. pERC decisions are based on four sets of criteria (see Table 3 below for further definitions):

- Clinical benefit;
- Patient-based values;
- Economic evaluation;
- And adoption feasibility.

45. Further definitions of these criteria and the level of evidence required for each of them is also described in pECR Terms of Reference.

Table 3. Criteria and sub-criteria definitions and sources of the pERC deliberative framework

Criteria	Criteria definition	Sub-criteria (sources)	Sub-criteria definitions
Overall clinical benefit	A measure of the net health benefit of using the drug to diagnose or manage a cancer related condition (e.g., lung cancer) or cancer care related issue (e.g., skeletal related events in metastatic disease)	Effectiveness (systematic review in the Clinical Guidance Report)	The potential health impact of the drug compared to the other drug and non-drug alternatives, measured in terms of relevant patient outcomes such as mortality, morbidity, quality of life. Magnitude, direction and uncertainty of effect should be considered.
		Safety (systematic review in the Clinical Guidance Report)	Frequency and severity of adverse effects associate with the new drug compared to other drug and non-drug alternatives.
		Burden of Illness (Clinical Guidance Report, patient advocacy group input)	Incidence, prevalence or other measure of disease burden on the population.
		Need (Clinical Guidance Report, patient advocacy group input)	Availability of an effective alternative to the drug technology.
Alignment with patient values	An assessment made after considering information on patient values	Patient values (patient advocacy group input)	Patient based values which bear on the appropriate use and impact of the drug.
Cost effectiveness	A measure of the net efficiency of the drug and companion technology compared to other drug and non-drug alternatives (no cut-off threshold)	<ul style="list-style-type: none"> • Economic evaluation • Costs, cost per QALY, cost per life year gained, cost per clinical event avoided • Uncertainty of net economic benefits (Economic Guidance Report and Pharmacoeconomic Model Review) 	A measure of the net cost or efficiency of the drug and companion technology compared to other drug and non-drug alternatives. The uncertainty of results should be considered.
Feasibility of adoption into the health system	An assessment of the ease with which the drug can be adopted into the overall health care and cancer care systems	• Economic feasibility – Budget impact assessment (evaluation of budget impact assessment in Economic Guidance Report)	The net budget impact of the new drug on other drug and health system spending, including companion testing technology.
		• Organisational feasibility (Provincial Advisory Group input)	The ease with which the new drug can be adopted, with an assessment of health system enablers and barriers to implementation, inclusive of all elements: operational, capital, human resources, legislative and regulatory requirements

Source: Pan-Canadian Expert Review Committee (2011 and 2014).

Cost-effectiveness threshold

46. Although some negative recommendations are based on the conclusion that the product is not cost-effective at the price listed, the actual cut-off point in terms of incremental cost per QALY gained (or other metric) is not made explicit. A review of 62 published drug reimbursement recommendations issued by CEDAC (former name of CDEC) showed that ICERs were considered in 40% of the cases (for 25 submissions which resulted in 12 negative recommendations and 13 positive recommendations). Positive recommendations generally had an ICER below CAD 80 000 per QALY but negative recommendations were issued for products with an ICER ranging from CAD 31 000 to CAD 137 000 per QALY. The study concluded that the implicit thresholds did not act as a clear demarcation line, because there was overlap between the ICER range for medications with a positive recommendation and the ICER range for medications with a negative recommendation (Rocchi et al., 2008 quoted by KCE, 2008).

Decision making in P/T public drug plans

47. After CDR or pCODR recommendations, each participating public drug plan may pursue evaluations to make its own decisions. Each provincial plan reviews cost-effectiveness and budget impact, makes reimbursement decisions and has the possibility to further negotiate prices with manufacturers.

48. In Ontario, for instance, the Committee to evaluate drugs (CED) assesses medicines to make recommendations on their inclusion in the Ontario Drug Benefit (public program covering seniors, beneficiaries of social assistance and people facing high out-of-pocket spending for drugs). It is composed of experts in medicine, pharmacy, pharmaco-economics and two members of the public. To assess cancer drugs, the CED collaborates with experts of the center of excellence Cancer Care Ontario. Cancer medicines can be funded through the Ontario Drug Benefit, the New Drug Funding Program or the exceptional access programme. The Ministry of Health takes decisions, which sometimes differ from CED's recommendations.

49. In Québec, the minister of health makes decisions following INESSS recommendations.

Consideration of budget impact

50. Each public drug plan uses Budget Impact Analyses (BIA) to predict the financial impact of introducing a new drug into the system. Whilst the CDR is used at a national level to aid decisions at the local level, there is no common method for BIAs and the approach differs across the public drug plans. However, the PMPRB published in 2007 guidelines for Conducting Pharmaceutical Budget Impact Analyses for Submission to Public Drug Plans (PMPRB, 2007). Inputs for the BIA include price of comparator treatments, market forecasts for the reference case and for the new drug, and drug price estimations.

Outcomes of the process

51. Gamble et al. (2011) assessed the impact of the implementation of the CDR on 11 public plan decisions: nine public plans from P&T, the federal Non-insured Health Benefits program, and Quebec drug plans – which does not participate to the CDR. Their conclusion is that the proportion of drugs listed by public plans decreased after the implementation of the CDR (though causality is not established) and that time-to-listing significantly decreased for some small provinces but may have increased for others.

52. Authors observed CDR recommendations and plan listing for innovative drugs which were granted a marketing authorisation between May 2004 and May 2009. Up to February 2010, the CDR had given positive recommendations for 45% of the 53 drugs it assessed. The percentage of drugs listed in drug plans varied from 11.5% in the Prince Edward Island to 59.8% in Québec. The majority of drugs were

listed with restriction (except in PEI): from 53% in Alberta and Manitoba to 68% in Newfoundland and Labrador. The median time-to-listing⁸ ranged from 292 days in Québec to 692 in Ontario and the median time-to-listing for drugs with listing restrictions ranged from 320 days in Québec to 815 days in Ontario.

53. Decisions made by drug plans were in accordance with CDR's recommendations (positive or negative) in the majority of cases: the concordance ranged from 60% of cases in Ontario to 90% in New Brunswick or Nova Scotia. Discordances were more often "not listed" drugs in spite of a positive recommendation from CDR, more rarely "listing" in spite of a negative recommendation from CDR (this happened four times in British Columbia, 10 times in Ontario and 12 times in Québec).

54. Hughes (2012) compared the reimbursement status in 2011 of cancer drugs in different indications in three Canadian provinces: Québec, Ontario and British Columbia. He found discordances in decisions for seven product-indications, with Quebec being in general more restrictive than other provinces.

8. Time elapsed between the marketing authorisation and listing in a given plan.

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