

**Canada's Research-Based Pharmaceutical Companies'
(Rx&D)**

***International Comparison of
Canadian Expert Drug Advisory Committee (CEDAC)
Common Drug Review (CDR) Recommendations***



November 2006

PURPOSE

This study aims at identifying the differences and similarities between listing recommendations made by national listing/reimbursement agencies and the Canadian Expert Drug Advisory Committee (CEDAC) of the Common Drug Review (CDR). It also aims at providing a rationale for those decisions where differences were observed and/or made publicly available. The goal is to give readers a tool to evaluate differences in cost-effectiveness analyses between international actors.

METHODOLOGY

The 50 reviewed drugs were selected based on recommendations made by the Canadian Expert Drug Advisory Committee of the Canadian Agency for Drugs and Technologies in Health (CADTH) up to the end of October 2006.

This analysis is restricted to a comparison between Canada, France, United Kingdom¹, Switzerland¹ and New Zealand², given that we could not confirm the reimbursement status of these drugs in many other jurisdictions. Reimbursement status of these drugs is also included for Sweden³ and Australia for illustrative purposes only and is not discussed in key findings below. Finally, we also looked at two randomly selected American states (Ohio and Oregon) to determine the number of plans under Medicare that cover these CDR reviewed drugs.

SUMMARY DESCRIPTION OF JURISDICTIONS ANALYZED

Canada

On September 1, 2003, a permanent Common Drug Review (CDR) process was implemented by the Canadian Coordinating Office of Health Technology Assessment (CCOHTA), thereby fulfilling a September 2001 commitment by the Federal/Provincial/Territorial (F/P/T) Conference of Ministers of Health to increase collaboration related to pharmaceutical benefits plan management. CCOHTA was renamed the Canadian Agency for Drugs and Technologies in Health (CADTH) in April 2006.

¹ The U.K. and Switzerland are home to some large trans-national pharmaceutical corporations. This provides industrial policy benefits to those jurisdictions. The UK and Switzerland each has its own way of managing health costs, but the evidence shows that making more pharmaceutical choice available does not impede their ability to manage costs.

² New Zealand is the home of Reference-based Pricing and has quite a restricted drug list. The budget for pharmaceutical expenditure is fixed for the year and cannot be exceeded according to Wayne McNee, Chief Executive, Pharmaceutical Management Agency, New Zealand. This limits New Zealand's ability to add new drugs to the formulary.

³ "Approximately 2 000 currently reimbursed medicines have not yet been tested against the new system for the reimbursement of medicines which entered into force in October, 2002. In the transition to a new system it was not practically possible to simultaneously review all medicines. The medicines which had been reimbursed in the old system were therefore allowed to maintain their reimbursement status until further notice. The review of the entire reimbursement list will take approximately five years. The review commenced at the end of 2003 [...]" from Läkemedelsförmånsnämnden (LFN) [Swedish Pharmaceutical Benefits Board], *2,000 pharmaceuticals reviewed for reimbursement*, p. 1.

As part of the CDR process, members of the Canadian Expert Drug Advisory Committee (CEDAC) conduct critical appraisals of new drugs (new chemical entities and new combinations) based on the best available clinical and pharmacoeconomic evidence and make recommendations whether to list a new drug for reimbursement to participating federal, provincial and territorial (F/P/T) drug benefit plans in Canada. These drug benefit plans make the final decisions on whether to reimburse or not.

United Kingdom - National Institute for Health and Clinical Excellence (NICE)

“NICE is an independent organization responsible for providing national guidance on treatments and care to the National Health Service (NHS) in the UK. Like the CDR, NICE evaluates the clinical- and cost-effectiveness of pharmaceuticals, and then issues evidence-based recommendations (called ‘guidance’ and ‘guidelines’) to local NHS organizations. NICE also relies on a combination of internal and external expert advice to inform final recommendations made by a committee of experts, the Technology Appraisal Committee.

NICE was not designed with the intention of reviewing all pharmaceutical products, nor all new pharmaceutical products. Instead, NICE undertakes a pharmaceutical review at the request of the Department of Health. Requests for evaluations focus on both new and established technologies for which “national guidance” would be beneficial, including those that are likely to be important to the health system (in terms of costs or health impact), those where availability and access varies across the NHS, and those for which the appraisal is likely to be controversial (in terms of clinical or cost-effectiveness). Once NICE is directed to review a drug, it works with the NHS Health Technology Assessment (HTA) Program to identify independent academic centers most suited to undertake an initial critical assessment of the drug.”⁴

Switzerland

Reimbursement status corresponds to the inclusion on the “*positive list*”. It is determined by the BSV (Federal Social Insurance Agency) assisted by the EAK (Federal Drug Commission) using the following criteria:

- Medical need, reliability and cost-effectiveness
- Efficacy in comparison with other products in the same therapeutic group
- Cost per day or total cost in comparison with others in the same therapeutic group
- Prices of the product in comparator countries: Denmark, Germany, Netherlands
- R&D cost

Typically it takes 1-2 years to obtain a reimbursement status.

⁴ *The Common Drug Review: a NICE Start for Canada*, McMahon, Morgan, Mitton, *Health Policy*, 2006 Aug; 77(3):339-51. Epub 2005 Oct 6.

France (centralized funding)

The Transparency Commission (*Commission de la Transparence* or CT) evaluates the medical benefit provided by a drug in a measure called *Amélioration du Service Médical Rendu* (ASMR). The CT is a scientific body whose primary focus is on the medical benefit provided by a drug, and it is composed as follows:

- Chairman + 2 vice chairmen
- A representative of the Department of Health
- A representative of the Department of Social Security
- A representative of the French health product safety agency (AFSSaPS)
- A representative of the National Association of Physicians
- A representative of the National Association of Pharmacists
- 4 representatives of third-party payers
- A representative of the French equivalent of Rx&D (LEEM)
- 6 scientific experts chosen according to their medical or scientific expertise

The CT makes its recommendations to the *Comité économique des produits de santé* (CEPS), which would be the Canadian equivalent of the PMPRB (except that negotiations between companies and the CEPS are not public). The CEPS is free to follow the CT's recommendations or not when determining price/reimbursement levels. The CEPS acts in accordance with sectoral agreements (*Accords Sectoriels* (AS)) developed and concluded in collaboration with the pharmaceutical industry in France.

NOTES TO READERS

International Comparison (ANNEX A) - Listing Decisions: It is essential to understand the color coding specific to each jurisdiction if one is to draw appropriate conclusions from this first table (for details, see notes below table).

Detailed recommendations (ANNEX B): This table lists a summary of the detailed recommendations concerning those preparations recommended not to be reimbursed in Canada and recommended for reimbursement in France. Canada, France and the UK were the only jurisdictions offering detailed reasons for recommendation. However, given that NICE did not systematically review all drugs, we have limited our bilateral comparison to Canada and France as a judicious compromise between rigour and coverage.

United States (ANNEX C): For illustrative purposes only, we concentrated on United States 'Medicare' coverage only because it more closely resembles Canadian public drug coverage. Despite these similarities, there are still significant differences between Canadian and American public plans. For one, in the USA, those enrolled for prescription drug coverage under Medicare can choose their provider and the type of plan they wish to benefit from.

Our preliminary conclusions show that a significant⁵ number of plans in Oregon and Ohio make 18 out of 24 non recommended drugs in Canada available for coverage on their plans. While more plans cover the non recommended CDR reviewed drug in that particular state, it is understood that each plan may have conditions attached to the use of particular drugs in accordance with clinical practice guidelines or require prior authorization, limit quantities or require step therapy. For example, in the case of Ohio, various drug plans list drugs as a Tier 1, Tier 2, Tier 3 or Tier 4 drug (Tier 1 has the lowest co-payment). The number of plans that list a particular drug as Tier 1 through 4 varies.

KEY FINDINGS

Out of the 50 drugs reviewed, CEDAC recommended only 26 for listing while Sweden reimburses 41, Switzerland is reimbursing 40; France recommended 29 for reimbursement and the UK were reimbursing 38 out of those 50 drugs. A detail of the decisions can be found under the table “CDR International Comparison” in **ANNEX A**.

- In summary, as of October 30, 2006, CEDAC recommends around 58% fewer drugs for reimbursement than Sweden, 54% less than Switzerland, 46% less than the UK and 12% less than France. CEDAC recommends 63% more drugs than Australia and 333% more drugs than New Zealand.

The next step was to identify the reasons that could explain such a significant difference in availability of medicines. Only France and Canada published detailed reasons for listing recommendations. We found troubling differences when looking at some drugs not recommended for listing in Canada but that were recommended for listing in France.

The results of this comparison are summarized in the table entitled “Detailed recommendations for those preparations recommended for listing in France and recommended not to be listed in Canada” in **ANNEX B**.

France’s Approach:

The data show that France and CEDAC recommend roughly the same number of drugs for reimbursement. However, there are differences in what is covered. The French Transparency Commission (*Commission de la transparence* or CT, hereinafter) is the only other body that publishes publicly available, detailed final decisions for all drugs recommended for reimbursement.

What the CT does and CEDAC doesn’t:

Interestingly, the first step in their review is to establish what kind of a burden for the French health care system the preparation’s target condition represents. The burden is measured in the form of a threat to a vital prognostic, or the degree to which it deteriorates the quality of life of patients. A drug that relieves a high burden will have a greater SMR (*service médical rendu*) rating.

⁵ 70% or more.

For conditions in which there are many types or degrees of severity, the CT may issue a different SMR rating for each (ex: diabetes type 1 & 2). The CT then evaluates a desirable/adverse effect ratio. The cost effectiveness perspective is taken into consideration while comparing the reviewed drug with existing treatments and rating the ASMR (*amelioration du service médical rendu*) or improvement over existing therapies.

There are 6 ASMR categories (comparable to the PMPRB's 3 categories) that will later be taken into consideration when negotiating prices. Another major difference is that the CT will issue a "best prescribing practice" according to the ASMR in its final recommendation. Based on cost effectiveness, the preparation will be recommended as a first or second line therapy as long as it brings similar or improved therapeutic outcomes to patients. A second line therapy would be used by doctors in the specific case where first line therapies did not work or where there are specific counter indications for the individual.

CEDAC: Cost effectiveness as a sine qua non condition

In many cases where drugs have shown a statistically and clinically significant improvement over existing therapies, they were not recommended on the grounds of poorly demonstrated cost effectiveness or due to an "inconclusive pharmacoeconomic study". In this way CEDAC believes it "supports decision makers who are exploring what technologies *should* be used to achieve the best outcomes both on patient health and the health care system"⁶.

On the contrary, this leaves Canadian physicians with restricted choices and does little to help patients who may not respond well to an existing therapy. This approach is in stark contrast to the French *Transparency Commission's* approach, which places a more appropriate weight on consideration for individual patient needs and an appreciation of the therapeutic value of medicines.

Finally, we noted that when provincial plans follow a recommendation to list, there is an average delay of more than 216 days between CDR's recommendation and the provinces' decision, illustrating the inefficiency and redundancy of the current system.

CONCLUSION

Why them and not me?

- CDR's restrictive criteria have left Canadian patients with about half the choices in medication their French, Swiss, Sweden or British counter-parts may benefit from.

More Choice does not Mean More Cost

- Choice does not translate *de facto* into costs. The Switzerland and Sweden examples illustrate this well:

⁶ <http://www.cadth.ca/index.php/en/media-centre>

- In Switzerland 40 / 50 drugs are reimbursed against 26 / 50 recommended for reimbursement in Canada, yet, total drug expenditure per capita in Switzerland is about 21% less than in Canada (498\$/capita against 634\$/capita respectively⁷, in current CAD PPP). And it is important to remember that a positive CEDAC recommendation does not guarantee provincial reimbursement.
- In Sweden, the facts are even more convincing: 41 of the studied drugs are made available for reimbursement in Sweden (national level) and yet total drug expenditure per capita in Sweden is about 46% less than in Canada (340\$/capita against 634\$/capita respectively⁸, in current CAD PPP).

Clearly, if other countries can offer more choice and maintain lower per capita expenditures on drugs, it is time Canadian governments find better ways to address the factors⁹ that contribute to the sub-optimal use of medicines.

While further research regarding the differences in medical practice between these countries would be required to determine why per capita costs on drugs are lower in Switzerland and Sweden – despite the broader access to a wider range of drugs – it is possible that a more enlightened approach to better managing utilization of medications (as opposed to restricting access through uninspired cost containment measures) could explain, in part, the differences in level of access between these two European countries and Canada.¹⁰

- Allowing a broader choice of medicines for patients, as many other governments throughout the world have done, recognizes that “One drug does not fit all” and incremental innovation has its advantages:
 - “Newer agents of a class, or new formulations of existing agents, often enable new cost-effective uses or more efficient treatment for the original indication. Incremental pharmaceutical innovations can reduce costs for health care providers and insurers and in some cases can improve employee productivity. Savings can come from reduced overall treatment costs due to shortened or eliminated hospital stays, less need for surgery, and increased worker efficiency and less absenteeism.”¹¹

⁷ CIHI – Drug Expenditure in Canada 1985-2005, p32 Table 5 and OECD Health Data 2005, October 2005 version.

⁸ CIHI – Drug Expenditure in Canada 1985-2005, p32 Table 5 and OECD Health Data 2005, October 2005 version.

⁹ Use of non prescribed medicines; Wrong choice of medicine; Appropriate choice of medicine, but wrong dose; Adverse reaction with other medicines; Duplication of prescriptions; Adverse reaction with pre-existing known/unknown condition; Lack of patient monitoring and/or follow-up: List excerpted from Presentation by Johanne Monette, MD, FRCPC, MSc, Solidage, Groupe de Recherche Université de Montréal/Université McGill sur les services intégrés pour les personnes âgées, Centre d’Épidémiologie Clinique et de la Recherche en Santé Publique, Division de Gériatrie, Hôpital général juif, Université McGill; presented at *Symposium sur l’utilisation optimale du médicament*, May 20 and 21, 2004, Québec.

¹⁰ This is achieved notably through the introduction of local demonstration projects aimed at improving the appropriate use of medications.

¹¹ Albert Wertheimer, Richard Levy and Thomas O’Connor: “Too Many Drugs? The Clinical and Economic Value of Incremental Innovations” in *Investing in Health: The Social and Economic Benefits of Health Care Innovation*, Volume 14, p77-p118, Elsevier Science Ltd, 2001.

- Restricting access, on the other hand, may have untold implications for patients and overall costs in the health care system
 - “Restricted formularies based on uncritical assumptions about therapeutic equivalence may lead to inferior care and therefore inefficient cost control, as when, for example, a patient completes a failed trial of a formulary drug when another drug in the same class would have been initially effective.”¹²

Provincial Summary

- Public payers do not always follow CDR’s recommendations (whether positive or negative). This reinforces the duplication of the CDR process and shows that provinces continue to make health care decisions.
- The CDR Review process averages 187 days. The average time to listing (TTL) following a positive CEDAC recommendation is 216 days.¹³ This means that it takes an average of 403 days from the date of a CDR submission to get a drug listed on a public formulary in Canada. This has a number of implications:
 - The CDR process has been unsuccessful in eliminating redundancies of drug review processes on a provincial level
 - Public access to therapy that has been determined to be cost-effective by very high standards is being delayed. This means that:
 - Patients do not have appropriate access to drugs on a timely basis; and
 - Governments are foregoing the benefits of cost-effective drug therapy for over a year, resulting in increased costs to taxpayers.

¹² Frederick K. Goodwin, M.D., Impact of Formularies on Clinical Innovation, *J Clin Psychiatry* 2003;64[suppl.17]:11–14).

¹³ CDR Tracker, Wyatt Health Management, October 30, 2006.

ANNEXES
***International Comparison of
Canadian Expert Drug Advisory Committee
(CEDAC)
Common Drug Review (CDR)
Recommendations***

**The information in these annexes is
accurate as of October 30, 2006 (except
where indicated)**

CDR International Comparison

Brand	Indications	Manufacturer	CDR	UK	FR	CH	NZ	Sw	Au
Adderall XR	ADDH and narcolepsy in children.	Shire							
Advicor	Cholesterol	Oryx	List						
Aldurazyme	Enzyme deficiency	Genzyme							
Amevive	Chronic plaque psoriasis	Lundbeck				Lwc			
Aptivus	HIV	Boehringer-Ing	Lwc						
Avodart	Benign prostatic hyperplasia	GSK	Lsm						
Axert / Almogran?	Migraine	Janssen-Ortho	Lsm						
Caduet	Hypertension, chronic stable angina	Pfizer	Lwc						
Ciprodex	Urinary infections	Alcon							
Combigan	Intraocular pressure	Allergan	Lwc						
DuoTrav	Oral: high blood pressure; ophthalmic: open-angle glaucoma	Alcon Canada	Lwc						
Ebixa	Alzheimer's type dementia	Lundbeck				Lwc			
Enablex	Urinary infections	Novartis							
Evra	Contraception; menopause	Janssen							
Fabrazyme	Enzyme deficiency	Genzyme							
Forteo / Forsteo	Osteoporosis	Lilly						Lwc	
Fosavance	Osteoporosis	Merck							
Gynazole.1	Infections caused by Candida	OM Pharma							
Humira	Osteoporosis	Abbott	Lwc						
Iressa	Lung cancer	AstraZeneca							
Kivexa	HIV-1 infection	GSK	Lsm						
Lantus	Diabetes (type I and II)	Aventis						Lwc	
Levemir	Diabetes (type I and II)	Novo Nordisk						Lwc	
Lyrica	Neuropathic pain - diabetes	Pfizer							
Macugen	Visual function	Pfizer							
Myfortic	Organ rejection	Novartis	Lsm						
Neulasta	Bone marrow transplant; cancer	Amgen	Lwc						
Norprolac Resub	High levels of the hormone prolactin- lactating women	Ferring	Lwc						
NovoMix 30	Diabetes	Novo Nordisk							
Pantoloc M	Gastro-intestinal	Altana	Lsm						
Pegasys RBV	Chronic hepatitis C	Roche	Lsm						
Raptiva	Chronic plaque psoriasis	Serono	Lwc					Lwc	
Relpax	Migraine with or without aura in adults	Pfizer							
Remodulin Resub	Pulmonary arterial hypertension - NYHA Class II - IV symptoms	Opopharma	Lwc						
Replagal	Enzyme deficiency	Drac							
Reyataz	HIV-1 infection	BMS	Lsm						
Sensipar / Mimpara	Secondary hyperparathyroidism; thyroid cancer	Amgen							
Somavert	Acromegaly	Pfizer							
Strattera	ADHD	Lilly							
Tarceva	Lung cancer	Roche	Lwc			Lwc			
Telzir	HIV - AIDS	GSK	Lsm						
Teveten Plus	Blood pressure	Solvay Pharma	Lsm						
Trelstar / Decapeptyl	Prostate cancer	Watson Labs	Lsm						
Trosec / Regurin	Overactive bladder	Oryx Pharma	Lwc						
Truvada	HIV-1 infection in adults	Gilead	Lwc						
VFEND Resub	Esophageal candidiasis, lung infections	Pfizer	Lwc						
Viread Resub	HIV-1 infection	Gilead	Lwc						
Xolair	Asthma	Novartis						Lwc	
Yasmin	Contraception; menopause	Schering	List						
Zavesca	Enzyme deficiency	Actelion							
Recommended			26	38	29	40	6	41	16
Total			50	50	50	50	50	50	50
Percentage			52.0%	76.0%	58.0%	80.0%	12.0%	82.0%	32.0%

LEGEND: Lwc=List with criteria/conditions
Lsm=List in similar manner
Details regarding colours on next page

White Spaces	Listing information, at the time of publication, could not be independently confirmed Listing statistics may be understated
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CDR International Comparison

Sources:

Canada http://www.cadth.ca/media/cdr/recommendations/Drug_Plans_Response_to_CEDAC_Recommendations_2006june7.pdf

Source: CEDAC (Canadian Expert Drug Advisory Committee). Color coding: CEDAC listing recommendations are red=do not list and green for any kind of favorable listing recommendation.

France http://www.afssaps.fr/html/has/sgt/hm/avis/html/act00a_z.htm

Source: Commission de la Transparence. Color coding: the CT database shows the positive recommendations for reimbursement in green, and the ones either not recommended for reimbursement or the ones that have no reimbursement status, in orange. (Web site last updated Dec 8th 2005)

UK <http://www.bnf.org/bnf/>

Source: The British National Formulary. Color coding: the British National Formulary database shows drugs that are reimbursed under the British Scheme in green and those that are not reimbursed or the ones that have no reimbursement status in orange.

Switzerland <http://www.kompendium.ch/Search.aspx?lang=fr>

Source: Le Compendium suisse des médicaments. Color coding: the CMS shows the reimbursed drugs (with or without restriction) in green, the drugs not reimbursed in red and those that have no reimbursement status in orange.

New Zealand <http://www.pharmac.govt.nz/interactive/index.asp>

Source: PHARMAC. The color coding: PHARMAC's database shows the reimbursed drugs (with or without restriction) in green and the drugs either not listed or not launched in New Zealand in orange.

Sweden <http://www.lfn.se>

Source: Läkemedelsförmånsnämnden (LFN) [Pharmaceutical Benefits Board]; N.B. NR - Contraceptives are not reimbursed

Australia <http://www9.health.gov.au/pbs/scripts/listgpindex.cfm?IndexType=P&StartCode=A>

Source: PBS. The color coding: the Pharmaceutical Benefits Schedule's database shows the reimbursed drugs (with or without restriction) in green and the drugs either not listed or not launched in Australia in orange.

Detailed recommendations for those preparations recommended for listing in France and recommended not to be listed in Canada

	Ca	CDR - CADTH (Canada)	Fr	CT (France) [Our translation from original French]
Ebixa		1. 2/3 RCTs reported statistically significant improvement results. Insufficient scientific evidence to establish clinical importance. 2. Time to institutionalization was only reported in studies where low rates were observed. 3. Pharmacoeconomic study is inconclusive.		In severe cases of Alzheimer's disease, EBIXA (memantine) provides significant improvement in the medical service rendered (level II) when providing treatment to patients. In moderately severe cases, EBIXA (memantine) does not provide an improvement in the medical service rendered (level V) in relation to the reference compounds in the absence of comparative studies. The level of medical service rendered by EBIXA is significant. The efficacy/adverse reactions of this drug is modest. Reimbursement rate: 65%
Fabrazyme		1. Trials failed to show the benefit of agalsidase beta. 2. Renal function improved with no statistical difference. 3. No difference in pain control. 4. No significant improvement in any of the clinically oriented endpoints... 5. Validity and generalizability are difficult to assess. 6. Infusion reactions. 7. Antibodies may develop. 8. Per-patient treatment cost is high.		The level of medical service rendered by this drug is significant. FABRAZYME represents significant improvement in the medical service rendered (level II), in the treatment of FABRY's disease.
Forsteo Forsteo		1. Randomized trial showed a decrease in vertebral and non-vertebral fracture rates. 2. Results of an unpublished randomized trial were considered. 3. No trial with approved dose provided evidence of a decrease in fracture rates in men. 4. No cost effectiveness evidence compared to anti-resorptive therapy. 5. Cost effectiveness was not demonstrated. 6. In rats, increased evidence of osteosarcoma.		The condition treated with this drug is characterized by progressive disability and/or a deterioration in quality of life as well as sometimes serious complications. This drug is part of curative treatment. The efficacy/adverse reactions of this drug is significant. The medical service rendered by FORSTEO is significant. In women with at least two vertebral fractures and a vertebral bone mineral density T score of less than -2.5, teriparatide (FORSTEO) provides a moderate improvement in the medical service rendered (IMSR III) as compared to bisphosphonates. Reimbursement rate: 65%
Lantus		1. 20 RCTs did not find (according to CEDAC) statistically or clinically significant improvements when compared to NPH insulin. 2. Nosignificant differences in the incidence of severe hypoglycemia. 3. Inconsistent results. 4. Quality of life improvement is inconsistent for T1 diabetes and insignificant for T2. 5. 3X as costly as NPH insulin.		IMSR III (moderate) in relation to NPH insulin in terms of tolerance with less nocturnal hypoglycemia and in terms of convenience of use (one injection per day without resuspension). Type 1 diabetes: This drug is a first-line drug. Type 2 diabetes: This is a second-line drug. There are alternatives. The level of medical service rendered is significant. Reimbursement rate: 65%
Lyrica		1. 12 RCTs were evaluated. Most compared with placebo, not enough with comparative treatment. 2. Statistically significant improvement compared to placebo. 3. High withdrawal rates decreases confidence in the results. 6. Cost of treatment is higher than comparators.		LYRICA does not provide any improvement in the level of medical service rendered (IMSR V) as compared to the usual treatments for peripheral neuropathic pain. The medical service rendered by LYRICA in treating peripheral neuropathic pain is significant. The medical service rendered by LYRICA in treatment associated with focal seizures is significant. The efficacy/adverse reactions is modest. Reimbursement rate: 65%
Relpax		1. Eleven randomized controlled trials compared eletriptan to placebo and other existing triptans and showed that it is more effective in relieving migraine. 2. The drug may increase the risk of adverse effect. 3. Eletriptan has not clearly shown to be more cost-effective than other triptans.		The condition treated by these drugs is characterized by progressive disability and/or a marked deterioration in quality of life. The efficacy/adverse reactions of this drug is significant. Eletriptan is a second-line drug in the treatment of migraines. The level of medical service rendered is significant. RELPAX does not provide an improvement in the medical service rendered as compared to the Triptans. Reimbursement rate: 65%
Replagal		1. Improvement in proportion of glomeruli, significant difference in renal function favoring the treatment, better LV mass. 2. Infusion reactions. 3. Antibodies may develop. 4. Difficulty to assess the validity and generalizability of survey data. 5. Cost of treatment. <u>Note:</u> The drug has demonstrated a biological effect in a debilitating disease for which patients have no other options to treat their underlying disease.		The condition treated by this drug causes a decrease in life span and drastically alters the patient's quality of life. This is a curative first-line drug. The efficacy/adverse reactions of this drug is moderate. FABRAZYME (agalsidase beta) is the only other treatment option. The level of medical service rendered by this drug is significant. REPLAGAL and FABRAZYME share, when providing treatment for FABRY's disease, significant improvement in the medical service rendered (level II).

Detailed recommendations for those preparations recommended for listing in France and recommended not to be listed in Canada

Sensipar Mimpara	1. Nine double-blind randomized controlled trials found that Cinacalcet significantly reduced parathyroid hormone and serum calcium levels. 2. There was insufficient evidence in these trials that cinacalcet has any effect on clinically important outcomes. 3. The cost: 4000\$ to 23,500\$ per year.		MIMPARA provides significant improvement in the medical service rendered (IMSR II) in terms of efficacy, in the treatment strategy for hypercalcemia in patients with cancer of the parathyroid, in cases of failure of or negative reactions to parathyroidectomy. Reimbursement rate: 65%
Zavesca	1. Lack of adequate control group and focus on biochemical outcome. 2. 90% of patients had diarrhea, 50% had weight loss, poor follow-up. 3. Better evidence required to justify cost.		Gaucher's disease is a rare and serious illness that involves a deterioration in quality of life and that calls into question the vital prognosis. This drug is part of a curative treatment. It's efficacy/adverse reactions is modest. This is a second-line drug reserved for failed treatments or cases in which enzymatic replacement (CEREZYME) cannot be used. There is only one medicinal alternative. The level of medical service rendered by this drug is significant. This drug may attract interest in rare cases in which individuals cannot be treated with CEREZYME.

CDR/CEDAC

Source: http://www.cadth.ca/index.php/en/cdr/recommendations/search?&order_field=brand_name

CT Source: <http://www.afssaps.fr/html/has/sgt/hm/avis/html/act00000.htm>

Recommended for listing
 Not recommended

US Reimbursement (To date: Nov. 30, 2006)

Brand	Manufacturer	CDR	OHIO		OREGON	
			# Plans	% Plans	# Plans	% Plans
Adderall XR	Shire		109	76.8%	84	71.8%
Advicor	Oryx	List	93	65.5%	68	58.1%
Aldurazyme	Genzyme		103	72.5%	73	62.4%
Amevive	Lundbeck		85	59.9%	64	54.7%
Aptivus	Boehringer-Ingelheim	Lwc	140	98.6%	116	99.1%
Avodart	GSK	Lsm	135	95.1%	104	88.9%
Axert / Almogran?	Janssen-Ortho	Lsm	75	52.8%	62	53.0%
Caduet	Pfizer	Lwc	101	71.1%	76	65.0%
Ciprodex	Alcon		117	82.4%	92	78.6%
Combigan	Allergan	Lwc	NL	N/A	NL	N/A
DuoTrav	Alcon Canada	Lwc	NL	N/A	NL	N/A
Ebixa	Lundbeck		NL	N/A	NL	N/A
Enablex	Novartis		100	70.4%	81	69.2%
Evra	Janssen		NL	N/A	NL	N/A
Fabrazyme	Genzyme		133	93.7%	113	96.6%
Forteo / Forsteo	Lilly		142	100.0%	117	100.0%
Fosavance	Merck		NL	N/A	NL	N/A
Gynazole.1	OM Pharma		78	54.9%	60	51.3%
Humira	Abbott	Lwc	139	97.9%	115	98.3%
Iressa	AstraZeneca		111	78.2%	96	82.1%
Kivexa	GSK	Lsm	NL	N/A	NL	N/A
Lantus	Aventis		139	97.9%	116	99.1%
Levemir	Novo Nordisk		117	82.4%	89	76.1%
Lyrica	Pfizer		138	97.2%	117	100.0%
Macugen	Pfizer		NL	N/A	NL	N/A
Myfortic	Novartis	Lsm	109	76.8%	95	81.2%
Neulasta	Amgen	Lwc	114	80.3%	87	74.4%
Norprolac	Ferring	Lwc	NL	N/A	NL	N/A
NovoMix 30	Novo Nordisk		NL	N/A	NL	N/A
Pantoloc M	Altana	Lsm	NL	N/A	NL	N/A
Pegasys RBV	Roche	Lsm	NL	N/A	NL	N/A
Raptiva	Serono	Lwc	114	80.3%	86	73.5%
Relpax	Pfizer		112	78.9%	87	74.4%
Remodulin	Opopharma	Lwc	55	38.7%	45	38.5%
Replagal	Drac		NL	N/A	NL	N/A
Reyataz	BMS	Lsm	140	98.6%	112	95.7%
Sensipar / Mimpara	Amgen		142	100.0%	117	100.0%
Somavert	Pfizer		135	95.1%	113	96.6%
Strattera	Lilly		126	88.7%	97	82.9%
Tarceva	Roche	Lwc	142	100.0%	117	100.0%
Telzir	GSK	Lsm	NL	N/A	NL	N/A
Teveten Plus	Solvay Pharma	Lsm	74	52.1%	62	53.0%
Trelstar	Watson Labs	Lsm	89	62.7%	79	67.5%
Trosec	Oryx Pharma	Lwc	NL	N/A	NL	N/A
Truvada	Gilead	Lwc	140	98.6%	116	99.1%
VFEND	Pfizer	Lwc	108	76.1%	86	73.5%
Viread	Gilead	Lwc	142	100.0%	117	100.0%
Xolair	Novartis		100	70.4%	75	64.1%
Yasmin	Schering	List	98	69.0%	97	82.9%
Zavesca	Actelion		89	62.7%	74	63.2%
Total Number of Plans in the State			142		117	

While higher percentages in green mean that more plans cover the drug in that particular state, it is understood that each plan may have conditions attached to the use of particular drugs in accordance with clinical practice guidelines. For example, in the case of Ohio, various drug plans list drugs as a Tier 1, Tier 2, Tier 3 or Tier 4 drug (Tier 1 has the lowest co-payment). The number of plans that list a particular drug as Tier 1 through 4 varies. These drug plans may also require prior authorization, limit quantities or require step therapy.

How and What are they Looking for: a CEDAC / CT / NICE Comparison

	Canada	France	UK
Name	<i>Canadian Expert Drug Advisory Committee</i>	<i>Commission de la transparence</i>	<i>National Institute for Health and Clinical Excellence</i>
Criteria	<p>The criteria that CEDAC considers in making recommendations include:</p> <p>clinical studies assessing the <u>efficacy and safety</u> of the drug in appropriate populations; <u>therapeutic advantages and disadvantages</u> relative to current accepted therapy; <u>cost-effectiveness</u> relative to current accepted therapy.</p> <p>CEDAC may recommend that a drug be listed, a drug be listed with criteria or conditions, or a drug not be listed, or a recommendation may be deferred pending clarification of information.</p>	<p>The notice from the Commission includes:</p> <p>The appraisal of the appropriateness, in relation to the medical service rendered (IMSR), of the registration of the medication on the lists or one of the lists; a comparison of the medication, in terms of medical service rendered, with the reference compounds from the pharmacotherapeutic class; the appraisal of the improvement in the medical service rendered (IMSR) by the medication; an appraisal of the terms and conditions for use of the medication, particularly, the length of treatment, dosage and other indications useful for proper drug prescription; and the estimate of the number of patients in connection with treatment indications for which the Commission finds that the registration is justified, based on the epidemiological data available.</p>	<p>NICE evaluates:</p> <p>-the clinical- and cost-effectiveness of pharmaceuticals (old and new alike)</p> <p>NICE issues:</p> <p>-evidence-based recommendations (called 'guidance' and 'guidelines') to local NHS organizations</p>
Is Recommendation's implementation mandatory?	no	no	yes
Emphasis on Cost effectiveness?	Explicit	Indirectly taken into consideration in ASMR and compared to existing therapies, but not in the case of an orphan drug (ASMR will point to a specific pricing category)	Explicit (QALY)
Measure of Health benefit	QALY	SMR	QALY
Review process is:	Systematic	Systematic	Case by case

Source: *The Common Drug Review: A NICE start for Canada?* By Meghan McMahon, Steve Morgan and Craig Mitton, Health Policy, 2006 Aug; 77(3):339-51. Epub 2005 Oct 6.

Source: <http://afssaps-prd.afssaps.fr/html/has/sgt/index.htm>* [Our translation from the original French]