



**Forum I: Options for Funding Drugs  
for Rare Disorders under  
Ontario's New Drug Legislation**

**Summary Proceedings**

**Tuesday October 24, 2006**

**9:00 am - 2:00 pm**

**Ontario Arts Council Boardroom**

**151 Bloor Street West, Toronto Ontario**

**Meeting Room – 6<sup>th</sup> Floor Board Room**

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**Forum I: Options for Funding Drugs for Rare Disorders  
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**Welcome and Objectives of Forum**

Durhane Wong-Rieger, CORD

**Access to Drugs for Rare Disorders (Current Mechanisms)**

- I. **Andreas Laupacis** (former Chair, CEDAC): **Canadian review mechanisms and applications to drugs for rare disorders: CDR/CEDAC Experience**
- II. **Peter Brenders**, BIOTECanada: **International Impact of Orphan Drug Policies: USA, Europe, Japan, Australia**
- III. **Ed Koning**, Canadian Fabry Association: **Case Studies (recent reviews)**

**Access to Drugs for Rare Disorders (Challenges and Emerging Strategies)**

- IV. **Chris Ward**, Ward Health: **Individualized Medicines**
- V. **Amir Attaran**, Institute of Population Health, University of Ottawa: **Ethical and Legal Issues**
- VI. **Mary Kim**, Canadian Arthritis Patient Alliance: **Ontario's Transparent Drug System for Patients Act**

**Current and Pending Drugs for Rare Disorders**

- Presentation of Case studies
- Implications within Canadian access framework

**CORPORATE PANEL**

- A. **Novartis: Philippe Martin-Widmer**
- B. **Genzyme: Monty Keast**
- C. **Actelion: Louise Boisjoly**
- D. **Pfizer: Catherine Fitzsimon**

**PATIENT PANEL**

- E. **Betty McPhee**
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**Issues Related to Access to Drugs for Rare Disorders**

**Access under Ontario's Transparent Drug System for Patients Act**

**Conclusions and Next Steps**

**Participant List**

## **Forum I: Options for Funding Drugs for Rare Disorders under Ontario's New Drug Legislation**

### Objectives:

- Review Ontario patient access to drugs for rare disorders within Canadian and international context
  - Review developing framework of "Expensive Drugs for Rare Disorders" under National Pharmaceutical Strategy
  - Develop understanding current and pending drugs for rare disorders: cases studies
  - Develop understanding of issues related to access to drugs for rare disorders
  - Develop recommendations for options toward appropriate access, including review process, funding and other access options, and on-going monitoring and evaluation
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### **Access to Drugs for Rare Disorders (Current Mechanisms)**

#### **I. Andreas Laupacis (former Chair, CEDAC): Canadian review mechanisms and applications to drugs for rare disorders: CDR/CEDAC Experience**

The issue of paying for expensive drugs is not unique to rare disorders. In fact, there is a cancer drug funding meeting later this morning which is the reason that I will not be able to stay for the entire session today.

Like many of you here, I am also a father, husband, and son (or rather a parent, spouse, and child). I have two children who we have decided to send to private school. So, while we know that funding for healthcare is important, we also have to ensure funding for other needs, for education, safety, and roads.

The issue of funding drugs for rare disorders is a complex ethical societal dilemma. Levels of evidence are different for treatments of rare disease. Even when a treatment is proven to be effective, it can be hard to get, as in the case of hip replacement surgery, or home care. So it's no surprise that access can be a problem where evidence is less convincing.

In the case of Fabryzyme's review by the CDR, we did not even want to accept it. It was clear that based on our criteria, even before the review, Fabryzyme would not meet standards of cost-effectiveness. But they gave it to us, so we reviewed it. Based on CDR criteria, it is clear that unless the treatment is curative, it will not meet conventional criteria for cost effectiveness. It becomes a societal, policy decision whether we, as a society, want to treat these drugs and patients differently because of the special issues in dealing with rare disorders. CEDAC is not appropriately constituted to make those societal decisions.

To further comment on the Fabryzyme review, we at CEDAC wanted to see better studies. We were disappointed that patients weren't followed longer and that the studies didn't have a somewhat larger number of patients.

Again, from an ethical and policy standpoint, there really is every reason for these types of studies to be absolutely well done from the beginning, since it's not feasible to repeat them.

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What I really don't like about the CDR process is that information from companies is submitted in private. Much of the submitted data is unpublished. CDR is not able to comment publicly on this information or on the quality of the trials. Personally I feel this is unacceptable. Industry should take this on and ensure transparency by making information public. It's a disservice to Canadians if – as we get better access to these drugs – we don't also get better *information* about them.

-*Question (Leanna Caron, Genzyme):* You started by saying that Fabry drugs really shouldn't have gone to the CDR as the CDR is not equipped to handle that type of decision. If not the CDR, then who is in a position to deal with the funding decision on Fabryzyme?

-*Dr. Laupacis:* Health Canada and Reimbursement Committees such as the CDR have very different mandates. Health Canada often deals with surrogate markers for drug efficacy. But in a reimbursement committee, you need to be able to determine how surrogate markers translate into morbidity and mortality.

There are many silos for drug assessments. I think it very valuable to have an independent body strictly to comment on the quality of evidence. But once we're done evaluating the evidence it should be decision makers such as Minister Smitherman and Helen Stevenson who decide whether a drug should be funded. It's not for CEDAC to decide whether a drug should be funded or not.

In the binders you all received, you have a copy of Joe Clarke's CMAJ article about access to medicines for rare disorders with the phrase "Condemning patients to death..." I actually submitted a reply to this article, which was also printed in CMAJ and I wish you had a copy of it here as well. To my knowledge, only 1% of patients in the trials for *Fabryzyme* actually died. In these situations it is really crucial that we all be honest about evidence – because there are so few people in the studies, because of the ethical issues around access to treatments for rare diseases. Our compassionate use policies exist because we want to provide medications to those who need them. But we shouldn't misrepresent the level of evidence behind these treatments by overstating the case.

-*Question (Lesia Babiak, OBC):* How can we advance discussion around these societal, ethical policy decisions you have pointed out?

-*Dr. Laupacis:* Debate needs to occur on many levels - including a citizen's council, and public involvement in decision-making.

We have been hearing a lot about this "genetic revolution" and how it will change medicine. There is a potential for those relatively "common" diseases like colon cancer to become 1000 different specific genetic variants of the disease with 1000 specific, targeted, treatments. This would make for many more rare disease / orphan drug scenarios.

Personally I am comfortable with an orphan drug program in Canada.

-*Question (Amir Attaran, U Ottawa):* You mentioned that pharmaceutical companies submit trial records to the CDR in private. What is the right of submission of information by governments

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and patients? Can they also submit information and do they have the right to keep this information private?

*-Dr. Laupacis:* Right now the only submissions are from manufacturers. Well, with only one exception probably – which is the Fabryzyme submission which was a provincial submission. Patients are not invited to submit to the CDR.

*-Comment (Peter Brenders, BIOTEC):* BIOTEC Canada wants to see the CDR adopt a public process also. We think it would make sense to distinguish special policies and procedures for reviewing biologics as they have many unique issues. We have been advocating for open CEDEC meetings like the FDA open meetings in the States. As far as privacy of data, most data from drug trials is posted and available on the FDA website and manufacturers aren't too concerned it seems.

*-Dr. Laupacis:* That may be the case but at CEDAC we have heard many times from industry that we are not permitted to comment on certain private information.

FDA open meetings may sound good but I would think having a town hall meeting around every drug review would perhaps be a bit much.

*Comment (Paul McCabe, Shire):* CEDAC is not even open to manufacturers (much less the public). There is no opportunity for companies to make a presentation to the CEDAC board, which doesn't seem right.

*-Dr. Laupacis:* It might be worthwhile to consider the comparison between the CDR and DQTC in Ontario. DQTC does allow presentations from companies. And they've found that it's only about 20% of the time that a presentation from a company would sway the committee. As for CDR, CEDAC sends their review back to the company and invites the company to comment on it (which is not done by DQTC).

*Comment (Lesia, OBC):* I'm hearing participants here say that the CDR should be revisited to make it more transparent and to invite much more public involvement. Then, with everything out in the open, it should be the responsibility of funders to make their final decisions.

*-Dr. Laupacis:* I want to also mention that while CEDAC met all timelines, unfortunately provinces ended up waiting quite a while, even months, before implementing funding recommendations.

I have to say that I would also like to see the CDR process opened up and made more transparent – because my bias is that people will start to understand **why** CEDAC says no.

Companies want transparency because they think that patients will see the decision making process and conclude that CEDAC is screwing up.

*Question (Amir Attaran, U Ottawa):* In the current system, how can patients advocate for themselves?

*-Dr. Laupacis:* Right now, there really is no avenue for patients to advocate.

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### **II. Peter Brenders, BIOTEC Canada: International Impact of Orphan Drug Policies: USA, Europe, Japan, Australia**

In terms of international orphan drug policies and drug funding, the basic situation is that access is not perfect anywhere else – but perhaps access is somewhat easier in other countries than it is in Canada.

Twenty years ago, this discussion we are having, about funding drugs for rare disorders, could not have happened. Yes, people were getting health care for rare diseases then – mostly, palliative care. But twenty years ago, people with rare diseases were beginning to look for something more than palliative care. They were asking for curative care.

At that time, Abby Meyers (National Organization for Rare Disorders, USA) had a child with Tourettes Syndrome who was participating in a drug study, when the drug company abruptly stopped the study. It wasn't financially viable for companies to do studies on treatments for rare diseases because (1) the market was too small, with patients too spread out; (2) payers were unlikely to pay before drug was approved; (3) treatments were not patentable, or patents were too short; and (4) there was little in-depth knowledge of orphan diseases. Such disorders were hard to study, and very hard to treat.

Abby linked up with Congressmen to do something about this. They wondered: could they force companies to do research and development for treatments for rare disorders? Could they pay them to do it? They ended up proposing incentives for rare disease drug R&D. The US response to this issue, the 1983 Orphan Drug Act, is why we are here today, in a position to have these discussions.

The Orphan Drug Act in the US gave companies working on treatments for rare diseases several incentives: 7 years market exclusivity; tax credits for research costs; grant programs to promote research by companies and research institutions; and quicker priority reviews. In 1983 when this legislation was passed there were 10 products classified as orphan drugs. By 1993 there were 216 products. During this time, mortality from rare disorders grew at a slower rate than for other diseases. It was estimated that for each one orphan drug approval, 500 deaths were prevented.

Japan followed with a similar approach in 1985. Australia adopted an orphan drug policy (not legislation) in 1997 which offered 5 year exclusivity, fee waivers, and protocol assistance for companies developing orphan drugs. In Europe, regulation on orphan diseases was adopted between 1997-1999.

As you are aware, Canada does not have such policies. When the issue has arisen in Canada, government has concluded that "existing mechanisms are adequate" for dealing with orphan diseases. Those mechanisms were: Emergency Drug Release (EDR) providing medications where the need exists. However, without an NOC (Notice of Compliance from Health Canada) one can't get these drugs paid for by private or public insurance so EDR only works with the assumption that the drug would be provided for free. In other words, the EDR program provides no incentive to companies.

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BIOTECanada does have an orphan drug policy white paper out there somewhere that has not been acted on by government.

The biotechnology industry has been advancing knowledge since the late 1970s. But so much is still unknown. Research is getting more complicated, and more expensive. There are many targets which we know little about.

There are 30 Canadian companies working on treatments for rare disorders. BIOTECanada, as an advocate, fears that if we aren't careful as we move forward with a drug policy, Canada may lose its place in biotech research and may ultimately become an "importer" of this technology. Given our good start with these Canadian companies, we have the opportunity to perhaps become an "exporter" of biotech solutions to the rest of the world.

Yes, there is a higher per-patient cost for rare disorders but it's essential to recognize that it's not significant, relative to total costs.

The question that remains for biotech companies is "Why come to Canada?" when CEDAC procedures are such that their products will never get funding.

I quote from Roberta Bondar in her role as Chair of the Science Advisory Board Committee on the Drug Review Process: *"A specific [Orphan Products] program, blending incentives, would bring new innovative talents into the therapeutics market, would add to Canada's exportable innovations, would offer opportunities for international joint ventures. More important, it would confirm in the public mind Health Canada's commitment to the health protection of all Canadians, including those whose needs are sufficiently rare as to escape the normal attention of the market."*

### **III. Ed Koning, Canadian Fabry Association: Case Studies (recent reviews)**

Fabry is an X-linked chromosome disorder - one of a few life-threatening lysosomal storage disorders. It's an ultra orphan disease with prevalence of 1 in 117,000. Life expectancy for males is between 40-50 years of age.

I was diagnosed with Fabry disease at 43 and for the last 5 years my health has deteriorated as a result. Fabry has been 'up to bat' recently as a case study of the drug funding struggle for rare disorders and I remain involved because I am looking for closure and progress towards resolution of these problems – not for myself, because I feel it's too late for me – but for family members and later generations dealing with Fabry disease.

Enzyme Replacement Therapy (ERT) is the only effective treatment for Fabry Disease. It was approved by Health Canada in Jan/Feb 2004 and is now available in over 40 countries – among them, Croatia, Argentina, Turkey, and Bulgaria. ERT is made using a recombinant genetic technology at a cost of \$250,000 per patient per year. In Canada it has only just been made available (August 2006) via a 3 Year Funding Agreement between Provincial/Federal governments and Companies as a research study, subject to Canadian Research Protocol approval. ERT for new patients is still not available. It seems that among developed countries, Canada has the most stringent criteria for approval.

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I really don't understand why things have happened this way in Canada. There have been several obstacles to funding – largely the problem seemed to be a ping-pong game back and forth between the Health Ministers and CDR & CEDAC. CDR announced a negative decision in November 2004 and again in May 2005, stating insufficient clinical evidence and that ERT is not cost effective. It seems clear that this is not the right process. All now agree that CDR is not the correct body to determine funding of life-saving orphan drugs. Health Ministers agreed to expedite the approval process in October 2005 and now that agreement has been reached to fund therapy through a Research Protocol, Health Ministers are suggesting that the Fabry agreement be used as a model for Expensive Drugs for Rare Disorders (EDRD), as part of the National Pharmaceutical Strategy (NPS).

What we really need is a better way to collect real-world, post-market data, on orphan drugs via international patient registries and standards of care. We should eliminate unnecessary bureaucracy and research protocols that provide little scientific or clinical value. The [Fabry] Research Protocol that has been agreed upon really is not set up to answer the outstanding questions we have about the drug, and there are too few patients in Canada to provide helpful data. There are existing models in place that would be less cumbersome and less expensive for providing access to Fabry medications.

I feel that decisions on how to spend public money should be public, and the CDR process really needs to be more open and transparent.

*Durhane:* The CDR response to the Fabryzyme file was really very puzzling. The committee re-reviewed the science and disagreed with the evidence, despite having less expertise on CEDAC compared to Health Canada review committees. It seemed CEDEC was not able to take into account the special issues with rare diseases, such as the fact that there is no other treatment available for this disease. They seemed to get stuck on technicalities, such as a significance level of .05 versus .056!

*Comment:* When a company is setting up research trials and choosing endpoints, you work with regulatory agencies and endpoints are agreed upon in advance. These endpoints are judged by experts in the field (not “drug experts”).

*Comment (Leanna, Genzyme):* These studies for rare conditions are driven by international (not “Canadian”) norms and standards of what the disease is. Endpoints that are chosen are the most appropriate **at that time**. But, of course, knowledge of the disease evolved immensely during the time when the registry was begun.

You're dealing with a disease that is quite heterogeneous. You understand certain things about the disease, then as time passes, you know the disease to be different than you thought at first – but there is no going back once a study has begun.

*Comment:* When you are dealing with the **first product** for a given disease, you **must** look at surrogate endpoints – hard endpoints come much later. Determining the surrogate endpoints is a critical first step.

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*Comment (Lesia, OBC):* In AIDS, surrogate markers are well validated now – but were they 10 years ago? When working with AIDS treatments, researchers and decision makers had to make decisions quickly in relative uncertainty.

*Comment:* Different jurisdictions (for example, CDR, CEDAC) shouldn't reinterpret or reject criteria accepted by Health Canada and the international research community.

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### Access to Drugs for Rare Disorders (Challenges and Emerging Strategies)

#### IV. Chris Ward, Ward Health: Individualized Medicines

I will share my observations on the status of drug funding. In my mind our policies are all about rationing access to medications. Governments are faced with many choices for resource allocation and they want to minimize their spending on drugs.

But the correct perspective on this is to see **illness** as the target (not treatments). **People being sick** is the problem – not the drugs that make them better.

In handling the growing problem of chronic disease management in Canada, we need to advance the individualized approach:

- Involving the patient
- Individualizing treatment (and there is nothing more individualized than rare diseases)
- Early detection and prevention
- Independence and choice – more often now, behaviour modification programs are paid for by employer health plans and other insurers.
- Focus on outcomes.

Keeping in mind that 90% of drugs work for just 30-50% of the population they are meant to treat, the field of pharmacogenetics is expanding its work to identify nonresponders and toxic responders so that treatment can be more successful and tailored to the patient.

#### V. Amir Attaran, Institute of Population Health, University of Ottawa: Ethical and Legal Issues

I have spent much of my career working in developing countries. What I have recognized since returning to Canada is that many problems around access to medications are the same in Canada as they are in developing countries. In fact, in some ways, we in Canada are worse off than Brazil, or South Africa. For example, in Brazil, every drug purchase in the public health system is publicly accessible and transparent. That is certainly not the case here in Canada.

There have been some interesting developments in the Canadian judicial system over the past decade which have an impact on access to health care and medications. Since 1999, the Supreme Court of Canada has demonstrated increasing willingness to apply the Charter of Rights and Freedoms to health.

The Supreme Court's **Chaoulli** decision was landmark. The Quebec government was denying a patient timely and effective health care because of long wait lists; and the patient could not access private care under Quebec law. This delay hurt the patient's health and his prognosis deteriorated over time. The government had plenty of time to act and had promised on numerous occasions to find a solution to the problem of waiting lists, but failed to act.

The **Chaoulli** case was won on a 4-3 split decision under the Quebec equivalent to the Charter of Rights and Freedoms. The Court did not prescribe action but instructed the province to get moving to solve the problem.

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The Canadian Charter of Rights and Freedoms, Sections 7 and 1, articulate each person's right to not be arbitrarily denied life, liberty, or security of the person. The current process of Drug Review is so far off the mark that it is inevitable that it will lead to legal challenge.

Arbitrariness is fairly rampant in the context of medicine. Fundamental justice involves (1) consideration of the relevant, not the irrelevant; (2) using normative guidelines to guide decisions; and (3) avoiding arbitrary delay: "justice delayed is justice denied."

The Charter also outlines a right to be heard, for example the right to "full answer and defence" in the criminal context. This right may vary by context. For example, the right to be heard in an immigration case may be interpreted as the right to make a case for yourself before an immigration tribunal (rather than in a court of law). It's unclear how this "right to be heard" may apply to patients affected by a drug licensing decision, but there is some basis for thinking that this right could be justified.

The Charter guarantees the rights and freedoms set out in it subject only to such reasonable limits prescribed by law as can be demonstrably justified in a free and democratic society. Does cost matter to Charter rights? The law is very unclear on this. There are cases where the ruling has been to protect Charter rights regardless of cost (for example, a deaf woman winning a case against the hospital, claiming the right to have an interpreter provided by the hospital during her labour). There are also many cases on the other side.

As my counterpart to the concept of "cost effectiveness," let me outline what I feel is a more useful concept: that of "judicial effectiveness." Judicial effectiveness takes into consideration much more than just cost effectiveness. Judicial effectiveness includes LOGOS (reasons; eg. cost effectiveness – on its own this is impoverished and inadequate) + ETHOS (politics) + PATHOS (testimony).

It is spectacularly naïve to think that Canada's drug policies will not be litigated. In this matter, however, I suggest that you take the long view: a bad case, a bad precedent, is worse than no case at all!

*Question:* In your knowledge, is there any requirement that persons rendering decisions have suitable training to do so?

*Prof. Attaran:* If you were to make the analogy with a judicial tribunal, you would probably end up with the conclusion that personal qualifications or expertise don't matter. When you look at administrative functions, you may have more of a case, but in my opinion, not the greatest chances of success.

*Comment:* In the US, decisions are made using the MCAC – a temporary group of experts, together with standing members and consultants for specific drug review.

*Question:* Where do you see lawsuits being filed? Would it be for provincial delay or possibly suits against the CDR itself?

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*Prof. Attaran:* Previous cases in South Africa and England have involved a patient seeking access to a certain drug or class of drugs.

### **VI. Mary Kim, Canadian Arthritis Patient Alliance: Ontario's Transparent Drug System for Patients Act**

Bill 102: Ontario's Transparent Drug System for Patients Act has introduced major changes in drug policy and drug funding in Ontario and perhaps has created new opportunities for funding drugs for rare disorders.

The drivers for reform leading to Bill 102 include:

- *Patients need better and faster access to drugs*
- *Public needs a voice in the system*
- *Government not getting value for money*
- *Government not using purchasing power*
- *Rising cost to employers of employee drug plans*

The Bill outlines a Rapid Review Process for drugs meeting certain criteria. Rapid Review would be made available for a new product qualifying as a "new chemical entity for treatment of immediately life-threatening disease or other serious disease." The rapid review would also be extended to new products offering substantial improvements on significant outcomes (including quality of life) over other available therapies; or for which no other effective drug therapy is currently available. These criteria may help to speed access to medications for rare diseases.

The Ontario government is also reforming the system to access drugs under special conditions. There will be a new process for accessing unlisted drugs in special cases, with a single point of approval sitting with the Executive Officer.

We are glad that Ontario is including two patients with full voting powers on its Committee to Evaluate Drugs (CED) and is redefining the committee's terms of reference to ensure meaningful patient input. Public participation will also be engaged through a Citizen's Council, consisting of members of the public, which will provide input on drug policies and ethical guidelines to the Committee to Evaluate Drugs and the Executive Officer.

Bill 102 is still very new in Ontario and it remains to be seen whether it will achieve its objectives. Things do look promising so far. In particular, the steps taken to involve patients in drug system decisions mark significant progress and we hope this will be sustained in all stages of implementation.

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### Current and Pending Drugs for Rare Disorders

- Presentation of Case studies
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#### **A. Novartis: Philippe Martin-Widmer**

Novartis, as a company, is committed to developing specialty drugs. We will share our experience now with our newly approved drug for treating iron overload: EXJADE. Iron overload is caused by multiple blood transfusions. This is a real problem, as the body has no mechanism to get ride of the excess iron. Currently there are 800-900 patients in Canada who are chelated with the current treatment, Desferal (patients with thalassemia, sickle cell disease, myelodysplastic syndrome, or other chronic anemias). Desferal reduces morbidity and mortality very successfully, but due to short plasma half-life, must be taken as a slow subcutaneous infusion 5-7 times a week, leading to poor compliance especially among teenagers and young adults. Poor compliance leads to decreased survival.

EXJADE is a once-daily oral chelator that Novartis has been developing and studying since 1998. EXJADE was given orphan drug status in the US, Europe, and Switzerland. EXJADE received priority review status by Health Canada and received NOC/c on October 18, 2006. Novartis is hopeful for CDR fast track review and is also submitting to the CED in Ontario for concurrent review. There will be some access to EXJADE for patients while the review is underway.

*Question:* What is considered "rare" in Canada? 900 or 3 or 10,000 patients?

*Answer (from audience member):* In the US, orphan diseases are defined as under 200,000 cases nationwide. It is also helpful to recognize that sometimes a disease is fairly common but specific side effects or issues related to the disease are "rare."

#### **B. Genzyme: Monty Keast**

Pompe Disease is characterized by progressive muscle degeneration, severely affecting skeletal and respiratory muscles and also causing cardiomyopathy/cardiomegaly in infants. It is

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an inherited disease with an incidence of 1/40,000 (<10,000 patients worldwide). There are 45-50 patients in Canada.

Patients with Pompe disease with onset in infancy have a markedly shortened life span (less than 10% survival at 24 months). In a trial with 18 patients treated with Myozyme, all patients survived to 18 months (compared to 2% of untreated historical controls) and most were *invasive* ventilator free. In results from Myozyme treatment in advanced Pompe disease, some other gains were reported including improvement in muscle strength and skills. There are no other treatments available for Pompe disease.

In Canada, Myozyme was granted priority review and was approved by Health Canada in August 2006. Twenty-three countries currently provide reimbursement for Myozyme, either full reimbursement or via a named patient program.

In the UK, rare conditions are funded nationally through NSCAG. The UK uses a Centres of Excellence model with a fixed annual budget for lysosomal storage disorders and Pompe Disease falls under this category.

In the Netherlands, there is a dedicated committee to evaluate drugs for rare diseases and make funding recommendations. This committee reviewed Myozyme and recommended funding retroactive to marketing approval.

In Germany, funding for Myozyme was approved simultaneously with marketing approval. In the US, there are public and private payors reimbursing Myozyme.

Genzyme as a company is committed to the CDR process. Additionally the company has had initial talks with Ontario and other provinces. Myozyme looks to be an excellent candidate to fall under the Bill 102 objective of "Improving patient access to drugs through new conditional listings, Exceptional Access, and rapid reviews of innovative drugs." Genzyme is pursuing a collaborative approach to reimbursement in Ontario, with direction being provided by both the Drug System Secretariat and the Drug Programs Branch.

### **C. Actelion: Louise Boistoly**

Actelion is a young pharmaceutical company founded in 1997 with headquarters in Switzerland and a Canadian affiliate employing 32 people. Actelion's research strategy focuses on the discovery, development, and marketing of innovative drugs for unmet medical needs.

Zavesca is indicated for the treatment of adult patients with mild to moderate Type 1 Gaucher disease for whom enzyme replacement therapy (ERT) is not a therapeutic option. It represents a new treatment approach by inhibiting the formation of substrate for the deficient enzyme. Zavesca is the only safe and effective oral alternative, and it offers substantial savings per patient compared with ERT.

Zavesca was submitted to CDR in May 2004 and CEDAC recommended that it not be funded. It was resubmitted and again refused in November 2004. All provinces follow the CEDAC recommendation, so Zavesca is not listed on any provincial drug plans at this point. Under the current system, CDR is not able to review the file again unless new clinical trials are done or a

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new price is determined.

Zavesca received orphan drug status for Type 1 Gaucher disease in the US and Europe. Its place in therapy has been identified by the European Working Group on Gaucher Disease. Zavesca is reimbursed in many countries, including the 7 countries listed in the PMPRB regulations (UK, US, Belgium, Germany, Italy, Sweden, and Switzerland).

The reimbursement challenges for orphan drugs are many. In study design, we face the challenges of a small number of research subjects, low statistical power in data analysis, and an ethical dilemma in assigning patients to a control group.

Study endpoints also create a challenge because of complex, multi-system clinical manifestations of the disease, variable rates of disease progression, and difficulties in quantifying and comparing disease manifestations between patients. It seems that the CDR review process does not take into consideration the realities of orphan drug research limitations.

Orphan diseases affect a very small number of patients but are often very debilitating. Patients suffering orphan diseases should have access to health care just as any other patient. It would be unethical to refuse access to care just because of cost. We need to see a better system for orphan drug review & assessment that is fair and equitable for orphan drugs.

### D. Pfizer: Catherine Fitzsimon

There are approximately 1580 Acromegaly patients in Canada. The disease is characterized by an over production of growth hormone by the pituitary gland caused by a pituitary tumor. This in turn may lead to cerebrovascular events, hypertension and heart disease, insulin-resistant diabetes, osteoarthritis, restrictive pulmonary disease, and coarsening of facial features. The average age of diagnosis is 43 years. Diagnosis is usually made 7-10 years after symptom onset and life expectancy with Acromegaly is reduced by 10 years.

Current therapy in Canada involves 1<sup>st</sup> line: surgical therapy, 2<sup>nd</sup> line: medical therapy, and 3<sup>rd</sup> line: radiotherapy. SOMAVERT is a growth hormone receptor antagonist, administered by subcutaneous injection. SOMAVERT is indicated for the treatment of acromegaly, in patients who have had an inadequate response to surgery, and/or radiation therapy, and other medical therapies, or for whom these therapies are not appropriate. The cost is approximately \$41-82K per year.

SOMAVERT was submitted to CDR and RAMQ in early 2006 and ultimately both committees recommended that Somavert **not** be listed. However, in October 2006, Ontario's DQTC recommended that Somavert be listed under specific criteria. Pfizer will await other provinces' decisions in the coming months.

The reasons CDR gave with its recommendation **not** to list Somavert were:

- Two Randomized Controlled Trials were reviewed. No difference was found in quality of life between placebo and Somavert.
- It is uncertain whether a reduction in IGF-I levels is a valid surrogate endpoint for improvement in clinical outcome, including survival.

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- Safety issues, namely elevated hepatic enzymes in 10% of patients who received SOMAVERT and a theoretical risk of an increase of the size of GH-secreting pituitary tumors.
- The estimated cost of SOMAVERT therapy (\$60,000-\$80,000 year/\$137,000 per QALY) submitted by Pfizer is an underestimation based on weak assumptions.

However, Somavert is publicly reimbursed in many other countries. In Canada only 200 patients are eligible for Somavert treatment and its place in therapy is well established by Canadian guidelines. We are encouraged by the positive signals from Ontario's DQTC about provincial listing.

### **E. Betty McPhee**

I was diagnosed in 2002 with Waldenstrom's Macroglobulinemia. Waldenstrom's Macroglobulinemia (WM) is a rare chronic blood cancer classified as a lymphoplasmacytic lymphoma or indolent non Hodgkins lymphoma. I wanted to learn as much as I could about the disease but it was much more complicated than I anticipated. Even more difficult than this, was the realization that not all treatments for my condition are available to me here in Canada.

My first treatment was 8 months of Rituxan + CVP (funded) mainly because of a pleural effusion (a rare complication in WM) which was becoming increasingly debilitating. It was difficult to climb stairs and just before treatment, to walk any distance without becoming very short of breath.

In my case I had excellent results – on my report it says a complete remission, however with WM it is really only a partial remission because it isn't curable. The results were amazing. I was even able to take a bike trip to the Gulf Islands, which was unimaginable given the problems I had been having previously.

A renowned expert in Waldenstrom's at the Dana Farber Cancer Institute in Boston, recommended maintenance rituxan to extend the response period. I had a second consult with Dr. Chan, Head of Respiriology at TGH and he concurred because a pleural effusion can be nasty to treat. He was concerned that I would develop another pleural effusion on relapse.

The problem for WM patients is that there have been no clinical trials, either for short-term or maintenance therapy. Like many other rare disorders, the numbers are too small to make it cost-effective. In the USA, maintenance rituxan is funded under the umbrella of NHL (non Hodgkin's lymphoma). In Ontario WM is considered 'distinct' from NHL. Dr. Chen and others at PMH have been reluctant to prescribe rituxan for WM because it is not approved, but primarily because it is not funded. They also felt it was unlikely to get Section 8 approval. My insurance would cover 80% of the drug, but not the infusion or other administrative costs. So, I had two options. I could go to a private clinic in Ontario at my own expense. The quote at Provis was \$43,000.00 of which \$22,400.00 were personal non-insured costs. My other choice was going to Roswell Cancer Institute in Buffalo because the non-insured costs were considerably less.

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In other provinces, such as BC and the Maritimes maintenance rituxan is approved. I know of patients in other provinces who are able to get this treatment and do not have to pay for it themselves.

Just a couple of weeks ago, I was able to access the new rituxan assistance program. Once my doctor signs the form (which could be another long wait), I will be able to get the infusion costs covered in Ontario at one of the new Bayshore Clinics. My insurance will pay 80% of the drug costs.

*Comment:* From Betty's experience we can see that orphan diseases or rare indications can fall through the cracks. This example is similar to the case of cyclosporine for aplastic anemia. Though it is known to be helpful for patients with aplastic anemia, no one will fund the treatment when it's not specifically indicated for that usage.

### **F. Mr Anand**

I have a 21-year old son who has been diagnosed with acromegaly. He went through two surgeries to try to achieve a cure for the condition. After surgery was not successful, he was able to access SOMAVERT and his physician is very happy with his response to this treatment. It is so important to us that we were able to get this help for our son. I just hope that as a result, he can have a normal life.

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### Issues Related to Access to Drugs for Rare Disorders Access under Ontario's Transparent Drug System for Patients Act

#### Comments from Helen Stevenson

*Helen Stevenson, Ontario Drug Strategy Secretariat:* It would be good to have another opportunity to work constructively together to build a model on access to drugs for rare disorders. Ontario has been working in concert with the National Pharmaceutical Strategy on these issues but we will keep going in Ontario regardless of how the NPS unfolds.

I have to say that I feel that the DQTC/CED *is* qualified to fulfill its mandate, but is faced with a very complex task when making its recommendations.

We have taken criticism in our Ontario Strategy for our cost savings measures – but this is how can afford to fund another drug!

Today has been a great start. We would like to continue to dialogue on these issues.

#### Open Discussion

*Peter Brenders:* We need clear recognition of a **need** to do this, to work on orphan drug policy in Canada. There has not been much pick-up on this issue since Roberta Bondar brought it forward into public awareness.

I have heard today the admission that CDR is not the correct process for reviewing orphan drugs. Since the CDR was established, **all** products for “unmet needs” have been rejected for funding. We need a new process.

*Comment:* Is it just that Canadians are too polite to actually force a change in this area? We have no orphan drug law, no orphan drug policy. There is a misperception that our health system in Canada is consistent and available, when in fact we have 10 provinces with 10 different policies. It's very hard to get the public to pay attention to these matters. It seems that a solution on a national level is what is really needed.

*Question (Wendy Perrow, Sigma Tau Pharmaceuticals):* Has there ever been an approval for funding for products treating rare disorders?

*Answer (audience member):* No. “Me too” drugs seem to be the main drugs that CDR has approved. Historically, yes, orphan drugs have achieved funding – especially the more targeted therapies. But it seems all of them have involved a fight to get funding.

*Comment:* Other countries seem to have a system for getting orphan drugs funded. Can CDR find out how this happens in other countries? What has worked elsewhere?

*Answer:* Several international cases may illuminate what has worked in other jurisdictions. In the UK, Christine Lavery filing a lawsuit for Herceptin access did create a change in drug access for all patients in similar circumstances. Having a well defined “orphan drug policy” definitely makes a difference in other countries and makes it easier to manage these issues. Also the UK

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Citizen's Council is a successful model, where transparency has been achieved, and patients and citizens are actually "players" – not just actors.

*Comment (Paul McCabe, Shire):* From this Forum I gather that we in Canada are far behind other countries in orphan drug policy. I wonder whether we could adopt a default mechanism, whereby a product that is approved in the seven PMPRB countries can be approved here automatically?

*Question:* As we continue this work, should we strive for a policy for all of Canada? Or would we be better off following the momentum in Ontario and then taking it province by province?

*Durhane:* If we wanted to take it province by province, the logical starting point is Quebec, since they do not participate in CDR and tend to be more generous. But the province-by-province approach is very tiring for patients. There are not enough advocates and people who do advocate are often not well, health-wise.

*Ed Koning:* In my opinion it's questionable whether the National Pharmaceuticals Strategy will ever come to fruition. CDR is not as big an issue as we think, since it actually isn't the process that we expect to be used in the future for orphan drugs. Health Canada is definitely not the problem here since drug approvals are progressing well.

The provinces are the ones paying for drugs – that is not going to change. There were aspects of the Fabry agreement between feds/provinces and companies that could be worth duplicating. However, it took 3½ to 4 years to accomplish and a lot of patient pressure, and that type of thing really should not be required for each specific new drug in question.

### **Conclusions and Next Steps**

CORD will follow up with participants after this meeting to provide copies of slide sets and the proceedings from today's meeting. Also we will canvas you for next steps. Today has been an Issue Identification session. We need to move forward from here to determine what our guiding principles are for addressing these problems, and to look at models for possible solutions.

We also hope to organize subsequent Forums on topics such as "Appropriate methodologies for R&D into rare disorders," and "Reimbursement and Funding Issues." CORD is seeking help in organizing future forums: finding speakers and coordinating logistics. Please help if you can.

We would like to get the Ontario Drug Strategy Secretariat engaged in the next session. Also it would be very helpful to bring in other decision makers to have a better chance for dialogue.

Thank you all for coming.

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