



Canada's long journey toward an Orphan Drug framework



At Last! Canada's Orphan Drug Policy!

Why is Canada the last developed country to adopt an orphan drug policy? Why, on October 3, 2012, after 17 years of inaction, did the federal government announce an Orphan Drug Framework “to increase access to new treatments?” And what else is needed to ensure patients actually have better access? The announcement was significant because it was the first official word since Health Canada’s 1996 recommendation that there was “no need for an Orphan Drug policy because Canadians already have access to drugs ... [with] ...Orphan Drug designation and marketing approval in the U.S.”

Criteria for orphan drug designation follow those of the E.U., namely, that the disease has a prevalence of not more than 5 in 10,000 persons and is life-threatening, or seriously debilitating.



USA and Europe: Blazing the Trail for Orphan Medicinal Products

In the decade prior to 1983, there were only 10 new approved drugs for rare conditions. Because of the small patient populations, it was difficult to conduct clinical trials and there was little likelihood of recovering the investment. But when Abby Myers was told that the company was abandoning the clinical trials in which her grandsons (diagnosed with Tourette’s Syndrome) were enrolled, she enlisted the aid of some Congressmen, and together they successfully lobbied for orphan drug legislation. The 1983 Orphan Drug Act defined rare diseases as those affecting fewer than 200,000 Americans. It provided support for R&D (clinical trial advice, fast track review, and reduced application fees) as well as commercial incentives to bring these drugs to market (enhanced patent protection and market exclusivity for 7 years). Now celebrating its 30-year anniversary, the Orphan Drug Act has granted orphan designations to over 2,800 drugs and approved more than 430.

In 2000, the European Medicines Agency introduced similar legislation, setting rare disease prevalence as “no more than 5 in 10,000 persons” with additional criteria for orphan status, namely, the condition must be life-threatening or chronically debilitating and there are either no other approved therapies or the proposed therapy offers a significant benefit. Since 2010, the U.S.A. FDA and the EMA have adopted a single “update” report and a common template to file for orphan status, considerably reducing filing time and costs and facilitating international clinical trials.

1996 Health Canada Says “No Go”

While acknowledging the challenge of licensing drugs for rare conditions, Health

Canada concluded that about 60% of U.S. designated orphan drugs were available in Canada through the normal drug approval process and the Emergency Drug Release Program (EDRP). However, they also acknowledged that drugs used “off-label” or brought in through EDRP were generally not covered by provincial drug plans and some private payers.

The 1996 recommendation concluded sufficient incentives existed to support R&D, including the Tax Incentive Program, and reduced fees for “small market drugs.” Finally, other sources of R&D funding were available, such as the Medical Research Council, National Research Council, and disease-specific associations.

Canada's Orphan Drug Framework:

The proposed Canadian Orphan Drug Regulatory Framework includes:

1. Orphan drug designation criteria and processes aligned with the U.S. and E.U. to facilitate collaboration

2. Advice for clinical trials by Health Canada or in conjunction with international regulators
3. Transparency and information sharing throughout drug lifecycle with timely access by key decision makers, including healthcare providers, health technology assessors, and patients
4. Posting of orphan drug designations, clinical trial registration and disclosure, post-market authorizations and post-market plans
5. Life-cycle approach to take into account a wide body of evidence before and after a drug is marketed

Criteria for orphan drug designation follow those of the E.U., namely, that the disease has a prevalence of not more than 5 in 10,000 persons and is life-threatening, or seriously debilitating. Moreover, the drug (for diagnosis, treatment, mitigation or prevention of the condition) is deemed necessary because there is no existing therapy or, if there is an existing therapy, the drug would provide substantial therapeutic benefit.

The Framework utilizes a life-cycle approach, with similar scientific requirements as for the regulation of [all] new drugs but includes built-in flexibility for small clinical trials and other types of information to support approval. Importantly, manufacturers may be asked to submit (in addition to the usual pre-clinical/clinical data) regulatory status in other countries, data limitations, and a plan for gathering information and conducting additional tests or studies to reduce uncertainties about benefits and harms.

Canada’s Orphan Drug Regulatory Framework is designed to facilitate filing for designation and setting up clinical trials in Canada at the same time as in the U.S. and E.U. The provisions for enhanced patent protection and market exclusivity may require more consultation and agreement by Industry Canada.

Milestones Toward Canadian Rare Disease Policy

In 1996, Health Canada stated, “there had not been significant pressure from industry or

Continued on page 21



Continued from page 20

special interest groups in Canada to develop an Orphan Drug policy.” Notwithstanding the lobbying efforts of the Canadian Drug Manufacturers Association (CDMA), it was not until 2004 that BIOTECCanada called for an Orphan Drug Policy, citing Canada’s biotechnology capabilities and the desire to encourage innovation and contribute to developing treatments for Canadians and others in need.

In February 2006, the patient community, under the leadership of the Canadian Organization for Rare Disorders (CORD), also proposed an Orphan Drug Policy, and in April 2007 CORD organized the 1st Canadian Conference on Orphan Drugs and Rare Disorders. This was an important milestone, bringing to Ottawa top representatives from the U.S. FDA, National Institutes of Health, the European Medicines Agency (EMA), international patient advocates and academics. Commitments were not forthcoming from federal and provincial officials in attendance, but a clear call for an Orphan Drug Policy was delivered and received.

Federal Government Starts Regulatory Process

In May 2008, MP Don Bell introduced a Private Member’s Motion in support of rare diseases, which was endorsed by all parties except the Bloc Québécois. Subsequently, in December 2009, CORD hosted a consultation on draft Orphan Drug regulations with David Lee, Director of the Office of Legislative and Regulatory Modernization, who had been quietly drafting a framework and policies. In January 2010, the first semi-public acknowledgement of rare diseases came from the Assistant Deputy Minister who wrote to Health Canada referencing “drugs for rare diseases regulatory & legislative modernization efforts.” This was a third significant milestone.

Provinces Open Pathways to Access

Meanwhile, several milestones in the provincial access had been achieved. In September 2005, Ontario, under intense lobbying from patient groups and clinicians, agreed to expand newborn screening to 21 inherited disorders. Other provinces have slowly followed suit (although Saskatchewan remains the leader with its decades-old program testing for 30+ disorders). Also in September 2005, CORD organized a demonstration by patients and families at the Federal/

Provincial/Territorial Health Ministers meeting, demanding funding for drugs for two rare lysosomal storage disorders (Fabry’s and MPS I), resulting in a rare on-site delivery of a “promise” to fund.

In 2006, an unprecedented three-year F/P/T plan to fund Fabry’s disease was announced along with a recommendation for a national “expensive drugs for rare diseases” strategy. By CORD’s analysis, only 50% of orphan drugs approved in the U.S. or E.U. were approved by Health Canada and of these, most were recommended as “do not list” by the Canadian Agency for Drugs and Technologies in Health (CADTH), the body that recommends drugs to the public plans.

Most rare disease drugs are funded under some form of “managed access scheme” with strict criteria for patients to start therapy (usually not “too advanced” symptomology, not “too early” stage disease but just enough symptoms to signify deteriorating status and likely benefit), defined “benchmarks” to stay on therapy, and sometimes criteria for stopping therapy.

In February 2008, with no national strategy in sight, the House of Commons Standing Committee on Health asked CADTH to develop a strategy for rare disease drugs. Modest changes have emerged.

In 2007, Quebec announced its intention to create a rare disease program, and in December 2008, Alberta promised a Rare Diseases Drug Program. But Ontario was the first to act. In January 2009, it introduced the Drugs for Rare Diseases Program; however, it was applicable only to ultra-rare diseases affecting between 1 in 100,000 and 1 in 150,000. British Columbia set up an Expensive Drugs for Rare Diseases Committee (which assesses individual applications) and Alberta has introduced two programs not limited to orphan drugs, Special Authorization Request and a fund for “off-label” drug usage.

Towards panCanadian Access Route

In July 2011, the orphan drug Soliris became the first drug to be funded through the emerging panCanadian Pricing Alliance, which negotiates one price for all provinces. And an analysis of recent CADTH and pan-Canadian Oncology Drug Review (pCODR) recommendations found that 80% of orphan drugs were recommended as “list with criteria” and only 20% as “do not list.” Although

provincial negotiations often add another 6 – 24 months to actual funding and not all provinces actually provide a listing, access has definitely improved.

Most rare disease drugs are funded under some form of “managed access scheme” with strict criteria for patients to start therapy (usually not “too advanced” symptomology, not “too early” stage disease but just enough symptoms to signify deteriorating status and likely benefit), defined “benchmarks” to stay on therapy, and sometimes criteria for stopping therapy. Companies may also enter financial agreements based on use (number of patients and/or doses) to manage total budgetary impact.

On May 2012, the Canadian Life and Health Insurance Association announced a “pooling plan” to cover “high cost” drugs (excess of \$25,000 per year), including drugs for rare disorders, that would be applicable across all insurance carriers for “fully insured” private drug plans.

Where Are We Now?

Regional multi-stakeholder consultations have been taking place with the goal of tabling the framework in fall 2013. By harmonizing with U.S. and E.U. criteria, Canadians will benefit from having drugs registered at the same time, opening the way for inclusion in clinical trials. But Canada can do even more. A number of research networks are engaged in identifying existing drugs that can be “repurposed” for orphan indications. Initiatives on personalized and targeted medicines will focus on drugs for genetically defined subgroups of more common diseases, including many forms of cancer. And considerable attention is being paid to engaging patients, drug review agencies, and the drug plans to ensure that clinical trials are designed to provide useful and meaningful data throughout the “lifecycle” of a drug from pre-market to post-market, including biomarkers, clinical outcomes, and patient-relevant outcomes. ❖