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Priority setting for orphan drugs: An international comparison

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ABSTRACT

Objectives: To describe the process of priority setting for two orphan drugs – Cerezyme and Fabrazyme – in Canada, Australia and Israel, in order to understand and improve the process based on stakeholder perspectives.
Methods: We conducted qualitative case studies of how three independent drug advisory committees made decisions relating to the funding of Cerezyme and Fabrazyme. Interviews were conducted with 22 informants, including committee members, patient groups and industry representatives.
Results: (1) Description: Orphan drugs reimbursement recommendations by expert panels were based on clinical evidence, cost and cost-effectiveness analysis. (2) Evaluation: Committee members expressed an overall preference for the current drug review process used by their own committee, but were concerned with the fairness of the process particularly for orphan drugs. Other informants suggested the inclusion of other relevant values (e.g. lack of alternative treatments) in order to improve the priority setting process. Some patient groups suggested the use of an alternative funding mechanism for orphan drugs.
Conclusions: Priority setting for drugs is not solely a technical process (involving cost-effective analysis, evidence-based medicine, etc.). Understanding the process by which reimbursement decisions are made for orphan drugs may help improve the system for future orphan drugs.

1. Introduction

Drug expenditures in every health system are rapidly increasing and account for a large proportion of health spending. This increase is partially due to the fact that per patient costs of some new drugs are extremely high, particularly for orphan drugs used to treat rare diseases. There is no universal definition of what constitutes a rare disease. Rare diseases in the European Union (EU) are defined as affecting fewer than 5:10,000 people and in the US fewer than 200,000 people [1]. Currently, over 6000 rare disorders have been identified [2]. Some governments have recognized the need to support the development of orphan drugs. The US Orphan Drug Act was the first major initiative to provide incentive for pharmaceutical development to aid with rare disorders [3]. This initiative provides incentives to pharmaceutical companies for research and development of orphan drugs [4].

Priority setting for orphan drugs involves complex value-laden choices that are often ethically controversial. This controversy arises, in part, because it involves conflicting moral obligations (e.g., beneficence versus distributive justice) which result in different levels of funding and

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opposing interests of a number of involved stakeholders, including government officials, pharmaceutical companies, patients and the public (who are ultimately paying for the drugs). Expensive orphan drugs present a challenge to many drug recommendation committees because they seldom meet the cost-effectiveness and clinical evidence criteria commonly used to evaluate drugs under review for reimbursement. Notably, orphan drugs cannot undergo large clinical trials due to the small number of people affected by the disease. The scope of this issue is potentially universal because, as the science of genomics advances, medical treatments are becoming increasingly more personalized therefore more treatments may gain quasi-orphan status [5,6]. As science progresses it is likely that treatments will become even more targeted towards a smaller disease group. Today's policy decisions for a few orphan drugs may determine funding for future products.

Cerezyme, used in the treatment of Gaucher disease, and Fabrazyme used in the treatment of Fabry disease, are two examples of enzyme replacement therapies which are the most expensive type of orphan drugs. These drugs were chosen for the case studies because they are both innovative and extremely costly orphan drugs. The purpose of this study was to identify the values used by three national drug reimbursement recommendation committees in Canada where the committees makes non-binding funding recommendations to the provinces, as well as Australia and Israel where their committees make national funding decisions for their public healthcare systems regarding these two drugs. To date, there have been few studies describing priority setting in the context of orphan drug reimbursement decisions [7]. Describing and comparing the values involved in the process of drug reimbursement decisions within an international context may be an essential first step towards understanding and improving the process.

2. Methods

2.1. Design

We conducted qualitative case studies of priority setting of the drugs central to our case studies in three committees, across three countries. Tables 1 and 2 provide more specific details about each of the aforementioned drugs. Data collection involved semi-structured interviews with 22 committee members, patients, and manufacturers, and the review of several relevant documents.

2.2. Data collection

Data collection involved in-depth qualitative interviews, and the collection of relevant documents (please refer to Tables 3–5). We conducted face-to-face interviews or one-on-one telephone interviews with committee members, patient groups and industry representatives. Specifically, we conducted interviews with members of the Canadian Expert Drug Advisory Committee (CEDAC); Australia's Pharmaceutical Benefits Advisory Committee (PBAC); and Israel's Basket Committee (IBC). Additionally, interviews were conducted with patients who use the drugs central to our case studies and participants from Genzyme which manufactures the drugs central to our case studies. Interviews were 30–60 min in length. All interviews were recorded and transcribed. Interviews explored decision making in drug reimbursement of the two selected drugs [see Example of Interview Guide for Committee Members Appendix B].

Relevant documents related to reimbursement decisions were sampled and analyzed to explore reimbursement decisions surrounding both the drugs central to our case studies (please refer to Tables 3–5).

2.3. Setting

This research was conducted within both reimbursement recommendation committees and the drug manufacturer (i.e., Genzyme). These committees were selected because they all make recommendations about public funds and they provide guidance on drug funding to governments and other funders. The manufacturer of the drugs central to our case studies, Genzyme, was included because of their potential insight into the drug reimbursement process. Tables 3–5 below provide an overview of each of the committees based on information from their

Table 1
Cerezyme (*imiglucerase*).

Manufacturer	Genzyme, approved by US Food and Drug Administration in 1994
Use/symptoms	Reduces and in some cases reverse the chronic and debilitating symptoms of type 1 Gaucher's disease Affects 1 in 40,000–60,000 individuals in the general population Higher prevalence in Jewish Ashkenazi community Some patients have no symptoms, while others develop serious symptoms that can be life threatening Bone-related symptoms can be painful and debilitating, impairing a patient's mobility Life expectancy is mildly decreased [8,9]
Cost	$350,000 US per patient per year. However, in Israel the cost has been reduced due to lowering the dosing scheme [10]
Reimbursement recommendation	Prior to establishment of Canadian Expert Drug Advisory Committee (CEDAC) and Israeli Basket Committee (IBC); Pharmaceutical Benefits Advisory Committee (PBAC) recommended funding through the Life Saving Drug Program (LSDP)
Research studies	1. *Replacement therapy for inherited enzyme deficiency—macrophage-targeted glucocerebrosidase for Gaucher's disease* Clinical trial lasting 9-months of 12 patients with type 1 Gaucher's disease Safety and efficacy regarding improving haemoglobin levels and platelet counts and in reducing splenic and hepatic enlargement were demonstrated within 5 years [11] 2. Enzyme therapy in type 1 Gaucher disease: comparative efficacy of mannose-terminated glucocerebrosidase from natural and recombinant sources Clinical trial comparing and demonstrating the safety and efficacy of imiglucerase with alglucerase [12] 3. Replacement therapy with imiglucerase for type 1 Gaucher's disease Clinical Trial comparing the frequency of administration of imiglucerase [13]