Health Policy and Technology (▮▮▮▮) ▮, ▮▮▮–▮▮▮

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journal homepage: www.elsevier.com/locate/hlpt

International differences in patient access to ultra-orphan drugs

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KEYWORDS
Ultra-orphan drugs;
Rare Diseases;
Reimbursement status;
Patient access

Abstract

Objectives: Reimbursement recommendations on (orphan) drugs are usually made at a national level and this can lead to variation in patient access to the same drug in different countries. We compared differences in patient access to ultra-orphan drugs between countries. Furthermore, we describe how reimbursed and non-reimbursed orphan drugs differ with respect to pharmacoeconomic properties.

Methods: We studied patient access to eight high-priced inpatient ultra-orphan drugs in nine countries. In addition, we determined whether differences with respect to cost per patient, budget impact and cost-effectiveness existed between orphan drugs with a positive and negative reimbursement status.

Results: Reimbursement status was available for 78 orphan drugs, of which 56 (72%) were positive. Large differences were observed between countries; while two countries had a positive status for two out of nine ultra-orphan drugs, four countries had positive status for all drugs it assessed. A number of drugs were reimbursed only after price negotiations and/or through specific orphan drug policies. The average cost per patient, budget impact and incremental cost-effectiveness ratios were lower for ultra-orphan drugs with a positive reimbursement status than for those with a negative status, although only cost-effectiveness ratios were statistically significant.

Conclusions: Large differences in patient access to ultra-orphan drugs were observed between countries. Future research should examine if similar findings can be seen in other countries and with other orphan drugs, and it should also determine which other factors play a role in reimbursement status of orphan drugs.

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https://doi.org/10.1016/j.hlpt.2017.12.001

Please cite this article as: Kanters TA, et al. International differences in patient access to ultra-orphan drugs. Health Policy and Technology (2018), https://doi.org/10.1016/j.hlpt.2017.12.001

Introduction

In the European Union, a drug is labeled as an orphan drug if the drug is intended to treat a life-threatening or chronically debilitating disease with a prevalence of less than 5 per 10,000 people [1]. Drugs for diseases with an even lower prevalence (i.e. less than 1:50,000 people) classify as an ultra-orphan drug [2]. Over time, orphan drug legislation has been passed in various countries and regions, including the United States (in 1983), Japan (1993), Canada (1996), Australia (1998) and the European Union (2000) to provide incentives for pharmaceutical companies to research, develop and produce orphan drugs [3,4]. Although incentives differ between countries, they generally include instruments such as market exclusivity, expedited review, assistance in trial design and waiving of licensing fees [5]. Before specific orphan drug legislation was passed, only a few orphan drugs were available, but orphan drug legislation has led to substantial growth in the number of orphan drugs – a growth that is likely to continue in the future [6,7]. In combination with high prices of orphan drugs, which can amount to prices well over €100,000 per patient per year, this also resulted in an increasing share of the total pharmaceutical budget spent on orphan drugs. For example, in Sweden this share increased from less than 1 percent in 2000 to 2.5% in 2012 and forecasted to reach 4.1% in 2020 [8]. For France, a similar growth was observed: from less than 1% in 2000 to a forecasted 4.9% in 2020. For the US, the proportion of pharmaceutical costs that is spent on orphan drugs is expected to double in an 11-year period: from 4.8% in 2007 to an expected 9.5% of total pharmaceutical costs spend on orphan drugs in 2018 [9].

Many countries have developed policies to contain health care expenditures by limiting the basic benefit package for their citizens. As a result, drugs that are considered safe and have proven efficacy face an additional hurdle before patients can actually use them. Pharmaceutical companies have to submit a reimbursement dossier to a reimbursement agency, which deliberates on whether or not the drug should be paid from public resources. In some countries, an agency issues a reimbursement decision, while in other countries agencies issue a reimbursement recommendation (for reasons of readability, we use recommendation to describe both recommendations and decisions in this study). Recommendations about whether to reimburse a drug are made on a national or regional level, and this is also the case for orphan drugs [10]. As reimbursement processes differ between countries, this can lead to variation in patient access to the same drug in different countries [11–13]. Although different countries use a variety of reimbursement criteria and the relative weights of criteria are implicit, reimbursement status on drugs are generally based on disease-specific, therapeutic and economic features, including cost-effectiveness [14,15]. Pharmacoeconomic properties have received much attention due to the high costs of orphan drugs. Little is known about how the criteria used to determine reimbursement status for non-orphan drugs apply to orphan drugs. Other factors, such as ethical considerations, can also play a role in reimbursement status of orphan drugs [16,17]. These considerations differ per country, leading to differences in reimbursement status of orphan drugs between countries [11,12]. In addition to the regular reimbursement procedures, many countries have installed specific policies to grant patients access to (ultra-) orphan drugs. Furthermore, payers and manufacturers have made specific agreements (particularly on price) to ensure patient access to these drugs.

The primary objective of this study was to compare access to ultra-orphan drugs in various high income countries. This study adds to existing literature (e.g. [11,12,18,19]) byexplicitly focusing on ultra-orphan drugs. The secondary objective was to describe differences in pharmacoeconomic characteristics between ultra-orphan drugs with positive and negative reimbursement status. As such, this study should be regarded as an important first step in exploring international differences in patient access to ultra-orphan drugs.

Methods

The ultra-orphan drugs included in this study are listed in Table 1, along with their respective indications. As the objective was to make a first step in exploring international differences in patient access to orphan drugs, the study sample was limited to all of the eight ultra-orphan drugs that were listed on the Dutch policy rule on orphan drugs for reasons of feasibility. The Dutch policy rule was designed to grant patients access to high-priced inpatient orphan drugs for diseases with high medical need under a coverage with evidence development scheme [18]. Only orphan drugs that were high-priced inpatient orphan drugs with a minimum budget impact of €600,000 in the Netherlands and indicated for diseases with a high unmet medical need could be listed on the Dutch policy rule. Canakinumab was the last ultra-orphan drug in this sample to obtain market approval in October 2010 (as shown in Table 1). The policy rule was stopped in 2012.

In the analyses, Pompe disease was divided into two indications (infantile Pompe disease and late-onset Pompe disease) to reflect the important disease based distinctions between these forms of this disease [20], which can translate into differences in reimbursement status. For the other orphan diseases in the study, no disease subtypes were analyzed.

Patient access was assessed in nine countries (Australia, Belgium, Canada, England, France, the Netherlands, New Zealand, Scotland, and Wales). These countries were selected on the basis of public availability of national reimbursement status for the majority of these eight ultra-orphan drugs (full dossiers or amended publications) and the language of the dossiers (English, French or Dutch). Reimbursement status was retrieved from websites of health technology assessment (HTA) agencies, websites of national ministries of health and advisory group reports. Treatments could also be available through specific policy instruments or finance schemes. Reimbursement status (established either from a regular reimbursement procedure or through a specific orphan drug policy) was publicly available for a total of 78 orphan drugs, while reimbursement status for three cases was not (yet) publicly available.

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