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Patient Access to Medicines for Rare Diseases in European Countries

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ABSTRACT

Background: The number of authorized orphan and non-orphan medicines for rare diseases has increased in Europe. Patient access to these medicines is affected by high costs, weak efficacy/safety evidence, and societal value. European health care systems must determine whether paying for expensive treatments for only a few patients is sustainable. **Objectives:** This study aimed to evaluate patient access to orphan and non-orphan medicines for rare diseases in 22 European countries during 2005 to 2014. **Methods:** Medicines for rare diseases from the Orphanet list, authorized during 2005 to 2014, were searched for in the IMS MIDAS Quarterly Sales Data, January 2005 – December 2014 (IQVIA, Danbury, CT). The following three measures were determined for each country: number of available medicines, median time to continuous use, and medicine expenditure. A medicine was considered available if uninterrupted sales within a 1-year period were detected. **Results:** From 2005 to 2014, 125 medicines were authorized and 112 were found in the search. Of those, between 70 (63%) and 102 (91%) were available in Germany, the United Kingdom, Italy, France, and the Scandinavian countries. These countries were also the fastest to enable continuous use (3–9 mo). Only 27% to 38% of authorized medicines were available in Greece, Ireland, Bulgaria, Romania, and Croatia, which took 1 to 2.6 years to begin continuous use. A country's expenditure on medicines for rare diseases in 2014 ranged between €0.2 and €31.9/inhabitant. **Conclusions:** Patient access to medicines for rare diseases varies largely across Europe. Patients in Germany, Scandinavian countries, Switzerland, France, and the United Kingdom can access larger numbers of medicines in shorter time.

Keywords: availability, medicine expenditure, orphan medicines, patient access, rare disease.

Rare diseases are usually chronic, life threatening, or chronically debilitating and affect up to 5 in 10,000 people [1–3]. They are often poorly diagnosed and treated [1,4]. Although each rare disease affects only a few individuals, together they affect around 6-8% of the total European population [1,3,5]. Several regulatory and financial incentives have enhanced the research and development of new medicines for rare diseases (e.g., the European Medicines Agency [EMA] orphan designation) [1,6,7]. These incentives have increased the number of authorized medicines for rare diseases [1,8,9]. In addition to the medicines with the orphan status, other medicines for rare indications that are not designated as orphans have been authorized [2,9]. The international European portal for rare diseases, Orphanet, provides a complete list of both based on the European Commission's Community Registers on orphan medicines and medicines suggested for orphan designation [9].

Patient access has several interpretations and is determined by several factors, including time to regulatory approval, market availability, or reimbursement; reasons for delays in these times; outcomes of technology appraisals; and conditions of reimbursement, including prescribing restrictions and copayments [9–14]. This study investigates the following three factors of patient access to medicines for rare diseases: how many medicines are available, median time to continuous use, and medicine expenditure.

The main concerns in providing patient access to these medicines are high cost and often weaker efficacy and safety evidence [8,10,15,16]. Nevertheless, they have important societal value because they improve patient quality of life and increase highly limited treatment options of a particular rare disease [16–18]. Different health technology assessment processes and decision-making policies can lead to important differences in access to these medicines among countries [11,15,19–21]. Nevertheless, each country faces the same decision—whether paying for an expensive treatment for only a few individuals is sustainable [8,10,17,20,22–26]. Therefore, orphan and non-orphan

Conflict of interest: Access to the IMS MIDAS Quarterly Sales Data (IQVIA, Danbury, CT) was made available by Astra Zeneca UK Limited Slovenia, and the use of the data was permitted by IQVIA. No financial incentives were obtained from the company, and all the authors declare that the study was performed for academic purposes only.

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medicines for rare diseases represent a challenge for all health care systems in Europe [17,20].

The aim of this study was to estimate patient access to different medicines for rare diseases from the comprehensive Orphanet list in various European countries in the past decade.

Methods

Patient access was estimated using the following three aspects: the number of medicines for rare diseases in continuous use, time to their first continuous use, and total medicine expenditure. The data analysis was performed in IBM SPSS v23.0 and Microsoft Excel. The data are presented as frequencies of available medicines and the median times to continuous use. Medicine expenditures are presented as the total annual sales (€).

Scope of Medicines for Rare Diseases

The study included medicines for rare diseases from the Orphanet list, authorized via centralized procedure at the EMA between 2005 and 2014 [1,10]. The Orphanet list comprises the medicines with a rare disease indication with and without the orphan designation from the EMA. Three medicines containing sitaxentan sodium, rilonacept, and dextromethorphan/quinidine were withdrawn from the European market during the inclusion period (2005–2014) and were thus excluded from the start of the study.

Selected European Countries

We included all the largest European countries, along with smaller ones for which the sales data from the IMS MIDAS Quarterly Sales Data, January 2005 – December 2014, were available. The following 22 European countries were analyzed: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom (UK).

Study Period

The medicines for rare diseases that were authorized between January 1, 2005, and December 31, 2014, were included. The sales data were obtained for the same period.

The IMS Health Data

Quarterly value sales from the IMS MIDAS Quarterly Sales Data, January 2005 – December 2014 (IMS Health Data; IMS Health Incorporated, Danbury, CT) were used [27]. These data were used for all medicines in the scope and for those European countries where sales data of the full medicines list could be found [27].

Each medicine from the Orphanet list was searched using the official product name at the EMA and the name of the active substance. This two-fold approach provided true information for the majority of the medicines. Some products may not have been identified because the IMS Health Data records the medicines under only one international name. In such cases, an internet search was performed to find other brand names of the product.

Despite the two-fold search, 13 products were not clearly identifiable because their product names were imprecise. Among these medicines were a tobramycin and mannitol inhalation powder; four human immunoglobulins; two filgrastim agents; and six other medicines containing everolimus, afamelanotide, lomitapide, bosentan, and a combination of human coagulation factor VIII and human von Willebrand factor. In cases of lomitapid, tobramycin inhalation powder, and one of the human immunoglobulins, similar product names were detected, but the sales data for these products appeared before the marketing authorization dates of the medicines originally searched. For the remaining 10 medicines, different product names were detected according to the search by active substance; however, these were approved for other indications (e.g., immunoglobulins were only detected according to "human immunoglobulin" showing products that could be used for several indications) or their sales data appeared before the marketing authorization date of the medicines originally searched. Therefore, we excluded these 13 products from the analysis to avoid potential bias (Tables S1 and S2 in the Supplementary Materials found at https://doi.org/10.1016/j.jval.2018.01.007).

The complete sales data for the medicines detected in the database were accessible for 22 European countries. For each country, the data were given either as hospital and retail panel separately or as hospital and retail combined. For 16 countries, both panels were given separately. In the case of Sweden, the combined data were reported. For Austria, Greece, Hungary, and Ireland, only retail sales data were available. Table S3 in the Supplementary Materials (found at https://doi.org/10.1016/j.jval.2018.01.007) presents the types of IMS Health Data reported for each country.

Data Analysis

First, the total number of medicines authorized between 2005 and 2014 was investigated according to the year of authorization. Main indication fields of these medicines were also searched using the Anatomical Therapeutic Chemical classification [28]. Furthermore, we investigated the following three main patient access measures for each of the 22 European countries: the number of medicines available, the median time to first continuous use after marketing authorization, and the medicine expenditure during the study period. All measures were observed for all medicines for rare diseases, together and separately, with and without the orphan status.

Medicine Availability

A medicine was considered available if continuous sales were detected in the database. Continuous sales were sales without interruption within a 1-year period, meaning that they were detected in four consecutive quarters (Q) (i.e., Q4-2010, Q1-2011, Q2-2011, Q3-2011). However, a 1-quarter gap (zero sales in one quarter) within the 1-year period was allowed (i.e., Q4-2010, gap, Q2-2011, Q3-2011 or Q4-2010, Q1-2011, gap, Q3-2011 or Q4-2010, Q1-2011, Q2-2011, gap). In all the presented cases, Q4-2010 was noted as the period of first continuous use. This way, one-time-only use or potentially nondistributed medicine supplies could be excluded.

The time to first continuous use was determined for each country for the available medicines. The time difference was calculated between the date of the first continuous use and the marketing authorization date. If continuous sales were detected before marketing authorization, the marketing authorization date was considered as the time of first continuous use. No negative times were considered because they could represent other means and mechanisms of patient access, such as compassionate use. The times were then compared among the countries as absolute times, and a pooled value was determined for all countries.

Medicine Expenditure

Medicine expenditure for each country was calculated directly from the sales at a manufacturer price reported in the IMS Health Data using constant euro exchange rate [27]. The proportions of medicine expenditure spent on medicines with and without orphan designation were also calculated. Furthermore, the sales