VALUE IN HEALTH ▮ (2016) ▮▮▮–▮▮▮

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Variation in Health Technology Assessment and Reimbursement Processes in Europe

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ABSTRACT

Background: It has been suggested that differences in health technology assessment (HTA) processes among countries, particularly within Europe, have led to inequity in patient access to new medicines. **Objectives:** To provide an up-to-date snapshot analysis of the present status of HTA and reimbursement systems in select European countries, and to investigate the implications of these processes, especially with regard to delays in market and patient access. **Methods:** HTA and reimbursement processes were assessed through a review of published and gray literature, and through a series of interviews with HTA experts. To quantify the impact of differences among countries, we conducted case studies of 12 products introduced since 2009, including 10 cancer drugs. **Results:** In addition to the differences in HTA and reimbursement processes among countries, the influence of particular sources of information differs among HTA bodies. The variation in the time from the authorization by the European Medicines Agency to the publication of HTA decisions was considerable, both within and among countries, with a general lack of transparency as to why some assessments take longer than others. In most countries, market access for oncology products can occur outside the HTA process, with sales often preceding HTA decisions. **Conclusions:** It is challenging even for those with considerable personal experience in European HTA processes to establish what is really happening in market access for new drugs. We recommend that efforts should be directed toward improving transparency in HTA, which should, in turn, lead to more effective processes.

Keywords: cancer, decision making, Europe, pharmaceuticals.

Introduction

In many countries, the efficacy, safety, and value of medical innovations are assessed through a formal health technology assessment (HTA) system. The goals of an HTA are to examine the consequences of the adoption of a particular technology and ensure that these represent good value for money. It has, however, been suggested that differences in HTA processes among countries, particularly within Europe, have led to inequity in patient access to new medicines.

Ensuring access to effective new medicines is challenging, with the introduction of expensive, innovative, and targeted agents having a substantial impact on health care costs, particularly in areas such as orphan diseases and oncology. Issues surrounding access to innovative medicines are exemplified by the large number of cancer treatments that have recently received European marketing authorization, but which are not always reimbursed in all European countries [1]. Europe has approximately one-quarter of global cancer cases, despite representing only one-eighth of the world population [2]. There is wide variation among European countries in the incidence of particular cancers and in cancer treatment and survival [3,4]. Some of the variation in cancer statistics is a reflection of differences in social and epidemiological factors. It has, however, been speculated that some of the variation in cancer outcomes may be due to the differences in health care systems and access to new interventions [5,6].

In 2005, a study of cancer drug access in Europe, focusing on the role of HTA, noted that some of the considerable variation in availability and uptake of new drugs was explained by differences in reimbursement processes [7]. For example, in Germany, cancer drugs were immediately available once marketing authorization was granted, whereas in Denmark and Austria drugs were typically available within 2 to 3 months of marketing authorization. In contrast, in France, Italy, and Spain, where the HTA process is a prerequisite for market access, there was a delay of 1 year on average because of the time required for formal reimbursement decisions [7]. This study is now a decade old—the purpose of the work reported here was to investigate whether its conclusions remain valid.

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1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2016.08.725

HTA and reimbursement processes were assessed through a review of published and gray literature, and through a series of interviews with HTA experts in eight European countries, representing a number of different health care systems and processes. To quantify the impact of differences among countries resulting from variations in processes, we studied the experience of 12 products introduced since 2009, including 10 cancer drugs approved by the European Medicines Agency (EMA) in 2010 to 2012.

Methods

Literature Review—Electronic and Gray Literature

Searches were carried out in April and May 2014 (for the full search strategy and search terms, see Appendix 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.08.725). When information in included references was presented only in graphical form (e.g., in the study by Benoff et al. [8]), data were digitally extracted using the GetData Graph Digitizer software (GetData Software, Hurstvile, Australia).

Expert Interviews

Semistructured, anonymized interviews were conducted with experts from eight European countries: France, Germany, Italy, Poland, Spain, Sweden, the Netherlands, and the United Kingdom (UK interviewees had specific experience of the National Institute for Health and Care Excellence [NICE]). Experts were recruited from an internal contact list from BresMed Health Solutions Ltd. (Sheffield, UK). Interview recruitment was double-blinded: the experts were not aware of the identity of the sponsor, and the sponsor was not aware of which experts were interviewed. Contact was made through gatekeepers and snowball sampling. For each country one clinical expert and one economic expert with knowledge of the local HTA and reimbursement systems were recruited. Additional interviews were conducted in Spain and Italy to capture the regional nature of the HTA and reimbursement processes in these countries. Efforts were made to engage with individuals who could provide insight into the country-specific reimbursement as well as HTA processes because of their previous or present involvement in those processes. A screening survey was developed to assess the participants' relevance. It comprised questions relating to their country's HTA and reimbursement processes and their experience with the 10 oncology products, including the extent to which they had been involved in the decision making.

Interviews were conducted between October 2014 and May 2015. In total, 18 interviews were conducted—8 with clinical experts and 10 with experts in health economics. Two interviews were carried out for each country, with an additional interview with a second health economics expert conducted in Italy and Spain to capture the regional nature of the HTA and reimbursement processes in these countries.

Interviewees were briefed about the objectives of the research and all gave their informed written consent to participate and for the interviews to be recorded. Participants were given flow diagrams of their country's HTA and reimbursement processes on the basis of the results of the literature review, and they were asked to provide their opinion on whether the information was a true representation of actual practice.

Interviewees were asked about sources of information and decision-making criteria used for HTA in their countries. Participants were asked to apply values to a series of decision criteria using a structured survey, with 5 points assigned to the most important decision criterion or criteria and 0 to the least important.

Qualitative analysis was carried out through coding the transcripts using the NVivo 10 software program (QSR International, Daresbury, United Kingdom) to identify any trends, differences, and similarities specific to the HTA and reimbursement processes, decision making, challenges, and promoting market access across the study countries. While presenting the results, anonymity of the participants was protected by removing names and creating broad interview categories (e.g., clinical expert and economic expert).

Product Case Studies

In total, 10 oncology products authorized by the EMA between 2010 and 2012 were selected for investigation. The selected products, presented in Table 1, were considered by the authors to be innovative drugs and/or novel entities—8 of the 10 were given ratings of I to IV of the Amélioration du Service Médical Rendu (ASMR) [The improvement in actual benefit (IAB)] by the Haute Autorité de Santé (HAS [French National Authority for Health]). For comparison, two nononcology products were also selected for investigation: Gilenya® (fingolimod; for multiple sclerosis) and Onbrez Breezhaler® (indacaterol; for chronic obstructive pulmonary disease).

The relevant HTA and reimbursement Web sites for each country were used to identify decision information and dates for specific products. Potential delays in market access were assessed as the difference between the date of EMA regulatory approval for each product and the date of country-specific HTA or reimbursement approvals as documented on the relevant agency Web sites. In Germany, market access is granted at the time of EMA authorization. Therefore, for this analysis the time from EMA approval to the publication of a recommendation by the Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) decision support unit was assessed. To investigate whether patient access was delayed by HTA and reimbursement processes, we assumed that product sales are a reasonable proxy for patient access. Quarterly product sales data for each country were obtained from IMS Health. For the United Kingdom, the IMS data included information for the whole country; nevertheless, only the

Table 1 – Products selected for analysis.

Disease area	Product brand name (generic name)
Oncology products	
Non–small cell lung carcinoma	Xalkori® (crizotinib)
Stomach neoplasms	Teysuno® (combination: tegafur, gimeracil, and oteracil)
Medullary thyroid cancer	Caprelsa® (vandetanib)
Breast cancer	Halaven® (eribulin)
Renal cell carcinoma	Inlyta® (axitinib)
Prostatic neoplasms	Jevtana® (cabazitaxel)
Hodgkin lymphoma	Adcetris® (brentuximab vedotin)
Melanoma	Yervoy® (ipilimumab) Zelboraf® (vemurafenib)
Non-Hodgkin lymphoma	Pixuvri® (pixantrone dimaleate)
Nononcology products	
Relapsing-remitting multiple sclerosis	Gilenya® (fingolimod)
Chronic obstructive pulmonary disease	Onbrez Breezhaler® (indacaterol)