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Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden

Alessandra Ferrario [a, b, *], Panos Kanavos [a, b]

[a] Department of Social Policy, London School of Economics and Political Science, United Kingdom
[b] LSE Health, London School of Economics and Political Science, United Kingdom

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ABSTRACT

Managed entry agreements are a set of instruments used to reduce the impact of uncertainty and high prices when introducing new medicines. This study develops a conceptual framework for these agreements and tests it by exploring variations in their implementation in Belgium, England, the Netherlands and Sweden and over time as well as their governance structures.

Using publicly available data from HTA agencies and survey data from the European Medicines Information Network, a database of agreements implemented between 2003 and 2012 was developed. A review of governance structures was also undertaken.

In December 2012 there were 133 active MEAs for different medicine-indications across the four countries. These corresponded to 110 unique medicine-indications. Over time there has been a steady growth in the number of agreements implemented, with the highest number in the Netherlands in 2012. The number of new agreements introduced each year followed a different pattern. In Belgium and England it increased over time, while it decreased in the Netherlands and fluctuated in Sweden.

Only 18 (16%) of the unique medicine-indication pairs identified were part of an agreement in two or more countries.

England uses mainly discounts and free doses to influence prices. The Netherlands and Sweden have focused more on addressing uncertainties through coverage with evidence development and, in Sweden, on monitoring use and compliance with restrictions through registries. Belgium uses a combination of the above.

Despite similar reasons being cited for managed entry agreements implementation, only in a minority of cases have countries implemented an agreement for the same medicine-indication; when they do, a different agreement type is often implemented. Differences in governance across countries partly explain such variations. However, more research is needed to understand whether e.g. risk-perception and/or notion of what constitutes a high price differ between these countries.

1. Introduction

A combination of high prices of new patented medicines, uncertainties relating to their clinical effectiveness and use in real life represent a dilemma for decision-makers and a potential barrier to access. These challenges, complemented by patients' demand for fast access to new medicines, have prompted countries to find ways to manage the introduction of new medicines and limit the impact of high prices and uncertainty. One way decision-makers are trying achieve this, is by implementing a heterogeneous group of instruments known as 'managed entry agreements' (MEAs) (Klemp et al., 2011).

The nature of MEAs can be very different between and within countries; some are conditional reimbursement decisions subject to reassessment of the relevant technology. Coverage with evidence development (CED) agreements require the manufacturer to provide additional data on a medicine's performance in real-life. This is common requirement of the Swedish Dental and Pharmaceutical Benefits Agency (TLV). For ropinirole (a medicine for the treatment of moderate to severe idiopathic restless legs syndrome) for example, the available data on the long-term effects and side-

* Corresponding author. LSE Health, London School of Economics and Political Science, United Kingdom.
E-mail address: a.ferrario@lse.ac.uk (A. Ferrario).

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effects of the medicine when it was first assessed were deemed insufficient because of large uncertainty around the cost per QALY. The medicine was therefore provisionally listed, on condition that the manufacturer would provide an updated economic model with real-life evidence (TLV, 2006). The review showed that the medicine was not cost-effective at the current price and a small price reduction was implemented to keep the medicine on the reimbursement list (TLV, 2012).

Other agreements represent a final coverage decision conditional on the provision of a MEA. When bortezomib (a medicine for multiple myleloma) was first assessed by the National Institute for Health and Care Excellence (NICE) in England, it was found to be effective but not cost-effective with an estimated incremental cost-effectiveness ratio (ICER) of GBP 38,000 per quality adjusted life year (QALY) (NICE, 2006). The willingness to pay for a QALY in England is broadly known to be up to GBP 30,000 unless end-of-life criteria apply. Following a reassessment of the medicine and the proposal of a payment by result agreement by the manufacturer including treatment interruption if the medicine does not achieve the expected response after four treatment cycles and reimbursement for failure, the ICER declined to GBP 20,700 and the medicine was recommended for use within the national health service (NICE, 2007).

Agreements are often divided into financial and health-outcome based agreements. The previous two examples would fall under the latter group although they both can have financial consequences. Purely financial agreements include price-volume agreements (PVAs) and dose/time capping schemes. PVAs define a threshold of expenditure after which a rebate is triggered and aim to limit budget impact or introduce certainty about a budget not being overrun. Capping schemes involve the establishment of either a time or dose cap after which the manufacturer pays for any additional doses required. This was the case for ranibizumab (for age-related macular degeneration) in England for which the manufacturer agreed to pay for any patients requiring more than 14 doses per affected eye (the scheme has now changed into a simple discount scheme following the introduction of a discount-based MEA for the diabetic macular odema indication of ranibizumab) (NICE, 2008).

Defining MEAs is often complicated by the use of country-specific terms to define them, the context in which they operate and the different views as to what constitutes a MEA. In the United Kingdom (UK) they are known as patient access schemes (PAS), Belgium uses the term conventions, while they are not known under a specific name in Sweden. In the Netherlands they were initially part of funding policies to improve access to expensive hospital and orphan medicines (2006–2011) and referred to as 'conditionally allowed specialist medicines' (CVZ, 2012b). Despite their diversity, MEAs have a common denominator, namely to facilitate access to new medicines in a context of uncertainty and high prices.

The body of evidence on MEA implementation to date is weak. Apart from exploring the impact of MEA from a theoretical economic perspective (Barros, 2011; Gandjour, 2009; Zaric and O'Brien, 2005; Zaric and Xie, 2009), few studies presenting cross-sectional evidence across settings exist (Adamski et al., 2010; Carbonneil et al., 2009; Carlson et al., 2010; Ferrario and Kanavos, 2013; Stafinski et al., 2010); only one attempts an analysis of the therapeutic focus (Ferrario and Kanavos, 2013), while another presents longitudinal data on MEAs for orphan medicines (Morel et al., 2013). Further, there are very few studies on the impact of MEAs (Pickin et al., 2009; Russo et al., 2010; Willis et al., 2010). Finally, there has been no published evidence comparing the different approaches used by countries to improve access and no comparison of governance structures around MEAs with the aim of explaining their implementation patterns.

A number of taxonomies have been proposed for their classification and some of them include only performance based risk-sharing agreements (Carlson et al., 2010; Casado et al., 2009; Ferrario and Kanavos, 2013; Garrison et al., 2013; Jaroslawski and Toumi, 2011; Launois and Ethgen, 2013; Towse and Garrison, 2010), as well as evaluation frameworks (Garrison et al., 2013; McCabe et al., 2010; Towse and Garrison, 2010). However, there is lack of an analytical framework that enables an understanding of how MEAs modulate key decision-making variables.

The aim of this study is to develop a conceptual framework for MEAs and to test it by exploring variations in MEAs implementation across countries and over time as well as their governance structures.

2. Methods

2.1. Data sources

Data on the medicine-indication pairs subject to a MEA, the types of MEAs implemented and their governance structures (relevant legislation, policies, guidelines and submission templates) were sourced from websites of HTA agencies, health insurers and governments (Dutch National Health Care Institute, 2014; INAMI-RIZIV, 2014b; NICE, 2014; TLV, 2014). Additional material based on primary data collection on MEA was used from a European survey of MEAs (Ferrario and Kanavos, 2013), supplemented by personal contacts with competent health authorities mainly to clarify or complement information retrieved from the data sources described. All MEAs reported by countries, from the date the first official MEA was implemented in each country, up to December 2012, were included in the analysis.

2.2. Study design

The study countries include Belgium (BE), England (EN), the Netherlands (NL) and Sweden (SE). These were selected because they implement MEAs, have either a publicly available list of MEAs or participated in a recent survey on MEAs (Ferrario and Kanavos, 2013), use health technology assessment (HTA) to guide their coverage decisions and have publicly available HTA reports, reflect a diversity in health system organisational structure (tax-based single purchaser systems (NHS) vs. social health insurance systems) and different perspective of HTA analysis (health system vs. societal perspective). Countries such as Poland or Italy which are well known to implement MEAs could not be included because in the first all agreements are in commercial confidence and in the second because complete up-to-date data on all MEAs implemented and HTA report was not available.

We only included MEAs for medicines with nationwide implementation or, in the case of England, MEAs with implementation within the entire devolved administration. For England, we included all PAS listed on NICE's website but we did not include information on PAS for medicines which had either not been reviewed by NICE or for medicines which had been rejected by NICE. Such cases exist (NHS Northern, 2014) but may not be implemented across the country. For Sweden, in addition to MEAs concluded by the Dental and Pharmaceutical Benefit Agency (TLV) at national level, we also included agreements concluded by the New Medicinal Therapies group (NLT) at regional level because these have nationwide implementation. We did not consider, as some other studies did (Carbonneil et al., 2009; Carlson et al., 2010), 'only in research' recommendations by NICE to be CED schemes