Objectives

Healthcare authorities are increasingly looking at budgets and requesting proven efficacy and cost-effectiveness evidence to support drug submissions; this presents a challenge for getting orphan drugs (ODs) approved. Between 2000 and 2010, only 65% of available ODs were approved by health technology assessment (HTA) bodies in the EU; 45% of these apps were for oncology indications. However, due to differences across EU states, reimbursement rates for ODs vary from 30% to 90%.

The rate of OD approvals appears to be falling, and ODs are more likely to gain approval in the USA than in the EU. One reason behind this trend could be the requirement of robust clinical data for cost-effectiveness calculations. These data are challenging to obtain when a very small population is affected by a disease. As such, cost-effectiveness data are often not included or are limited in OD HTA submissions. Furthermore, the impact of an OD is often only significant for the individual, not the whole population, making HTAs naturally biased against ODs because the objective of the HTA is to maximise public health.

This research explores the current and alternative approaches to assessing the economic value of ODs within the existing HTA framework.

Methods

A structured literature search was completed in July 2014. There were two stages of searching:

1. A targeted search of published literature that discusses alternative approaches for assessing the economic value of ODs.
2. A targeted search of recent HTA submissions for ODs across six key EU markets (France, Germany, Ireland, the Netherlands, Sweden, and the UK).

Literature search

The search was kept broad in the initial electronic searches as the literature evidence base for ODs can be very small. Due to the varied nature of the papers, we focused on the screening efforts for the manual review of titles, abstracts, and full papers. A search protocol was produced, detailing inclusion and exclusion criteria as well as search methods.

The following databases where searched for this element of the review:

- MEDLINE
- MEDLINE In-Process (using PubMed)
- Cochrane Library (NHS Economic Evaluation Database and HTA database)
- Web of Science (to identify conference abstracts/materials)

Lack of long-term evidence

Linertová

Inability to identify subgroups or populations

- Web of Science (to identify conference abstracts/materials)

Hutchings

Pomalidomide

Insufficient evidence of economic value


HTA bodies, companies developing ODs, patients and society on both national and international levels must in further discussions continue to assess the value of ODs.

Access to ODs will continue to be unequal compared to non-ODs and across countries until approaches such as those described here are followed.

Results

Current challenges for ODs

The literature review identified several challenges for evaluating ODs within the existing HTA framework, which are listed here:

- Insufficient evidence of efficacy
- High uncertainty around clinical outcomes (especially when analysed using frequentist clinical trial statistics)
- Insufficient evidence for other important outcomes, e.g. quality of life and patient reported outcomes
- Lack of long-term outcomes
- Lack of information on the wider systemic impact of the disease
- High drug cost

Most of the issues are due to the low patient numbers available for clinical trials for ODs. This leads to inadequate evidence for HTAs and difficulties in quantifying the true benefit of ODs in terms of clinical outcomes and quality of life. These factors increase the uncertainty of both the clinical and the cost-effectiveness of the product, which, combined with high prices for ODs, lead to incremental cost-effectiveness ratios far beyond normal thresholds.

Inconsistent HTA decisions

The HTA review showed no difference in the clinical data or the approach taken by the manufacturer in the HTA submissions across the six EU markets. However, there were differences in the decision taken by the HTAs. This highlights a lack of consistency in the decisions taken by HTA bodies leading to unequal access to ODs across countries.

Alternative approaches

We identified several alternative approaches in the literature to overcome the challenges for HTA evaluation of ODs, which we have summarised below:

- Societal value, variable thresholds and weighted outcome measures
- Cost and burden of illness studies

There is a difference in values defined in cost-effectiveness thresholds and values defined by society when it comes to the evaluations. Different thresholds should be variable and determined by societal values, e.g. setting a higher threshold for ODs, or equity weights should be determined for outcomes in orphan diseases, increasing the health gain in evaluations of ODs.

- Cost and burden of illness studies

The cost and burden of illness for an orphan disease should be established before an economic evaluation, ideally including a standardised research for economic evaluation on the Disease level. This should focus on what are the appropriate outcomes to assess and the particular features of the disease. Such disease-specific reference cases already exist for other disease areas, but have only recently been developed for some orphan diseases through the BURGOL-RO project.

- Additional data collection and innovative early access schemes

More registries should be established and observational studies carried out in orphan diseases. Despite the absence of a capability to identify a specific group of patients, there is still a need for evidence for economic assessment of ODs. This should lead to reciprocal research and the real outcomes of the disease.

Conclusions

• Assessing the economic value of ODs within the existing HTA framework is a challenge mainly because of low patient numbers for clinical trials, lack of long-term data, lack of important outcomes and limitations in accepted statistical methods

• Alternative approaches have been discussed in published literature, but none of these approaches have been used in recent HTA submissions

• HTA bodies, companies developing ODs, patients and society on both national and international levels must in further discussions continue to assess the value of ODs

• Access to ODs will continue to be unequal compared to non-ODs and across countries until approaches such as those described here are followed

References


Further information is available on request. Please visit BresMed at Stand 106/107/208/207.

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