LEVERAGING RWE AND INTEGRATING MULTI-SOURCE DATA TO BUILD THE CASE FOR FUNDING AND ACCESS FOR RARE DISEASE DRUGS

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BACKGROUND

Decision making around funding and access of rare & orphan disease products is a well-known challenge for healthcare systems worldwide. Generation of clinical evidence is not straightforward; due to limited patient availability and small patient numbers, lack of comparators and/or use of surrogate endpoints. From an economic perspective, high “price density” with high one-off upfront costs can add to the existing challenge – mostly in the case of cell/gene-therapy approaches. Due to these issues, many rare disease products are granted a conditional marketing authorization (CMA) from the European Medicines Agency (EMA), with requirements to submit additional data to support the value of the product.

OBJECTIVES

This research aims to identify what additional data has been requested for orphan disease products which received a CMA from the EMA, and how these have been translated into recommendations and additional requirements by England’s and Germany’s Health Technology Assessment authorities (NICE and G-BA respectively).

METHODS

The research team identified all orphan disease drugs which have been granted CMA by the EMA (2012-2021), through their published “Medicine data: European public assessment reports (EPAR) for human medicines”[1].

The appraisals for England’s HTA body (NICE)[2] and Germany’s HTA body (G-BA)[3] were accessed via their respective public websites. The team identified and analysed the appraisals for orphan disease products which had received a CMA by the EMA; with an emphasis on identifying the outcome of the appraisal, as well as any additional data which these HTA bodies had requested of manufacturers for their appraisal.

Figure 1. Summary of orphan disease products with conditional marketing authorization by EMA and corresponding NICE & G-BA appraisal

9/23 submit final results of Ph2/3 to confirm efficacy and safety	**8/23** Post-authorization safety & efficacy studies requested	**3/23** submit long-term follow up data confirming efficacy & safety	**2/23** Additional open-label study to assess efficacy & safety requested

23 evaluations identified

Figure 2. Summary of NICE appraisals of orphan disease products with EMA conditional marketing authorization

13/19 available only through Managed Access Agreements & patient discount access schemes	**4/19** guidance under development (requested additional information)	**2/19** manufacturer did not provide evidence submission

19/23 appraisals identified

Figure 3. Summary of G-BA appraisals of orphan disease products with EMA conditional marketing authorization

11/17 non-quantifiable additional benefit	**4/17** minor additional benefit	**1/17** considerable additional beenfit	**1/17** mandated RWE collection prior to appraisal

17/23 appraisals identified

RESULTS

A total of 23 orphan disease drugs which have been granted CMA by the EMA were identified. **(Figure 1).** Many of these products had been evaluated using their Phase 2/3 interim data. Therefore, the EMA have typically requested that the manufacturer submit final results of their Ph 2 or Ph 3 studies or have requested additional long-term data to demonstrate efficacy & safety (in certain sub-groups and/or compared to SoC) along with post-authorization safety & efficacy studies.

The NICE (19/23) and G-BA (17/23) appraisals for these products were identified and analysed to understand outcomes and additional data requests by the HTA bodies. **(Figures 2 & 3.)**

NICE have typically recommended these products through the use of Managed Access Agreements (most commonly a simple discount patient access scheme) due to the perceived lack of data, where NICE can collect additional RWE to understand the efficacy & safety of the product.

G-BA has typically attributed a non-quantifiable (minimum for orphan drug) or a minor additional benefit to these products. However, with the exception of Zolgensma[4], the G-BA have not set up access agreements or registries to collect additional data.

Orphan disease products which received a CMA by the EMA had difficulty generating robust clinical evidence to demonstrate a positive benefit-risk ratio in their respective therapy areas. The high levels of clinical uncertainty was the primary driver of conditional marketing authorisation.

In many cases, this uncertainty was due to the lack of an appropriate comparator or timeframes for clinical evidence generation, which led to incomplete clinical data at the time of appraisal.

DISCUSSION

The availability of additional data from multiple sources (e.g. claims data, digital health technologies, electronic medical records, Tx and Rx data) can help reduce this uncertainty. For example, RWE acceptability by HTAs has increased significantly and presents a great opportunity for manufacturers to demonstrate the value of their products. The acceptability of RWE by NICE is already established, and even required in many cases where there is a lack of traditional RCT data. In the case of G-BA, the acceptability of this data has increased in recently years by the G-BA – with one of the first examples of RWE requirements in the case of Zolgensma in 2020[4] through the establishment of the procedure for requesting application-related data collection.

Non-comparative studies, uncontrolled studies, disease & drug registries, and other sources of RWE increasingly may be used to inform healthcare decision making in situation where RCTs are unavailable or might not be appropriate for ethical reasons.

Data engineering will be necessary to integrate the data from multiple sources, this will require pre-planning and often intensive time and financial resources. Modelling can be useful to address the issue of lack of comparative data by constructing artificial comparators out of real-world data.

With an increasing number of conditionally approved products for orphan diseases, there is a need to adapt HTA processes to address assessment challenges for clinical uncertainty and affordability. Innovative source data and financial engineering are promising solutions to overcome those barriers.

REFERENCES

1. Medicine data: European public assessment reports (EPAR) for human medicines [online]. Available at: https://data.europa.eu/data/datasets/epar-human-medicines?locale=en) [Accessed on 28 October 2021]
2. NICE guidance portal [online]. Available at: https://www.nice.org.uk/guidance [Accessed on 28 October 2021]
3. G-BA benefit assessment of drugs [online]. Available at: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/ [Accessed on 28 October 2021]
4. G-BA specifies procedures for application-related data collection - Zolgensma gene therapy first case [online]. Available at: https://www.g-ba.de/presse/pressemitteilungen-meldungen/874/ [Accessed on 28 October 2021]