Communicating the Value of an Orphan Drug

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A critical component in the global market access strategy for any therapy is to develop a concise, evidence-based value story that conveys the key elements of product value. Value story development is no less essential for a first-in-class orphan drug than for a product entering a large and competitive market. Particularly with rare conditions, where there may be low disease awareness and high concern about the cost of treatment, a thoughtfully developed value story can resonate not only with payers but with other internal and external audiences, as outlined in the following table.

A value story should answer the questions typically in the minds of healthcare decision makers evaluating the product.

- Why do we need to treat?
- Are the existing options good enough?
- What is special about this product?
- Does this product work? How well?
- Does this product improve quality of life and other outcomes meaningful to patients and caregivers?
- Is this product worth the cost? Can we afford it?

In rare diseases, there can be challenges in developing the body of evidence necessary to support a value story, making it especially important to deliver clear and specific messages about the key elements of product value. Often, the most compelling approach is to very clearly communicate the unmet need, and then focus on the ways in which the product addresses the unmet need. The following are some recommendations on how to highlight the value of orphan drugs in written submissions and live presentations to healthcare decision makers.

VARIOUS PERSPECTIVES ON THE ORPHAN DRUG VALUE STORY

Audience	*Important Take-Aways*
Payers	Paying for this product is a sensible use of my finite healthcare budget because it is justifiable from clinical, economic, and humanistic points of view.
Clinicians	With this product, I can better manage the disease, leading to the best possible outcomes for my patients.
Patients and/or Caregivers	This product controls the disease, allowing my family/me to have a more normal life with fewer disease-related disruptions.
Patient Advocates	Our population now has an effective treatment option; industry has partnered with us to develop a therapy that will improve our health and quality of life.
Internal Stakeholders	Our shared vision drives our research and commercial efforts. We feel good about our role in helping patients and caregivers face a devastating rare disease.

BURDEN OF ILLNESS

Due to the rarity of orphan diseases, healthcare decision makers may have limited awareness of the clinical, humanistic, and economic burden of disease. This can lead to well-intentioned but inappropriate restrictions on patient access to a potentially beneficial therapy. Particularly if a product is the first available treatment for the disease, it can be helpful to provide somewhat expanded disease background information, with references to current review articles, treatment guidelines, and other top-line sources. When possible, real-world evidence or patient/caregiver surveys can help to demonstrate the true burden of an under-recognized illness.

UNMET NEED

An unfortunate reality of orphan diseases is that patients and families often undergo invasive, inconvenient, and/or inadequate therapies that would not be considered acceptable for large populations. Patients may have to travel great distances to undergo procedures at specialist centers, or they may be unable to hold a job or attend school due to an unrelenting treatment schedule. In other cases, the existing standard of care does not allow patients to achieve acceptable therapeutic goals,

but it is thought to be "the best we can hope for in these cases."

A key focus in the orphan drug value story must, then, be the urgency of unmet need, particularly at the level of the patient, caregiver, and family. It is important to emphasize the impact of existing treatments, with an emphasis on suboptimal outcomes. When data on unmet need are scant, the best initial evidence may even come from the registrational trial(s) for the new product: baseline data on enrolled patients sometimes can be a good source of real-world evidence about the status of patients receiving standard care.

CLINICAL EFFICACY AND COMPARATIVE EFFECTIVENESS

Healthcare decision makers may challenge the design of trials for orphan drugs. Trials are typically small, due to the very small patient population. The pivotal trial may employ surrogate endpoints, because it would be inappropriate to delay filing—thereby prolonging patients' wait for an effective treatment option—while waiting for long-term outcomes. Moreover, due to the large unmet need in many orphan conditions, it may be considered unethical to conduct a placebo-controlled trial, and there may be no acceptable active comparator. Likewise, it can be difficult to undertake indirect treatment comparisons due to the paucity of clinical trial data in an orphan indication.

It is essential, therefore, to be upfront and clear about the appropriateness of the trial design for an orphan drug, and then to keep the message focused on the product's key efficacy benefits in a disease characterized by substantial burden and unmet need.

Quality of life (QoL) and patient-reported outcomes (PROs) can lend further support to the core efficacy message, particularly in diseases with substantial humanistic burden. One potential pitfall is the use of general QoL or PRO scales that are not developed for or validated in the disease being studied. It is often worthwhile to develop and validate a PRO scale specific for the rare disease, to ensure that it addresses the often unusual circumstances patients face, as well as the unique attributes of the population (e.g., spending considerably more time and effort on managing their disease due to distance from specialized treatment facilities; using extremely inconvenient or invasive treatments because they are the only option; psychosocial concerns arising from a low-visibility condition.)

ECONOMIC VALUE

Economic value is one of the most challenging issues in market access for orphan drugs. The high price of most orphan drugs—due to the low patient population and the need to recoup development costs—means that it is unlikely that an orphan drug can be demonstrated to be cost effective according to traditional incremental cost-effectiveness ratio (ICER) thresholds. Different countries are evolving in terms of how they approach economic evaluation for orphan drugs, but in general, the budget impact argument is more effective than a cost-effectiveness analysis. Due to the rarity of an orphan disease, the overall budget impact of an orphan drug is likely to be modest or minimal, particularly after accounting for cost offsets such as reduced need for invasive procedures or reduced risk of organ damage or costly clinical events. In markets that require a cost-effectiveness analysis, the outputs of economic modeling should be discussed in the context of equity and, again, the product's clinical value in a burdensome disease with inadequate existing options.

Scientific and clinical innovation is the driving force behind the uptick in orphan drugs coming to market. Likewise, innovation and creativity are essential for developing strong evidence-based value propositions that help to maximize patient access to these potentially transformative therapies.

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